e-ISSN:2602-2079

Volume 7
Issue 12
2023

JOURNAL of Surgery and Medicine

International Medical Journal

JOSAM

Editorial Team

Prasenjit Das, Professor, MD, DNB, MNAMS, MNASc
Department of Pathology
All India Institute of Medical Sciences
New Delhi, India
Website

Seyed Vahid Hosseini, Professor
Shiraz University of Medical Sciences, Shiraz, Iran
Website

Vol. 7 No. 12 (2023):

Published: 2023-12-31

Research Article

Case Report

J Surg Med. 2023;7(12):748-753.
DOI: 10.28982/josam.7856

Research article

Journal of Surgery and Medicine
e-ISSN: 2602-2079
https://jsurgmed.com/

The role of oxidative stress levels and S100B levels in children with functional neurological disorder

Esra Sizer [1], Tuğba Çobanoğlu [2], İbrahim Kaplan [3]

[1] Department of Child and Adolescent Psychiatry, Diyarbakır Pediatric Hospital, Diyarbakır, Turkey
[2] Department of Child and Adolescent Psychiatry, Faculty of Medicine, Turgut Özal University, Malatya, Turkey
[3] Department of Biochemistry, Faculty of Medicine, Dicle University, Diyarbakır, Turkey

ORCID ID of the author(s)

ES: 0000-0001-8675-6770
TÇ: 0000-0001-5611-2739
İK: 0000-0003-2813-1064

Corresponding Author
Esra Sizer
Diyarbakır Pediatric Hospital, Department of Child and Adolescent Psychiatry, Diyarbakır, Turkey
E-mail: dr.esra.mngsr@gmail.com

Ethics Committee Approval
The study was approved by the Dicle University ethics committee with decision number 276 dated October 17, 2018.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

Financial Disclosure
The authors declared that this study has received no financial support.

Published
2023 December 7

Abstract

Background/Aim: Although stressors and traumatic life events are known to be predisposing factors for developing functional neurological disorder (FND), the etiology of the disorder has not been fully elucidated. In this study, oxidative stress parameters and serum levels of S100B protein were investigated in pediatric patients with functional neurological disorder. The association of these parameters with stress factors and traumatic life events was investigated.

Methods: This case-control study included a control group of 35 patients aged 8-18 years and 32 healthy subjects diagnosed with functional neurological disorder. The Childhood Trauma Scale and Dissociative Experiences Scale were applied to both groups. Serum levels of the patient and control groups were compared by blood sampling: total oxidant status (TOS), total antioxidant status (TAS), oxidative stress index (OSI), and S100B.

Results: It was found that the Childhood Trauma Scale total score, emotional neglect, emotional abuse, physical neglect and the Dissociative Experiences Scale were statistically significantly higher in the FND group than in the control group ($P<0.001$, $P<0.001$, $P=0.013$, $P=0.017$, $P<0.001$). Stressors were found to be statistically significantly higher in the FND group than in the control group ($P=0.020$). There was no statistical difference between the FND group and control groups regarding the TAS, TOS, OSI, and S100B levels ($P=0.965$, $P=0.228$, $P=0.268$, $P=0.517$, respectively).

Conclusion: Our study is the first to investigate TOS, TAS, OSI and S100B in children with FND. In our study, although stressors and traumatic experiences were significantly higher in the functional neurological disorder group compared to the control group according to the stress susceptibility model, contrary to expectations, there was no significant difference in oxidative stress parameters and serum S100B levels. It was thought that the interaction between FND, which is characterized by biopsychosocial interaction and can manifest itself with various clinical symptoms, and stress may not be linear as initially thought, and the interaction between genetic predisposition and environmental factors may play a more complex role. The absence of significant differences observed in oxidative stress parameters and serum S100B levels may suggest that we should focus on different pathways and different potential biomarkers that need to be investigated in the future to understand the etiology and diagnosis of FND. However, the limitations noted above may affect the generalizability of the study findings.

Keywords: pediatric, functional neurological disorder, oxidative stress, S100B

How to cite: Sizer E, Çobanoğlu T, Kaplan İ. The role of oxidative stress levels and S100B level in children with functional neurological disorder. J Surg Med. 2023;7(12):748-753.

Introduction

Functional neurological disorders refer to clinical presentations characterized by neurological symptoms such as voluntary or motor issues in the body, despite the absence of any identifiable physical or physiological problems [1]. In adults, the prevalence of the disorder is two to ten times higher among females compared to males, while in children it is more common among girls. The condition usually first appears in adolescents and young adults, often between the ages of 10 and 35 [2]. The incidence of functional neurological disorder is estimated to be 2% to 5% per year in large-scale population-based studies. Studies have found that early childhood trauma, emotional life stress, and conflict are associated with functional neurological disorder symptoms [3,4].

Chung et al. reported irregularities in the hypothalamus-pituitary-adrenal (HPA) axis in children and adolescents with functional neurological disorders. They observed a weakened or inverted cortisol awakening response, which is typically associated with chronic stress [5]. Additionally, one adult study found a decreased cortisol awakening response in FND patients using a transdiagnostic approach. This findings suggests that the previously activated system exhibits a more chronic stress or disorder pattern. Therefore, the flow effect can be more complex than a simple activation [6]. Additionally, the irregularities in the HPA axis can be triggered by glucocorticoids, and it can disrupt the oxidant-antioxidant balance [7]. In aerobic organisms, oxidant and antioxidant systems are actually in balance. Although oxidants in trace amounts are known to play a role in signal transduction and immune responses in the cell, in cases where the antioxidant balance is disturbed, excess oxidants damage membrane lipids, enzymes, structural proteins, and DNA by oxidation and play a role in the development of neurodegenerative and neuropsychiatric conditions [8-10]. The brain is particularly sensitive to stress due to its physiological and structural properties and high metabolic rate [11]. Some studies have shown that serum oxidant levels are elevated in mood disorders, depressive disorders, and neurodevelopmental disorders [12-14].

S100B is produced and released by astrocytes, contributing to the modulation of calcium ion signaling, maintenance of internal balance, protein phosphorylation, cellular growth, genetic transcription, cellular differentiation, enzymatic function, and internal cellular processes [15]. While nanomolar concentrations of S100B are a neurotrophic factor that reduces stress-induced damage and stimulates neuronal and astrocyte growth and differentiation, recent observations show that micromolar concentrations of S100B trigger apoptotic cell death by causing an increase in reactive oxygen species, the release of cytochrome C, and activation of the caspase cascade [16,17]. Studies have shown that serum S100B levels increase in psychosis, depression, and other mood disorders and revert with treatment in some disorders [18-21].

No study in the literature has examined the levels of oxidative stress and S100B that could contribute to the etiology of functional neurological disorder in childhood. It has already been mentioned that stressors and traumatic life events are predisposing factors for the development of functional neurological disorders. We aimed to look at the etiology of functional neurological disorder from a neuroinflammatory standpoint by examining oxidative stress parameters and serum levels of S100B protein in pediatric patients with functional neurological disorder and investigating the association between these parameters and predisposing factors.

Materials and methods

Study design

This case-control study was carried out by the Dicle University Faculty of Medicine, Department of Child and Adolescent Mental Health and Diseases. This study was approved by the Dicle University Ethics Committee with decision number 276 dated 17.10.2018. Study reporting was done following the STROBE guidelines [22]. The data were collected between October 30, 2018 and May 30, 2019.

Evaluation of functional neurological disorder groups

Thirty-seven patients (6 boys, 29 girls) aged 8-18 years and diagnosed with functional neurological disorder were enrolled in the study. The diagnostic criteria from the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) were used to diagnose functional neurological disorder, and the patients were evaluated by two different psychiatrists. To meet the criteria, one or more changes in voluntary motor or sensory function had to be present. Based on DSM-5 criteria, clinical findings should demonstrate evidence of inconsistency or incompatibility between the symptom in question and known neurological or general medical conditions. The symptom or deficit should be better explained by another physical or mental health condition. Furthermore, the symptom or deficit should cause clinically significant distress or impairment in social, occupational, or other important areas of functioning or warrant medical evaluation.

According to the diagnostic criteria, acute functional neurological disorder (FND) is defined as the presence of symptoms for fewer than six months, while persistent FND is defined when symptoms have been present for six months or longer [1]. In our study, the mean time between the onset of symptoms and the first visit to a psychiatry outpatient clinic was 6.41 (10.9) months, and patients with persistent FND were included in the study. In our study, we found that 21.6% of the FND group initially visited the psychiatry clinic, which is consistent with the literature, but 78.4% came to our unit after referral. It was observed that, prior to seeking psychiatry admission, 45.7% of the patients visited pediatric neurology, 22.9% visited pediatrics, 22.9% visited emergency services, and 8.6% visited related clinics for their symptoms. Consequently, the time between the onset of symptoms and admission to psychiatry was prolonged. When the subtypes were examined according to the symptoms in the FND group, it was found that 21 (60.0%) patients came mainly with seizures or seizure attacks. In the other subtypes, there was one patient (2.9%) with weakness or paralysis, three (8.6%) with unusual movements, one (2.9%) with difficulty swallowing, and one (2.9%) with speech signs *(aphonia),* anesthesia, or sensory loss. It was observed that there was one (2.9%) patient with sensory loss,

three (8.6%) patients with specific sensory symptoms, and four (11.4%) patients with mixed symptoms.

Evaluation of control groups

At the Dicle University Faculty of Medicine, Department of Child and Adolescent Mental Health and Diseases where our study was conducted, there is a pediatric outpatient clinic that provides services for healthy children, including growth development, vaccinations, puberty issues and other follow-ups. We invited eligible children and their families to participate in this study at our clinic. Those who agreed underwent a psychiatric evaluation conducted by two different psychiatrists and met the exclusion criteria before being included in the control group. In our study, 32 healthy volunteers were included in the control group.

Exclusion criteria

For the patients and control groups, exclusion criteria included severe neurological or chronic medical illness, head injury, acute infection or inflammation, mental retardation, psychotic disorders, bipolar disorder, moderate psychiatric disorders, alcohol and substance use disorders, use of psychotropic drugs, a diet high in oxidants and antioxidants, intake of antioxidants such as vitamin E and C, and obesity in their past and/or present lives.

Participant selection

Prior to commencing, the necessary sample size was determined employing the G Power 3.1 analytical software. Through power analysis, a sample size of 34 patients was computed, considering a significance level (α) of 0.05, a statistical power (1-β) of 80%, and a medium effect size. The recruitment was concluded upon reaching an adequate number of participants within the stipulated timeframe. Subsequently, three individuals from the control group were excluded from the analysis due to their expressed intention to withdraw from the study.

Data collection

The Childhood Traumas and Dissociative Experiences Scale was completed in the FND and control groups. After 12 hours of fasting, blood samples were drawn from the antecubital vein into a biochemistry tube containing EDTA for the patient and control groups. It was centrifuged at 3500 rpm for five minutes (NF 048, NUVE). The sera obtained were stored at -80 C°.

Measurement of total antioxidant status (TAS)

The total antioxidant capacity (TAS) of serum samples was measured by the automated measurement method developed by Erel using an autoanalyzer (Architect C16000, Abbott). In this method, the characteristic color of ABTS* $^{+}$' is bleached by the antioxidants present in the sample. This reaction can be monitored spectrophotometrically, and the rate of bleaching is inversely proportional to the TAS of the sample. The reaction rate is calibrated with Trolox, widely used as a conventional standard for TAS measurement assays, and the appraisal results are expressed in mmol Trolox equivalent/L. The assay has a sensitivity of less than 3% [23].

Measurement of total oxidant status (TOS)

In the method developed by Erel, the oxidants present in the sample oxidize the ferrous ion-*o*-dianisidine complex to ferric ions. The oxidation reaction with glycerol molecules is accelerated and increased up to threefold. The iron (III) ion forms a colored complex with xylenol in an acidic environment. The color intensity, which can be measured spectrophotometrically, is related to the sample's total amount of oxidant molecules. The assay is calibrated with hydrogen peroxide, and the results are determined in micromolar hydrogen peroxide equivalents per liter (expressed in μmol H_2O_2 Equiv./L) [24].

Calculation of oxidative stress index (OSI)

After aligning the measurement units, the oxidative stress index (OSI) was calculated by dividing the total oxidant content (TOS)/by the total antioxidant content (TAS) [24].

Measurement of S100B level in serum

The serum level of human S100B (Sunred Biological Technology, catalog number: 201-12-4851 Shanghai, China) was determined by the enzyme-linked immunosorbent assay (ELISA) method with commercially available kits following the kit procedures.

Childhood Trauma Questionnaire

This assessment instrument, developed by Bernstein et al., consists of 28 questions. The scale determines a total score of five subscores related to childhood sexual abuse, physical abuse, emotional abuse, and emotional and physical neglect [25]. The Turkish validity and reliability study of the Childhood Trauma Scale was conducted in 2012 by Şar et al. [26].

Dissociative Experiences Scale

This is a 28-question self-report scale developed by Bernstein and Putnam in 1986 that measures the frequency of various dissociative experiences. Subjects give a score between 0 and 100 for each item, and the result is obtained by calculating the average of the total score obtained [27]. The Dissociative Experiences Scale was translated into Turkish by Şar et al. [28] in 1997, and a validity and reliability study of the Turkish version of the scale was conducted.

Statistical analysis

Statistical analysis was performed using the package program SPSS 21.0 for Windows (SPSS, Inc.; Chicago, USA). Descriptive values are expressed as number (n), percent (%), mean (mean), standard deviation (SD), and median (median). Pearson's chi-square and Fisher's exact test were used to compare categorical variables. Continuous variables were compared with parametric tests (independent samples t-test) if they conformed to the normal distribution determined by the Kolmogorov-Smirnov and Shapiro-Wilk tests, If they did not conform to the normal distribution, a nonparametric test (Mann-Whitney U test) was used. The relationship between variables was assessed with the Spearman correlation test. The significance level was accepted as *P*-value <0.05.

Results

The functional neurological disorder group (FND) consisted of 35 participants (29 [82.9%] female, 6 [17.1%]) male with a mean age of 14.20 (2.33) years. The mean age of the 32 participants (27 [84.4%] female, 5 [15.6%]) male in the control group was 14.22 (2.29) years. The mean educational level in the FND and control groups was nine years. There was no statistically significant difference between the groups regarding age and gender (*P*=0.974, *P*=0.867). It was found that in the

FND group, from the onset of symptoms to admission to psychiatry was, on average, 6.41 (10.9) months.

When evaluating the results of the Childhood Trauma Scale and the Dissociative Experiences Scale, it was found that the total scores of the Trauma Scale, emotional neglect, emotional abuse, physical neglect, and Dissociative Experiences Scale were statistically significantly higher in the FND group than those in the control group (P<0.001, P<0.001, P=0.013, P=0.017, P<0.001) **(**Table 1).

Table 1: Childhood trauma scale and dissociative experiences scale results between groups

Groups	Parameter	n	mean (SD)	DF	*t*	*P*-value
FND group	Emotional abuse	35	7.75 (3.54)	65	0.192	0.013
Control group		32	6.37 (2.21)			
FND group	Physical abuse	35	5.94 (2.37)	65	0.589	0.081
Control group		32	5.51 (1.55)			
FND group	Physical neglect	35	7.46 (3.09)	65	1.950	0.017
Control group		32	6.19 (1.71)			
FND group	Emotional neglect	35	12.54 (6.02)	65	4.052	<0.001
Control group		32	7.04 (2.86)			
FND group	Sexual abuse	35	5.40 (1.09)	65	0.570	0.084
Control group		32	5,08 (0.27)			
FND group	CTQ Total	35	40.11 (12.75)	65	3.132	<0.001
Control group		32	31.57 (5.48)			
FND group	DES Total	35	28.77 (22.70)	65	2.481	<0.001
Control group		32	21.87 (13.66)			

FND: functional neurological disorder, CTQ: Childhood Trauma Questionnaire, DES: Dissociative Experiences Scale, n: number, SD: Standard deviation, DF: Degree of freedom, *t*: Independent t-test value

There was no statistical difference between the FND and control groups regarding TAS level and OSI (P=0.965, P=0.268). TOS and S100B levels were slightly higher in the FND group, and there was no significant difference between the two groups (P=0.228, P=0.517) (Table 2 and 3). There was no significant relationship between the total score of the Childhood Trauma Scale, the Trauma Scale subgroups and the Dissociative Experiences Scale score, and the TAS, TOS, S100B, and OSI (Table 4).

Table 2: TAS, TOS, OSI INDEX scores between groups

Groups	Parameter	n	mean (SD)	DF	*t*	*P*-value
FND group	TAS, mmol Trolox equiv/L	35	1.53 (0.18)	65	0.200	0.911
Control group		32	1.53 (0.18)			
FND group	TOS, μmol H_2O_2 equiv/L	35	25.80 (10.93)	65	1.252	0.596
Control group		32	22.66 (9.45)			
FND group	OSI	35	1.71 (0.82)	65	1.296	0.540
Control group		32	1.47 (0.64)			

FND: functional neurological disorder, n: number, SD: Standard deviation, DF: Degree of freedom, *t*: Independent t test value

Table 3: S100B values of the between groups

Groups	Parameter	n	Median	Mean Rank	U	*P*-value
FND group	S100B, ng/L	35	333.35	34.48	544.500	0.846
Control group		32	322.71	33.56		

FND: functional neurological disorder, n: Number, Median: Median value, Mean Rank: Mean Ranks, U: Mann Whitney U test value

Table 4: Correlation of childhood trauma scale and dissociative experiences scale scores with parameters measured in blood

FND group		TAS mmol Trolox equiv/L	TOS μmol H_2O_2 equiv/L	S100B ng/L	OSI
Emotional abuse	r_o	0.113	0.190	0.033	-0.114
	p	0.253	0.130	0.423	0.251
Physical abuse	r_o	0.001	-0.205	-0.136	0.239
	p	0.498	0.112	0.211	0.077
Physical neglect	r_o	-0.002	-0.156	0.026	0.181
	p	0.496	0.179	0.439	0.141
Emotional neglect	r_o	-0.132	-0.035	-0.035	0.000
	p	0.219	0.419	0.419	0.499
Sexual abuse	r_o	-0.099	-0.163	-0.064	0.174
	p	0.280	0.167	0.362	0.152
CTQ Total	r_o	-0.046	-0.030	0.024	0.036
	p	0.393	0.429	0.444	0.416
DES Total	r_o	0.054	-0.030	-0.030	-0.002
	p	0.376	0.429	0.433	0.494

FND: functional neurological disorder, CTQ: Childhood Trauma Questionnaire, DES: Dissociative Experiences Scale, p: Spearman correlation significance value (*P*-value), r_o : Spearman Correlation Number

When asked about stressors, 8 subjects (22.9%) reported family stressors, 9 subjects (25.7%) reported school problems, 6 subjects (17.1%) reported social relationship issues, and 12 subjects (34.1%) reported no stressors in the functional neurological disorder group. In the control group, 3 individuals (9.4%) reported family stressors, 2 individuals (6.3%) reported school problems, 1 individual (3.1%) reported social relationship issues, and 26 individuals (81.3%) reported no stressors. It was found that stressors were statistically significant more frequently in the FND group (P=0.020). In the FND group, when the stressors (65.9%) and those who did not have stressors (34.1%) were considered separately, there was no statistically significant difference in serum levels of TAS, TOS, OSI and S100B (P=0.185, P=0.286, P=0.098, P=0.710).

Discussion

Our study investigated the relationship between stressors and adverse childhood experiences, which are considered predisposing factors for the development of functional neurological disorder, oxidative stress parameters, and serum levels of S100B protein. One of our important findings is that stressors and traumatic life events were more prevalent in the functional neurological disorder group, as expected. Another important finding is that measurements of oxidative stress indicators and S100B concentrations exhibited no notable distinctions among pediatric patients with functional neurological disorder when compared to the control group. There was no significant correlation between the extent of adverse childhood experiences and oxidative stress parameters and S100B levels.

If we consider stress from a psychoneuroimmunological perspective, studies have shown that psychological stress induces a cascading effect of hypothalamic-pituitary-adrenal axis dysregulation that activates both the immune system and oxidative stress [29,30]. According to the stress diathesis model of Keynejad et al. [31], the interaction of different combinations, such as a low or high genetic load of the individual and the severity and frequency of traumatic experiences in childhood, result in the individual having a different risk of developing functional neurological disorder. Monocytes and glial cells are activated following emotional trauma, which triggers the inflammatory system. Although the link between traumatic experiences in childhood and S100B is unknown, it is thought to affect the transition of S100B into the serum by producing cytokines and disrupting the blood-brain barrier [32].

Falcone et al. described adverse childhood experiences and showed that serum S100B levels were higher in pediatric patients hospitalized with a diagnosis of mood disorder and psychotic disorder compared with the control group [33]. However, in our study, no significant difference was found between serum S100B levels in the functional neurological disorder group with high adverse childhood experiences compared with the control group. Adverse childhood experiences can explain the stress diathesis model, and stressors cause mental disorders other than childhood functional neurological disorder. However, the differences in serum S100B protein levels according to the type of psychiatric disorder suggested that the disorder may have caused varying degrees of changes in the

different brain regions specifically affected by the condition. This indicates that imaging and neuroinflammatory studies might provide clearer results.

In an examination carried out by Büyükaslan et al. [34] involving 25 adult female and 12 male patients with conversion disorder, between 18 and 60 years, it was observed that the functional neurological disorder group exhibited notably elevated levels of total oxidative status, oxidative stress index, and S100B compared to the control group. Furthermore, a significant reduction in total antioxidant status was also identified in the same functional neurological disorder group. Our study found that the TAS, TOS, and OSI scores did not differ significantly between the pediatric functional neurological disorder and control groups. Studies show the effects of childhood traumatic experiences on oxidative stress in the brain [35,36]. Research has indicated that glial cells, which possess immunological memory within the brain and contribute significantly to the brain's reaction to stress, might be involved in either safeguarding or disturbing the stress equilibrium. Additionally, microglial neuroimmunity is believed to have a crucial impact on alterations in experience-dependent plasticity among individuals with functional neurological disorders [5,37-39]. Recent neuroimaging studies have shown that different brain regions are affected in children and adolescents with functional neurological disorder more than in adults. These neuroplastic changes in children with short disease duration may not correspond to those in adult patients with chronic disease duration [40-42]. Therefore, long-term follow-up of patients with childhood functional neurological disorder and investigation of the effects of oxidative stress and neuroinflammatory changes may provide more important information for understanding the condition.

In our study, oxidative stress parameters were studied in total. Özdemir et al. [ref#?] did not find a significant difference in total oxidant and antioxidant parameters in their study with adults with post-traumatic stress disorder; however, a significant difference in lipid peroxidation markers and prolidase among sub-parameters was found in other studies [43-45]. These data led us to understand the functional neurological disorder better, and assessing oxidative stress sub-parameters might be more useful before the deterioration of oxidative capacity affects total antioxidant capacity.

Limitations

The results of our study could be limited due to the small number of participants, the absence of long-term follow-ups, the lack of research on how these parameters respond to treatment, and the long time elapsed until the patients presented to our psychiatry clinic. Furthermore, given that S100B can be released extracranially, certain investigations have suggested the importance of assessing S100B within cerebrospinal fluid (CSF), coupled with the calculation of a serum/CSF ratio [46-48]. FND encompasses a wide variety of clinical presentations and often requires multiple-site evaluation before initiating psychiatric treatment. These assessments may include specialists from neurology, pediatrics, or other related disciplines. Due to the nature of FND, patients typically do not seek emergency psychiatric care in the acute phase of the disorder [49]. This situation led us to believe that our results might have been compromised due to the inability to obtain blood samples in the acute phase and also the examination of serum S100B levels instead of CSF. Furthermore, because there is no standardized measurement method for functional neurological disorder severity, the effect of disease severity on oxidative stress and S100B parameters was not examined. Begue et al. [50] noted that creating standardized measurement tools to classify the FND by demographics, duration of disease severity, symptoms, comorbidities, and functionality for neurobiological studies in functional neurological disorder would increase the biological specificity of the studies.

Conclusion

Our study is the first to investigate TOS, TAS, OSI and S100B in children with FND. In our study, although stressors and traumatic experiences were significantly higher in the functional neurological disorder group compared to the control group according to the stress susceptibility model, contrary to expectations, there was no significant difference in oxidative stress parameters and serum S100B levels. It was thought that the interaction between FND, which is characterized by biopsychosocial interaction and can manifest itself with various clinical symptoms, and stress may not be linear as initially thought, and the interaction between genetic predisposition and environmental factors may play a more complex role. The absence of significant differences observed in oxidative stress parameters and serum S100B levels may suggest that we should focus on different pathways and different potential biomarkers that need to be investigated in the future to understand the etiology and diagnosis of FND. However, the limitations noted above may affect the generalizability of the study’s findings.

References

1. American Psychiatric Association, DSM-5 Task Force. (2013). Diagnostic and statistical manual of mental disorders: DSM-5™ (5th ed.). American Psychiatric Publishing, Inc., 2013 doi: 10.1176/appi.books.9780890425596.
2. Sadock B, Sadock V, Ruiz PK. Sadocks synopsis of psychiatry: Behavioral sciences/clinical psychiatry. Philadelphia: Wolter Kluwer, Lippincott Williams & Watkins; 2015.
3. Roelofs K, Keijsers GPJ, Hoogduin KAL, Näring GWB, Moene FC. Childhood abuse in patients with functional neurological disorder . Am J Psychiatry. 2002;159:1908-13. doi: 10.1176/appi.ajp.159.11.1908.
4. Maqsood N, Akram B, Luqman N, Amin R. Functional neurological disorder: Psycho-Social Stressors And Life Events In Children. Professional. 2014;21:489-94. doi: 10.21649/akemu.v23i2.1584
5. Chung J, Mukerji S, Kozlowska K. Cortisol and α-amylase awakening response in children and adolescents with functional neurological (conversion) disorder. Aust N Z J Psychiatry. 2023;57(1):115-29. doi: 10.1177/00048674221082520.
6. Weber S, Bühler J, Vanini G, Loukas S, Bruckmaier R, Aybek S. Identification of biopsychological trait markers in functional neurological disorders. Brain. 2023;146(6):2627-41. doi: 10.1093/brain/awac442.
7. Spiers JG, Chen HJ, Sernia C, Lavidis NA. Activation of the hypothalamic-pituitary-adrenal stress axis induces cellular oxidative stress. Front Neurosci. 2014;8:456. doi: 10.3389/fnins.2014.00456.
8. Halliwell B. The antioxidant paradox: less paradoxical now? Br J Clin Pharmacol. 2013;75:637-44. doi: 10.1111/j.1365-2125.2012.04272.x.
9. Sies H, Cadenas E. Oxidative stress: damage to intact cells and organs. Philos Trans R Soc Lond B Biol Sci. 1985;311:617-31. doi: 10.1098/rstb.1985.0168
10. Nunomura A, Tamaoki T, Motohashi N. Role of oxidative stress in the pathophysiology of neuropsychiatric disorders. Seishin Shinkeigaku Zasshi. 2014;116:842-58.
11. Jellinger KA. Recent advances in our understanding of neurodegeneration. J Neural Transm. 2009;116(9):1111-62. doi: 10.1007/s00702-009-0240-y
12. Selek S, Altindag A, Saracoglu G, Celik H, Aksoy N.Prolidase activity and its diagnostic performance in bipolar disorder. J Affect Disord. 2011;129:84-6. doi: 10.1016/j.jad.2010.09.003
13. Kul M, Unal F, Kandemir H, Sarkarati B, Kilinc K, Kandemir SB.Evaluation of oxidative metabolism in child and adolescent patients with attention deficit hyperactivity disorder. Psychiatry Investig. 2015;12:361. doi: 10.4306/pi.2015.12.3.361
14. Bal N, Acar ŞT, Tamer L. Altered Levels of Malondialdehyde and Vitamin E in Major Depressive Disorder and Generalized Anxiety Disorder. Dusunen Adam. 2012;25:206-11. doi: 10.5350/dajpn2012250302
15. Qin B, Panickar KS, Anderson RA. Cinnamon polyphenols attenuate the hydrogen peroxide-induced down regulation of S100β secretion by regulating sirtuin 1 in C6 rat glioma cells. Life Sci. 2014;102:72-9. doi: 10.1016/j.lfs.2014.02.038
16. L Schroeter M, Sacher J, Steiner J, Schoenknecht P, Mueller K. Serum S100B represents a new biomarker for mood disorders. Curr Drug Targets. 2013;14:1237-48. doi: 10.2174/13894501113149990014
17. Huttunen HJ, Kuja-Panula J, Sorci G, Agneletti AL, Donato R, Rauvala H. Coregulation of neurite outgrowth and cell survival by amphoterin and S100 proteins through receptor for advanced glycation end products (RAGE) activation. J Biol Chem. 2000;275:40096-105. doi: 10.1074/jbc.M006993200
18. Carlton E, Falcone T, Batra A, Fazio V, Franco K, Janigro D. Do systemic inflammation and blood-brain barrier failure play a role in pediatric psychosis? Cleve Clin J Med. 2009;76:93.

19. Rothermundt M, Missler U, Arolt V, Peters M, Leadbeater J, Wiesmann M, et al. Increased S100B blood levels in unmedicated and treated schizophrenic patients are correlated with negative symptomatology. Mol Psychiatry. 2001;6:445-9. doi: 10.1038/sj.mp.4000889
20. Schroeter ML, Abdul-Khaliq H, Diefenbacher A, Blasig IE. S100B is increased in mood disorders and may be reduced by antidepressive treatment. Neuroreport. 2002;13:1675-8. doi: 10.1097/00001756-200209160-00021
21. Machado-Vieira R, Lara DR, Portela LV, Gonçalves CA, Soares JC, Kapczinski F, et al. Elevated serum S100B protein in drug-free bipolar patients during first manic episode: a pilot study. Eur Neuropsychopharmacol. 2002;12:269-72. doi: 10.1016/s0924-977x(02)00029-9
22. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Int J Surg. 2014;12:1495-9.
23. Erel O. A novel automated direct measurement method for total antioxidant capacity using a new generation, more stable ABTS radical cation. Clin Biochem. 2004;37:277-85. doi: 10.1016/j.clinbiochem.2003.11.015
24. Erel O. A new automated colorimetric method for measuring total oxidant status. Clinical biochemistry. 2005;38:1103-11. doi: 10.1016/j.clinbiochem.2005.08.008
25. Bernstein D, Fink L. Manual for the childhood trauma questionnaire. New York: The Psychological Corporation; 1998.
26. Sar V, Ozturk E, Ikikardes E. Validity and reliability of the Turkish version of Childhood Trauma Questionnaire. Turkiye Klinikleri Tip Bilimleri Dergisi. 2012;32(4):1054-63.
27. Carlson EB, Putnam FW, Ross CA, et al. Validity of the Dissociative Experiences Scale in screening for multiple personality disorder: a multicenter study. Am J Psychiatry. 1993;150(7):1030-6. doi: 10.1176/ajp.150.7.1030.
28. Sar V, Kundakci T, Kiziltan E, Bakim B, Yargic LI, Tutkun H. The reliability and validity of the Turkish version of the Dissociative Experiences Scale (DES-II). Proceedings of the 33rd National Congress of Psychiatry. Antalya: Psychiatric Association of Turkey; 1997.
29. Gu HF, Tang CK, Yang YZ. Psychological stress, immune response, and atherosclerosis. Atherosclerosis. 2012;223(1):69-77. doi: 10.1016/j.atherosclerosis.
30. Biswas SK. Does the interdependence between oxidative stress and inflammation explain the antioxidant paradox? Oxid Med Cell Longev. 2016;2016:5698931. doi: 10.1155/2016/5698931.
31. Keynejad RC, Frodl T, Kanaan R, Pariante C, Reuber M, Nicholson TR. Stress and functional neurological disorders: mechanistic insights. J Neurol Neurosurg Psychiatry. 2019;90:813-21. doi: 10.1136/jnnp-2018-318297.
32. Shalev H, Serlin Y, Friedman A. Breaching the blood-brain barrier as a gate to psychiatric disorder. Cardiovasc Psychiatry Neurol. 2009;2009:278531. doi: 10.1155/2009/278531.
33. Falcone T, Janigro D, Lovell R, et al. S100B blood levels and childhood trauma in adolescent inpatients. J Psychiatr Res. 2015;62:14-22. doi: 10.1016/j.jpsychires.2014.12.002.
34. Büyükaslan H, Kandemir SB, Asoğlu M, et al. Evaluation of oxidant, antioxidant, and S100B levels in patients with functional neurological disorder. Neuropsychiatr Dis Treat. 2016;12:1725. doi: 10.2147/NDT.S109174.
35. Schiavone S, Colaianna M, Curtis L. Impact of early life stress on the pathogenesis of mental disorders: relation to brain oxidative stress. Curr Pharm Des. 2015;21:1404-12. doi: 10.2174/1381612821666150105143358.
36. Schiavone S, Jaquet V, Trabace L, Krause KH. Severe life stress and oxidative stress in the brain: from animal models to human pathology. Antioxid Redox Signal. 2013;18:1475-90. doi: 10.1089/ars.2012.4720.
37. von Bernhardi R, Eugenín-von Bernhardi J, Flores B, Eugenín León J.Glial cells and integrity of the nervous system. Adv Exp Med Biol. 2016:1-24. doi: 10.1007/978-3-319-40764-7_1.
38. Stephenson CP, Baguley IJ. Functional neurological disorder (functional neurological disorder): a role for microglial-based plasticity mechanisms? Med Hypotheses. 2018;111:41-8. doi: 10.1016/j.mehy.2017.12.010.
39. Kozlowska K, Spooner CJ, Palmer DM, et al. "Motoring in idle": The default mode and somatomotor networks are overactive in children and adolescents with functional neurological symptoms. Neuroimage Clin. 2018;18:730-43. doi: 10.1016/j.nicl.2018.02.003.
40. Kozlowska K, Griffiths KR, Foster SL, Linton J, Williams LM, Korgaonkar MS. Grey matter abnormalities in children and adolescents with functional neurological symptom disorder. Neuroimage Clin. 2017;15:306-14. doi: 10.1016/j.nicl.2017.04.028.
41. Aybek S, Nicholson TR, Draganski B, et al. Grey matter changes in motor functional neurological disorder. J Neurol Neurosurg Psychiatry. 2014;85:236-8. doi: 10.1136/jnnp-2012-304158.
42. Perez DL, Williams B, Matin N, et al. Corticolimbic structural alterations linked to health status and trait anxiety in functional neurological disorder. J Neurol Neurosurg. Psychiatry 2017;88:1052-9. doi: 10.1136/jnnp-2017-316359.
43. Ozdemir PG, Kaplan I, Uysal C, et al. Serum total oxidant and antioxidant status in earthquake survivors with post-traumatic stress disorder. Acta Neuropsychiatr. 2015;27:153-8. doi: 10.1017/neu.2014.47.
44. Demir S, Bulut M, Atli A, et al. Decreased prolidase activity in patients with posttraumatic stress disorder. Psychiatry Investig. 2016;13:420. doi: 10.4306/pi.2016.13.4.420.
45. Atli A, Bulut M, Bez Y, et al. Altered lipid peroxidation markers are related to post-traumatic stress disorder (PTSD) and not trauma itself in earthquake survivors. Eur Arch Psychiatry Clin Neurosci. 2016;266:329-36. doi: 10.1007/s00406-015-0638-5.
46. Gonçalves CA, Leite MC, Guerra MC. Adipocytes as an important source of serum S100B and possible roles of this protein in adipose tissue. Cardiovasc Psychiatry Neurol. 2010:790431. doi: 10.1155/2010/790431.
47. Tubaro C, Arcuri C, Giambanco I, Donato R.100B protein in myoblasts modulates myogenic differentiation via NF-kappaB dependent inhibition of MyoD expression J Cell Physiol. 2010;223:270-82. doi: 10.1002/jcp.22035.
48. Rothermundt M, Peters M, Prehn JHM, Arolt V. S100B in brain damage and neurodegeneration. Microsc Res Tech. 2003;60:614-32. doi: 10.1002/jemt.10303.
49. Kozlowska K, Nunn KP, Rose D, Morris A, Ouvrier RA, Varghese J. Conversion disorder in Australian pediatric practice. J Am Acad Child Adolesc Psychiatry. 2007;46(1):68-75. doi: 10.1097/01.chi.0000242235.83140.1f.
50. Bègue I, Adams C, Stone J, Perez DL. Structural alterations in functional neurological disorder and related conditions: a software and hardware problem? Neuroimage Clin. 2019;22:101798. doi: 10.1016/j.nicl.2019.101798.

J Surg Med. 2023;7(12):754-759.
DOI: 10.28982/josam.7583

Research article

Journal of Surgery and Medicine
e-ISSN: 2602-2079
https://jsurgmed.com/

Endometrial pathologies in clinical follow-up of patients with hormone receptor-positive/negative breast cancer

Sefa Kurt [1], Samican Ozmen [2], Onur Yavuz [1], Orkun Ilgen [1], Emine Cagnur Ulukus [3]

[1] Department of Obstetrics and Gynecology, Dokuz Eylul University School of Medicine, Izmir, Turkey
[2] Department of Obstetrics and Gynecology, Karacabey State Hospital, Bursa, Turkey
[3] Department of Pathology, Dokuz Eylul University, School of Medicine, Izmir, Turkey

ORCID ID of the author(s)

SK: 0000-0002-5144-0634
SO: 0000-0001-6050-4110
OY: 0000-0003-3716-2145
OI: 0000-0002-0296-8504
ECU: 0000-0003-3023-9218

Corresponding Author
Samican Ozmen
Karacabey State Hospital, Mecidiye Mah., Bursa Çanakkale Yolu Şifa Sokak No:2, 16700, Karacabey, Bursa, Turkey
E-mail: samicanozmen@hotmail.com

Ethics Committee Approval
The study was approved by Non-Interventional Health Research Ethics Committee of Dokuz Eylul University (Date: May 6, 2021, approval number 2021/14-45 and protocol number 6167-GOA).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

Financial Disclosure
The authors declared that this study has received no financial support.

Published
2023 December 7

Abstract

Background/Aim: Breast cancer is the leading cause of cancer-related fatalities in women. Tamoxifen, a selective estrogen receptor modulator (SERM), is frequently employed for chemoprevention in hormone receptor (HR)-positive breast cancer patients due to its anti-estrogenic impact on breast tissue. Nevertheless, tamoxifen exhibits agonistic effects on the endometrium, particularly in postmenopausal women. This study aims to assess gynecological issues and endometrial pathologies that emerge during the treatment and follow-up phases of women diagnosed with HR-positive/negative breast cancer.

Methods: This cohort study involved a data review from 857 breast cancer patients diagnosed over a decade at a tertiary center. Histopathological endometrial findings were evaluated for 166 patients who underwent gynecological consultations before breast cancer treatment with normal examination results and underwent invasive assessments due to gynecological symptoms that arose during treatment and follow-up. The study encompassed cases culminating in total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH+BSO).

Results: The study analyzed 166 cases meeting the inclusion criteria. The mean age at breast cancer diagnosis was 48 years with a standard deviation of 8.4 years, and the average follow-up duration was 4.1 (3.8) years. The predominant histopathological type was invasive ductal carcinoma (75.3%). Of the cases, 68.6% occurred during premenopausal and 31.4% during postmenopause. HR positivity was identified in 136 cases (81.9%), while 30 (18.1%) exhibited negative HR status. Among HR-positive cases, 113 (83.0%) received tamoxifen treatment, while 23 (17.0%) were treated with letrozole. Common clinical findings during and after treatment encompassed increased endometrial thickness (ET) and abnormal uterine bleeding (AUB). Histopathological evaluation of invasive procedures prompted by increased ET indicated the following frequent endometrial findings: proliferative endometrium (33.1%), endometrial polyp (20.5%), and endometrial hyperplasia (EH) without atypia (9%). The histopathological outcomes of invasive procedures prompted by AUB included atrophic endometrium (11.4%), proliferative endometrium (3.6%), and endometrial cancer (1.8%). Among the endometrial malignancies, three occurred in the premenopausal phase and four in the postmenopausal phase. Notably, three of the seven endometrial malignancies were observed in the tamoxifen hormone therapy group, all HR-positive. Four cases were from the non-tamoxifen hormone therapy group with negative HR status.

Conclusion: Globally, breast cancer ranks as the most prevalent malignancy in women. Tamoxifen, a frequently utilized adjuvant therapy post breast cancer surgery, can exert diverse effects on gynecological organs, encompassing benign pathologies like increased ET and malignant pathologies like uterine neoplasia. There is a rising suspicion that etiopathogenetic factors contributing to breast cancer progression might also precipitate uterine cancer, irrespective of tamoxifen use. Vigilant patient monitoring is paramount for detecting uterine neoplasia and other gynecological pathologies.

Keywords: breast cancer, endometrial pathologies, tamoxifen

How to cite: Kurt S, Ozmen S, Yavuz O, Ilgen O, Ulukus EC. Endometrial pathologies in clinical follow-up of patients with hormone receptor-positive/negative breast cancer. J Surg Med. 2023;7(12):754-759.

Introduction

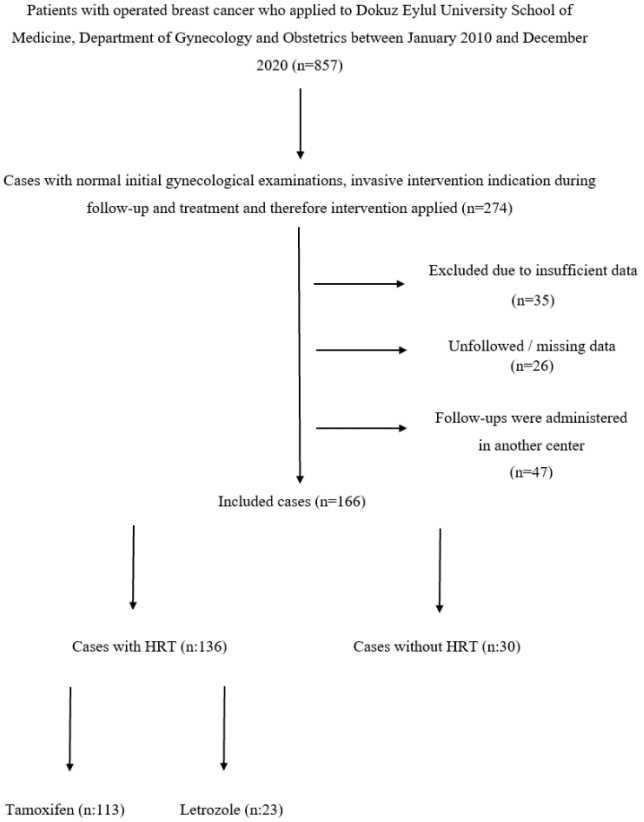
Breast cancer holds the unfortunate distinction of being the most prevalent cancer among women globally, and it maintains its grim position as a leading cause of cancer-related fatalities in this demographic. Despite its prevalence, advancements in early diagnostic capabilities, coupled with a multidisciplinary treatment approach encompassing surgery, radiotherapy, collaboration with medical oncologists, and diligent post-treatment monitoring, have collectively contributed to reducing breast cancer mortality rates [1,2]. Originally conceived as a contraceptive measure, tamoxifen emerged as a selective estrogen receptor modulator (SERM) and was initially employed as an oral contraceptive. However, its significance has evolved considerably, finding its niche in preventing and managing hormone-dependent breast cancer. Its anti-estrogenic properties have proven valuable in offering chemoprevention for women at elevated risk of cancer, particularly those afflicted with estrogen receptor (ER) positive breast cancer. Renowned for its low toxicity and widespread availability, tamoxifen has become one of the most commonly prescribed anticancer medications globally [3,4].

Tamoxifen hormone therapy introduces a spectrum of effects encompassing the development of endometrial polyps, hyperplasia, atypia, and even uterine malignancies [4]. These consequences are notably more prevalent among postmenopausal women. Research has illuminated a concerning trend—underlying endometrial pathology coupled with prolonged tamoxifen treatment exceeding 2 years escalates the risk of uterine malignancy, particularly aggressive histopathological variants such as type 2 endometrial cancer and sarcoma, by a factor of 2 to 7 [4,5]. With this backdrop, the primary objective of this study is to scrutinize the trajectory of endometrial pathologies emerging during and post breast cancer treatment in a cohort of patients who presented no initial evidence of uterine pathology during their initial gynecological examination, regardless of their adherence to adjuvant tamoxifen therapy.

Materials and methods

The study was conducted at a tertiary center from January 2010 to December 2020. Cases were assessed through the utilization of the diagnosis code 'ICD-C50'. Non-Interventional Health Research Ethics Committee of Dokuz Eylul University clearance was secured (Date: May 6, 2021, approval number 2021/14-45 and protocol number 6167-GOA). All patients provided informed consent both prior to treatment and examination. The study entailed the analysis of 857 cases over 10 years. Of these, 166 breast cancer cases were identified that aligned with the stipulated inclusion and exclusion criteria, warranting their inclusion in the evaluation. The assessment encompassed a spectrum of data, including demographic attributes of breast cancer patients, tumor histology, hormone receptor (HR) positivity, administration of adjuvant hormone therapy, mean duration of follow-up, the emergence of gynecological complications during follow-up, and the endometrial pathologies ascertained via preoperative and postoperative invasive procedures. Procedures such as probe curettage, fractionated curettage, and hysteroscopy constituted the 'preoperative' endometrial biopsy interventions, while the term 'postoperative' was associated with the final pathology post total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH+BSO). The patient cohort was bifurcated into two distinct groups: those subjected to hormonal therapy and those who were not. HR positivity was established upon detecting at least one of three receptors – estrogen, progesterone, or human epidermal growth factor receptor 2. Within the hormonal therapy subgroup, patients were further categorized into two subdivisions: those utilizing tamoxifen and those employing aromatase inhibitors (Figure 1).

Figure 1: Flowchart for defining and recording the study criteria.



Determination of menopausal status was guided by serum follicle-stimulating hormone (FSH) and estradiol (E2) levels, circumventing factors such as age and duration of amenorrhea [6]. Cases with serum FSH levels surpassing 75 mIU/ml were deemed postmenopausal, while those exhibiting serum FSH levels below 25 mIU/ml were classified as premenopausal. E2 levels came into play for cases with serum FSH levels ranging between 25 and 75 mIU/ml; E2 levels below 20 pg/ml pointed to postmenopausal status, while levels exceeding 20 pg/ml indicated perimenopausal status. The study's purview included patients devoid of any gynecological pathology at the outset of breast cancer treatment, individuals undergoing invasive interventions (probe, fractionated curettage, hysteroscopy) due to gynecological symptoms during treatment, and subsequently receiving hysterectomy and salpingo-oophorectomy. Exclusions comprised patients who had undergone hysterectomy prior to breast cancer diagnosis, those undergoing hormonal therapy or intrauterine device medication for premalignant endometrial conditions, individuals with a history of gynecological or colon cancer, and those with concurrent or preceding malignancies, whether synchronous or asynchronous. Cases lacking pertinent patient information, subjects continuing care at another facility, and patients treated

outside the study's parameters were also omitted from the analysis.

Statistical analysis

The statistical analysis was executed using IBM SPSS Statistics 24 software. Continuous variables were presented in the form of mean (standard deviation) or median (minimum-maximum) values, while categorical variables were expressed as n (%). The data's adherence to normality was assessed using the Kolmogorov-Smirnov test. Comparative statistical analysis was conducted between outcomes of breast cancer patients who underwent surgery following the detection of uterine pathologies during their follow-up and the relevant dependent and independent variables. The Mann-Whitney U test was employed to evaluate non-parametric independent data, while the categorical data analysis utilized the Chi-square and Fisher precision tests. A significance level of $P<0.05$ was deemed statistically meaningful.

Results

The demographic characteristics of the 166 patients included in the study are presented in Table 1. The participants' mean age was 48 (8.4) years, with a gravida of 2 (1.7) and parity of 2 (1.0). The median follow-up period for breast cancer was 4.1 (3.8) years. The predominant histopathological types of breast cancer were invasive ductal carcinoma (75.3%) and invasive lobular cancer (16.3%). Under the category 'other,' which accounted for 8.4%, histopathological types included ductal/lobular, mucinous, and medullary. HR positivity was observed in 136 (81.9%) cases, while HR negativity was observed in 30 (18.1%) cases. Of the HR-positive cases, 113 (83.0%) received tamoxifen, and 23 (17.0%) received letrozole treatment. Among the cases, 114 (68.6%) were in the premenopausal period, and 52 (31.4%) were in the postmenopausal period. Specifically, 91 (66.9%) of the HR-positive cases were premenopausal, and 45 (33.1%) were postmenopausal. In contrast, 23 (76.6%) of the HR-negative cases were premenopausal, while 7 (23.4%) were postmenopausal (Table 1).

Table 1: Demographic characteristics of all cases

Parameter	Value
Age, years, mean (SD)	48 (8.4) (min-max: 31-81)
Menopausal status of the cases (pre/postmenopause)	114 (68.6%) / 52 (31.4%)
Menopausal status of HR-positive cases (pre/postmenopause)	91 (66.9%) / 45 (33.1%)
Menopausal status of HR-negative cases (pre/postmenopause)	23 (76.6%) / 7 (23.4%)
Gravida, mean (SD)	2 (1.7) (min-max: 0-12)
Parity, mean (SD)	2 (1) (min-max: 0-6)
Follow-up period, years, mean (SD)	4.1 (3.8) (min-max: 0-22)
The histopathological type of breast cancer	
Invasive ductal carcinoma	125 (75.3%)
Invasive lobular carcinoma	27 (16.3%)
Other	14 (8.4%)
HR status	
*Positive	136 (81.9%)
Tamoxifene	113 (83.0%)
Letrozole	23 (17.0%)
*Negative	30 (18.1%)
Invasive procedure indications	
Endometrial thickness increases	114 (68.7%)
Abnormal uterine bleeding	28 (16.9%)
Genetic	13 (7.8%)
Other	11 (6.6%)

SD: standard deviation, HR: Hormone receptor

The most frequently reported gynecological symptoms during and after breast cancer treatment included vaginal dryness, dyspareunia, and vaginal bleeding. Notably, the most common finding was increased endometrial thickness (ET). Invasive interventions were primarily indicated for increased ET and abnormal uterine bleeding (AUB), accounting for 68.7% and 16.9%, respectively (refer to Table 1). Genetic mutation analysis revealed BRCA 1-2, STK-11, and PALB-2 mutations in 11 out of 13 cases in the genetic mutation group. Additionally, 11 cases fell under the 'other' category, while 6 exhibited benign adnexal masses. Furthermore, myoma uteri, previously undetected, was identified in five cases (Table 1).

Diagnostic invasive procedures were performed on cases with the indications above before surgery. Subsequently, all cases underwent a postoperative TAH+BSO (total abdominal hysterectomy and bilateral salpingo-oophorectomy) procedure. In instances of malignancy, supplementary treatments were administered based on the malignancy type and the frozen pathology examination results obtained during the operation. The preoperative and postoperative endometrial histopathology findings are detailed in Table 2. Notably, the final pathology report revealed hyperplasia with atypia among five cases initially diagnosed with benign pathologies from endometrial sampling. Similarly, all cases initially diagnosed with endometrial cancer from endometrial sampling were confirmed as endometrial cancer in the final pathology results (Table 2). A comparison of postoperative final pathology results concerning preoperative endometrial biopsy indications is provided in Table 3. Proliferative endometrium emerged as the most frequent histopathological outcome among cases operated on due to increased ET (33.1%).

Table 2: Preoperative and postoperative endometrial histopathological results of all cases

Endometrial histopathology	Preoperative (n=166)	Postoperative (n=166)
Proliferative endometrium	71 (42.8%)	69 (41.6%)
Endometrial polyp	40 (24.1%)	37 (22.3%)
Atrophic endometrium	26 (15.7%)	26 (15.7%)
Hyperplasia without atypia	19 (11.4%)	19 (11.4%)
Hyperplasia with atypia	3 (1.8%)	8 (4.8%)
Malignancy	7 (4.2%)	7 (4.2%)

Table 3: Final pathology results according to preoperative endometrial biopsy indications

	Postoperative histopathological results (n=166)					
Indications	Proliferative endometrium	Endometrial polyp	Endometrial atrophy	Hyperplasia without atypia	Hyperplasia with atypia	Endometrial malignancy
Endometrial thickness increasing	55 (33.1%)	34 (20.5%)	0 (0.0%)	15 (9%)	7 (4.2%)	3 (1.8%)
Abnormal uterine bleeding	6 (3.6%)	0 (0.0%)	19 (11.4%)	0 (0.0%)	0 (0.0%)	3 (1.8%)
Genetic mutations	4 (2.4%)	1 (0.6%)	4 (2.4%)	3 (1.8%)	0 (0.0%)	1 (0.6%)
Other	4 (2.4%)	2 (1.2%)	3 (1.8%)	1 (0.6%)	1 (0.6%)	0 (0.0%)

Conversely, endometrial atrophy constituted the prevailing histopathological outcome (11.4%) in patients operated on for AUB. The correlation between preoperative ultrasonically measured ET values and postoperative histopathological results for all cases is outlined in Table 4. Notably, proliferative endometrium was elevated in cases with 5-10 mm ET measurements, while endometrial polyps were significantly more frequent in cases with ET >15 mm ($P<0.001$). Conversely, ET <5 mm cases exhibited significantly higher instances of endometrial atrophy ($P<0.001$). Within the four cases with ET measurements below 5 mm, 1 displayed endometrioid adenocarcinoma, while the remaining three exhibited serous carcinoma histology. Cases with ET measurements between 10-15 mm showed significantly higher instances of endometrial hyperplasia (EH) with or without atypia compared to other groups ($P<0.001$, $P<0.001$, respectively).

Notably, there were no noteworthy differences between ET measurement groups in terms of endometrial malignancy.

Table 4: Distribution of endometrial thickness values measured by ultrasound in all cases according to final histopathological diagnoses

	<5 mm n=36	5-10 mm n=73	10-15 mm n=31	>15 mm n=26	*P*-value
Proliferative endometrium	6 (16.6%)	55 (75.3%)	7 (22%)	1 (3.8%)	<0.001*
Endometrial polyp	0 (0.0%)	8 (10.9%)	9 (29%)	20 (76.9%)	<0.001*
Endometrial atrophy	26 (72.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	<0.001*
Hyperplasia without atypia	0 (0.0%)	7 (9.5%)	9 (29%)	3 (11.5%)	<0.001*
Hyperplasia with atypia	0 (0.0%)	1 (1.3%)	6 (19.3%)	1 (3.8%)	<0.001*
Endometrial malignancy	4 (11.1%)	2 (2.7%)	0 (0.0%)	1 (3.8%)	0.1

Table 5 presents a comparison of histopathological findings based on menopausal status. Among the cases, 114 were premenopausal (68.6%), while 52 were postmenopausal (31.4%). The diagnosis of proliferative endometrium was notably higher in the premenopausal group than the postmenopausal group (P<0.001, respectively; 35.5% vs. 6%). Conversely, the diagnosis of endometrial atrophy was significantly more prevalent in the postmenopausal group (P<0.001, respectively; 6% vs. 9.6%). Comparable results were observed between the groups regarding other final histopathological findings. Notably, among endometrial cancer cases, 4 were identified in the postmenopausal period, while 3 were identified in the premenopausal period.

Table 5: Comparison of histopathological findings according to menopausal status

	Premenopause n=114 (68.6%)	Postmenopause n=52 (31.4%)	*P*-value
Proliferative endometrium	59 (35.5%)	10 (6%)	<0.001*
Endometrial polyp	23 (13.9%)	14 (8.4%)	0.331
Endometrial atrophy	10 (6%)	16 (9.6%)	0.001*
Hyperplasia without atypia	15 (9%)	4 (2.4%)	0.327
Hyperplasia with atypia	4 (2.4%)	4 (2.4%)	0.207
Endometrial malignancy	3 (1.8%)	4 (2.4%)	0.193

Discussion

This study presents findings on endometrial pathologies observed during the clinical monitoring of breast cancer patients with positive and negative HR statuses. Notably, our study highlights the significant increase in ET due to hormonal therapy and the heightened occurrence of endometrial pathologies associated with this increase in ET. Interestingly, our results diverge from existing literature, revealing a higher incidence of endometrial malignancies among patients who did not undergo hormone therapy.

Breast cancer exhibits diverse biological behaviors and treatment responses, thus constituting a heterogeneous spectrum of pathologies. Roughly half of all cases are linked to risk factors, including reproductive elements and proliferative breast disorders, with another 10% attributed to familial history and genetic influences [1,2]. Furthermore, environmental factors, encompassing demographic and lifestyle considerations, play a role in breast cancer risk [1–3].

Around 20% of breast cancer cases in the United States are diagnosed within the 45-54 age bracket [7]. Correspondingly, our study indicates an average age of diagnosis at 48 (8.4) years. The prevailing literature reflects that 75% of breast cancer cases exhibit HR positivity, thus making the HR-positive type the predominant form of breast cancer [1]. Our findings mirror these previous studies, with 81.9% of cases displaying HR-positive breast cancer.

Research indicates that HR-negative breast cancer predominantly occurs during the premenopausal phase, with prevalence rates ranging between 15–20% [8]. Our study aligns with this trend, as HR-negative breast cancer constituted 18.1% of all cases, consistent with existing literature.

Tamoxifen, a commonly employed adjuvant therapy for breast cancer patients, functions as a competitive inhibitor of estrogen receptors, binding to estrogen receptors within the breast to hinder tumor proliferation. This agent yields diverse impacts across different tissues. Despite its anti-estrogenic role in breast tissue, it can manifest as an estrogen agonist within distinct regions of the female reproductive system [3,4]. In premenopausal women, the antagonistic effect of tamoxifen on the endometrium is due to its interaction with endogenous estradiol, which surpasses its agonistic influence. Conversely, the postmenopausal endometrium experiences lower endogenous estrogen levels, prompting tamoxifen to assume an agonistic role [3–5].

Reports indicate that as many as 67% of women undergoing tamoxifen treatment for breast cancer may encounter endometrial pathologies [9,10]. Uterine gynecological issues manifest incidentally during pelvic imaging or present symptomatically, such as abnormal uterine bleeding. A frequently observed pelvic imaging finding is an escalation in ET. Likewise, within our study, the most prevalent outcome during monitoring breast cancer patients receiving hormone therapy was an augmentation in ET, evident in 68.7% of cases. Following this, cases featuring AUB were recorded in 28 instances (16.9%). In extant literature, AUB surfaces in approximately 50% of premenopausal cases and 25% of postmenopausal cases [10–13]. Notably, the preponderance of cases within our study was situated in the premenopausal period, and the routine gynecological surveillance of breast cancer patients is more frequent within our country due to medical practices. This might account for the comparatively reduced occurrence of cases with AUB compared to the literature.

Within our study, the histopathological outcomes of most cases that underwent invasive evaluation due to heightened ET predominantly indicated benign conditions, with proliferative endometrium (33.1%) and endometrial polyps (20.5%) being the primary findings.

While the prevalence of endometrial polyps within the general population fluctuates between 0-10%, patients undergoing tamoxifen treatment face an elevated risk, with incidence rates ranging from 6-42% [9–12]. Although endometrial polyps are benign, the likelihood of malignant transformation among endometrial polyps in the broader population is approximately 2% during the premenopausal phase and 5% during the postmenopausal phase. This risk escalates to 11% among women employing tamoxifen [14,15]. In alignment with existing literature, our study reveals a comparable risk of endometrial polyps among patients receiving hormone therapy, with a prevalence of 21.1%, thereby holding statistical significance.

Research has revealed an increased risk of EH in postmenopausal women using tamoxifen, whereas no elevated risk has been established for premenopausal patients. The NSABP P-2 study highlighted an annual rate of atypical EH at 0.77 per 1000 women among postmenopausal patients receiving tamoxifen, alongside a rate of 3.63 per 1000 women for simple hyperplasia [11,16]. An additional retrospective study depicted a

risk of approximately 12% for simple hyperplasia, 3% for complex hyperplasia, and approximately 2% for endometrial cancer among postmenopausal breast cancer patients subjected to four years of tamoxifen treatment [10]. However, our study's outcomes deviate from the literature. Among the 27 instances of EH, 19 encompassed simple hyperplasia without atypia, and eight exhibited hyperplasia with atypia. Of these cases, 19 occurred during the premenopausal period, while 8 manifested during the postmenopausal period. Intriguingly, 50% of the hyperplasia with atypia cases were identified in the premenopausal phase. A noteworthy 88.8% (24/27) of hyperplasia cases were under hormone therapy. Although progesterone and levonorgestrel intrauterine devices can serve as treatment options for EH, HR-positive breast cancer patients without fertility expectations should prioritize hysterectomy as their treatment choice [17,18].

Determining the menopausal status is crucial in assessing tamoxifen's impact, as neoplastic transformations typically manifest more prominently during the postmenopausal phase. Following a five-year course of tamoxifen treatment, the incidence of endometrial cancer stands at 0.3% among postmenopausal patients and 0.1% among premenopausal patients [14,19,20]. Interestingly, the American College of Obstetricians and Gynecologists (ACOG) affirms that the risk of uterine cancer does not rise in premenopausal women undergoing tamoxifen therapy and suggests that routine gynecological monitoring suffices for these patients [20]. In this context, our findings diverge from existing literature. Among the seven malignancies identified in our study, four occurred during the postmenopausal period, while 3 emerged during the premenopausal phase. Consequently, we advocate for a case-specific evaluation that considers individual dynamics. We further recommend meticulous assessment for all patients, irrespective of their menopausal status.

The risk of endometrial cancer attributed to tamoxifen is well-established and correlates with the duration of tamoxifen usage. Numerous studies indicate that postmenopausal patients using tamoxifen experience an endometrial cancer incidence that is 2-3 times higher than that of the general population [4,5,10,13,14]. Nonetheless, certain studies also highlight an elevated occurrence of HR-positive/negative endometrial cancer among breast cancer patients compared to the general population, irrespective of drug utilization [21,22]. This hints at a potential etiological similarity between various breast cancer subtypes and the onset of endometrial cancer [23]. Our study demonstrates a notable disparity in endometrial malignancy cases within the group that did not undergo hormone therapy. Consequently, we posit that gynecological assessments should form an integral component of the routine monitoring of breast cancer patients, regardless of the positive or negative HR status.

Extended tamoxifen usage has been linked to an elevated susceptibility to uterine sarcoma, and this risk may persist for a certain duration even after discontinuing tamoxifen therapy [24–26]. In alignment with this concern, ACOG advises that patients undergoing tamoxifen treatment be educated about and assessed for the risk of uterine sarcoma, alongside other potential risks [20]. It's worth noting that our study group did not yield any instances of uterine sarcoma.

Our study has several strengths, including utilizing a homogenous cohort within a single tertiary care center. Notably, the study employed stringent exclusion criteria, ensuring the robustness of the data. The extended follow-up period spanning a decade further contributes to the study's credibility. Worth mentioning is the fact that the absence of patient information was among the exclusion criteria, bolstering the quality of our findings. A limited number of patients was the major limitation of this study.

Conclusion

In summary, breast cancer is the most prevalent malignancy among women worldwide. Recent years have witnessed a decline in breast cancer mortality due to advancements in diagnostic and therapeutic approaches, transforming the ailment into a manageable chronic condition. Alongside tumor attributes, factors such as menopausal status, reproductive history, and current health status wield notable influence over the treatment trajectory. The research underscores the augmented susceptibility to uterine pathologies – such as endometrial polyps, endometrial carcinoma, EH, uterine sarcoma, and carcinosarcoma – in patients employing tamoxifen for breast cancer therapy. Consequently, vigilant surveillance and assessment of women receiving tamoxifen treatment for potential gynecological pathologies are important. Furthermore, it's imperative to recognize that etiopathogenetic factors implicated in breast cancer development might similarly contribute to endometrial cancer development, irrespective of hormonal therapies employed, thereby heightening the risk of endometrial cancer in such patients. Future investigations with larger sample sizes possess the potential to furnish insights into the impact of tamoxifen in breast cancer cases and the optimal frequency for follow-up care.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021 May 4;71(3):209–49.
2. Kesson EM, Allardice GM, George WD, Burns HJG, Morrison DS. Effects of multidisciplinary team working on breast cancer survival: retrospective, comparative, interventional cohort study of 13 722 women. BMJ. 2012 Apr 26;344(apr26 1):e2718–e2718.
3. Jordan VC. The SERM Saga, Something from Nothing: American Cancer Society/SSO Basic Science Lecture. Ann Surg Oncol. 2019 Jul 25;26(7):1981–90.
4. Emons G, Mustea A, Tempfer C. Tamoxifen and Endometrial Cancer: A Janus-Headed Drug. Cancers (Basel). 2020 Sep 7;12(9):2535.
5. Fleming CA, Heneghan HM, O'Brien D, McCartan DP, McDermott EW, Prichard RS. Meta-analysis of the cumulative risk of endometrial malignancy and systematic review of endometrial surveillance in extended tamoxifen therapy. British Journal of Surgery. 2018 Jul 11;105(9):1098–106.
6. Freeman EW, Sammel MD, Gracia CR, Kapoor S, Lin H, Liu L, et al. Follicular phase hormone levels and menstrual bleeding status in the approach to menopause. Fertil Steril. 2005 Feb;83(2):383–92.
7. Giaquinto AN, Sung H, Miller KD, Kramer JL, Newman LA, Minihan A, et al. Breast Cancer Statistics, 2022. CA Cancer J Clin. 2022 Nov 3;72(6):524–41.
8. Yin L, Duan JJ, Bian XW, Yu S cang. Triple-negative breast cancer molecular subtyping and treatment progress. Breast Cancer Research. 2020 Dec 9;22(1):61.
9. Cheng WF, Lin HH, Torng PL, Huang SC. Comparison of Endometrial Changes among Symptomatic Tamoxifen-Treated and Nontreated Premenopausal and Postmenopausal Breast Cancer Patients. Gynecol Oncol. 1997 Aug;66(2):233–7.
10. Cohen I, Altaras MM, Shapira J, Tepper R, Rosen DJD, Cordoba M, et al. Time-Dependent Effect of Tamoxifen Therapy on Endometrial Pathology in Asymptomatic Postmenopausal Breast Cancer Patients. International Journal of Gynecological Pathology. 1996 Apr;15(2):152–7.
11. Runowicz CD, Costantino JP, Wickerham DL, Cecchini RS, Cronin WM, Ford LG, et al. Gynecologic conditions in participants in the NSABP breast cancer prevention study of tamoxifen and raloxifene (STAR). Am J Obstet Gynecol. 2011 Dec;205(6):535.e1-535.e5.
12. Şahin Uysal N, Boyraz G, Usubütün A, Tuncer ZS. The evaluation of laparotomy results in breast cancer patients with gynecological pathologies. Journal of Obstetrics and Gynaecology Research. 2020 Oct 10;46(10):2126–33.
13. Jeon J, Kim SE, Lee DY, Choi D. Factors associated with endometrial pathology during tamoxifen therapy in women with breast cancer: a retrospective analysis of 821 biopsies. Breast Cancer Res Treat. 2020 Jan 20;179(1):125–30.
14. Cohen I. Endometrial pathologies associated with postmenopausal tamoxifen treatment. Gynecol Oncol. 2004 Aug;94(2):256–66.
15. Lee SC, Kaunitz AM, Sanchez-Ramos L, Rhatigan RM. The Oncogenic Potential of Endometrial Polyps. Obstetrics & Gynecology. 2010 Nov;116(5):1197–205.
16. Fisher B, Costantino JP, Redmond CK, Fisher ER, Wickerham DL, Cronin WM. Endometrial Cancer in Tamoxifen-Treated Breast Cancer Patients: Findings From the National Surgical Adjuvant Breast

and Bowel Project (NSABP) B-14 *. JNCI: Journal of the National Cancer Institute. 1994 Apr 6;86(7):527–37.
17. Romero SA, Young K, Hickey M, Su HI. Levonorgestrel intrauterine system for endometrial protection in women with breast cancer on adjuvant tamoxifen. Cochrane Database of Systematic Reviews. 2020 Dec 21;2021(2).
18. Feldman S, Shapter A, Welch WR, Berkowitz RS. Two-Year Follow-Up of 263 Patients with Post/Perimenopausal Vaginal Bleeding and Negative Initial Biopsy. Gynecol Oncol. 1994 Oct;55(1):56–9.
19. F. Machado, J.R. Rodríguez(h), J.P.H. León, J.R. Rodríguez, J.J. Parrilla, L. Abad. Tamoxifen and endometrial cancer. Is screening necessary? A review of the literature. Eur J Gynaecol Oncol . 2005;26(3):257–65.
20. Committee Opinion No. 601. Obstetrics & Gynecology. 2014 Jun;123(6):1394–7.
21. Guo J, Zhang Y, Qian H, Ma F, Cui X, Duan H. The clinical characteristics and prognosis of endometrial carcinomas that occur after breast cancer: does hormone receptor status of breast cancer matter? Arch Gynecol Obstet. 2019 Nov 1;300(5):1399–404.
22. Lortet-Tieulent J, Ferlay J, Bray F, Jemal A. International Patterns and Trends in Endometrial Cancer Incidence, 1978–2013. JNCI: Journal of the National Cancer Institute. 2018 Apr 1;110(4):354–61.
23. Liu J, Jiang W, Mao K, An Y, Su F, Kim BYS, et al. Elevated risks of subsequent endometrial cancer development among breast cancer survivors with different hormone receptor status: a SEER analysis. Breast Cancer Res Treat. 2015 Apr 13;150(2):439–45.
24. Engin H. High-grade endometrial stromal sarcoma following tamoxifen treatment. Gynecol Oncol. 2008 Jan;108(1):253–4.
25. Kloos I, Delaloge S, Pautier P, Di Palma M, Goupil A, Duvillard P, et al. Tamoxifen-related uterine carcinosarcomas occur under/after prolonged treatment: Report of five cases and review of the literature. International Journal of Gynecological Cancer. 2002 Sep;12(5):496–500.
26. Yildirim Y, Inal MM, Sanci M, Yildirim YK, Mit T, Polat M, et al. Development of uterine sarcoma after tamoxifen treatment for breast cancer: report of four cases. International Journal of Gynecological Cancer. 2005 Nov;15(6):1239–42.

J Surg Med. 2023;7(12):760-764.
DOI: 10.28982/josam.7452

Research article

Journal of Surgery and Medicine
e-ISSN: 2602-2079
https://jsurgmed.com/

Instagram and lumbar discectomy surgery: An evaluation of patients' perception of surgery in social media

Yigit Kultur [1], Sinan Karaca [2], Mehmet Nuri Erdem [3], Erdem Sahin [4], Elviz Gasimov [5], Mirza Biscevic [6], Mehmet Tezer [7]

[1] Taksim Training and Research Hospital, Department of Orthopedics and Traumatology, Istanbul, Turkey
[2] Yeni Yuzyil University, Department of Orthopedics and Traumatology, Istanbul, Turkey
[3] Işık University, Vocational School of Health Services, Operating Room Services Department, Istanbul, Turkey
[4] Erzurum Regional Training and Research Hospital, Department of Orthopedics and Traumatology, Erzurum, Turkey
[5] Azerbaijan Scientific-research Institute of Traumatology and Orthopedics, Department of Orthopedics and Traumatology Baku, Azerbaijan
[6] General hospital Sarajevo, Department of Orthopedics and Traumatology, Bosnia and Herzegovina
[7] Nisantasi Orthopedics Center, Department of Orthopedic and Traumatology, Istanbul, Turkey

ORCID ID of the author(s)

YK: 0000-0001-8201-6994
SK: 0000-0003-3403-8069
MNE: 0000-0001-7377-6393
ES: 0000-0001-8333-0803
EG: 0000-0002-6495-8897
MB: 0000-0002-8866-5749
MT: 0000-0001-6137-7432

Corresponding Author
Yigit Kultur
Taksim Training and Research Hospital, Katip Mustafa Celebi Siraselviler Street, No: 48 Beyoglu, Istanbul, Turkey
E-mail: yigitkulturr@hotmail.com

Ethics Committee Approval
This article is not a study with human participants. There are no experiments on animals. This article does not contain any studies on human participants or animals performed by the author. There is no identifying information of participants.

Conflict of Interest
No conflict of interest was declared by the authors.

Financial Disclosure
The authors declared that this study has received no financial support.

Published
2023 December 5

Abstract

Background/Aim: Most scoring systems in healthcare take into account the physical condition and pain status of a patient, but the impact of society on the individual is ignored. The aim of our study was to evaluate the social media posts made by patients regarding lumbar discectomy surgery. The objective was to identify and explore concerns and issues that may not be immediately evident during clinical evaluations but are significant to the patients themselves.

Methods: Public posts with the hashtags #discectomy, #lumbardisectomy, and #discectomyrecovery were examined on the Instagram application. The tone of the post, return to sports (RTS), rehabilitation or physical therapy (PT), return to work (RTW), incision site (e.g., scarring, sutures, and dressing), pain, activities of daily living (ADL), and X-ray/magnetic resonance imaging (MRI) data were evaluated. The "Instagram likes ratio" was determined by dividing the total number of likes received for each post by the number of followers.

Results: 272 posts were assessed, and 77.9% of them exhibited a positive tone. The topic that was most frequently discussed was ADL, which was discussed in 24.6% of the posts. Statistical analysis demonstrated a significant association between positive tone and ADL, as well as positive tone and RTS (P<0.001). A statistically significant correlation was observed between negative tone and neurological deficits, pain, and X-ray/MRI findings (P<0.001).

Conclusion: Our study offers a unique perspective on the experience and satisfaction of patients who have undergone lumbar discectomy. Neurologic deficits and pain were notably significant in the negative posts. However, in general, the majority of the posts maintained a positive tone. The results could provide insights into patients' experiences and perspectives that can potentially inform healthcare professionals in providing more comprehensive and patient-centered care.

Keywords: discectomy, Instagram, social media, post, hashtag, return to sports

How to cite: Kultur Y, Karaca S, Erdem MN, Sahin E, Gasimov E, Biscevic M, Tezer M. Instagram and lumbar discectomy surgery: an evaluation of patients' perception of surgery in social media. J Surg Med. 2023;7(12):760-764.

Introduction

Social media has become an indispensable and regularly used part of our daily lives. Carr and Hayes define social media as internet-based platforms that enable users to engage in interactive and self-presentation activities either in real time or asynchronously. These platforms cater to diverse audiences both broad and specific who derive value from user-generated content and the sense of interacting with others [1].

On average, a person spends at least six hours a week on the internet. Furthermore, 15% of internet users follow health-related data, and 34% of adult internet users follow health-related treatments through various online reviews, promotional sites, and blogs [2]. In 2010, Baker et al. [3] reported that approximately 30% of patients who opted for elective spinal surgery performed an internet search prior to the surgery. This indicates that a significant portion of patients actively seek information online before making decisions about their medical procedures.

As of January 2020, popular social media applications including WhatsApp, Facebook, Instagram, WeChat, and TikTok collectively had a staggering user base of 3.8 billion. This highlights the widespread reach and influence of social media platforms in connecting billions of individuals worldwide [4]. Instagram is a platform that allows its users to express themselves by taking photos and videos and sharing them on their accounts [5]. Since 2011, the platform has allowed its users to find posts by like-minded users by searching with hashtags (#) [6]. This allows patients to connect with online communities of individuals who have similar health problems.

The utilization of social media in the healthcare sector is experiencing continuous growth. This trend has been further accelerated by the global pandemic in recent years as patients increasingly seek convenient access to health-related information through various social media platforms. Consequently, such platforms have become a valuable resource for telemedicine, and healthcare professionals and patients are utilizing these platforms more intensively for communication and remote medical consultations.

This trend underscores the evolving role of social media in facilitating access to healthcare services and the dissemination of valuable health information. It signifies the increasing importance of social media platforms as effective tools for connecting individuals with healthcare resources and promoting health literacy in the digital age [7]. It may also be asserted that patients can express themselves more comfortably on social media than at the doctor’s office. Most scoring systems in healthcare take into account the physical condition and pain status of a patient, but the impact of society on the individual is ignored. However, considering that humans are bio-psycho-social beings, we believe that the evaluation of a patient’s clinical situation under influence of society, particularly social media, may offer physicians a different perspective.

The aim of this study was to assess the social media posts of patients who have undergone lumbar discectomy surgery. The objective was to identify any issues or concerns that may not be easily detected through conventional clinical evaluations but hold significant importance for patients. Essentially, our goal was to establish a connection between the operating room and social media platforms. By analyzing patients' posts related to their surgical experiences, we sought to gain insights into their needs and expectations, which could foster a stronger doctor-patient relationship and enhance overall awareness in the medical community.

Materials and methods

In July 2022, a search was conducted on Instagram's public accounts among posts from July 2020 to June 2022. In this cross-sectional study, public posts published with the hashtags #discectomy, #discectomyrecovery, and #lumbardisectomy were examined. The search results were evaluated by two researchers. To reach consensus, any differences between analysts were evaluated together. In cases of disputes, posts that were subject to contention were excluded from the study to ensure the integrity and reliability of the findings. By removing such posts, the aim was to maintain the validity and accuracy of the analyzed data. Since the posts were publicly available, ethics committee approval was not obtained.

The evaluation included the tone of the post, return to sports (RTS), rehabilitation or physical therapy (PT), return to work (RTW), incision site details (such as scarring, sutures, and dressing), pain, activities of daily living (ADL), and X-ray/magnetic resonance imaging (MRI) data. Furthermore, the timing of post-operative sharing was recorded and categorized as follows: posts shared within one week after surgery, posts shared more than one week after surgery, and posts shared on the anniversary of the surgery.

Inclusion and exclusion criteria

The search results revealed a total of 272 patients who had undergone lumbar discectomy. These patients were identified through the use of specific hashtags: #discectomy, #discectomyrecovery, and #lumbardiscectomy. For each patient, only the first and most relevant hashtag was included in the study. To ensure the relevance of the data, advertisements pertaining to rehabilitation or physical therapy, accounts of physicians, and accounts primarily focused on sharing general health-related content were excluded from the study. Posts were also excluded if they were shared preoperatively, contained video content, were specifically about cervical discectomy, were veterinary-related posts, or were written in a language other than English. Those who did not have a history of discectomy surgery in their social media statements were excluded from the study. Posts not detected as having positive or negative tones (neutral tones) were also excluded.

Statistical analysis

Statistical analysis was conducted using the program SPSS 15.0 for Windows. Descriptive statistics such as the mean, standard deviation, minimum, maximum, and median were used to summarize numerical variables. Categorical variables are presented as numbers and percentages. For non-normally distributed data, the Mann-Whitney U test was employed to compare two independent groups. The chi-squared test was used for comparing results within groups. A significance level of $P<0.05$ was used to determine statistical significance.

Results

Females constituted the majority of participants in the study, accounting for 79.4% compared to 20.6% males. A significant proportion of posts (66.9%) were shared after the initial week following the surgery. Posts shared within the first postoperative week accounted for 23.8%, while those shared on the anniversary of the surgery made up 9.1% of the total. A significant proportion of posts (77.9%) had a positive tone, while 22.1% had a negative tone. The most frequently mentioned topic in the posts was ADL (24.6%), followed by the incision site (22.7%), pain (21.3%), RTS (19.8%), X-ray/MRI (12.8%), RTW (4.4%), and PT (3.6%). No posts were excluded due to persistent disagreement.

The results of the statistical analysis indicated a significant correlation between positive tone and ADL as well as positive tone and RTS (P<0.001). A significant relationship was observed between negative tone and neurological deficit, pain, and X-ray/MRI (P<0.001) (Table 1). There were significant associations between pain and neurological deficit (P=0.003), as well as between X-ray/MRI and neurological deficit (P=0.043) (Table 2). However, no statistically significant relationships were found between post tone and sex (P=0.395), RTW (P=0.075), rehabilitation/physical therapy (P=0.125), and incision site (P=0.409). The average "Instagram like ratio" for the posts was 11%.

Table 1: The relationship between patient characteristics and the tone used in the posts.

		Tone				
		Negative n=60 (22.1%)		Positive n=212 (77.9%)		
		n	%	n	%	*P*-value
Gender	Female	50	83.3%	166	78.3%	0.395
	Male	10	16.7%	46	21.7%	
Timing of the post	≤1 week after surgery	26	43.3%	39	18.4%	<0.001
	>1 week after surgery	34	56.7%	148	69.8%	
	Anniversary of surgery	0	0.0%	25	11.8%	
Neurological deficit	No	49	81.7%	212	100%	<0.001
	Yes	11	18.3%	0	0.0%	
Post content	RTS	1	1.1%	53	25%	<0.001
	RTW	0	0.0%	12	5.6%	0.075
	ADL	2	2.3%	65	30.6%	<0.001
	Rehabilitation/PT	0	0.0%	10	4.7%	0.125
	Incision site	11	12.7%	51	24%	0.409
	Pain	50	58.1%	8	3.7%	<0.001
	X-ray or MRI	22	25.5%	13	6.1%	<0.001

ADL: activities of daily living, PT: physical therapy, RTS: return to sports, RTW: return to work. * Posts could have more than one post content *Significant p values are written in bold.

Table 2: The relationship between post characteristics and the presence of neurological deficit.

				Neurological deficit				
				No n=261 (96.0%)		Yes n=11 (4.0%)		
		n	%	n	%	n	%	*P*-value
Gender	Female	216	79.4%	205	78.5%	11	100%	0.128
	Male	56	20.6%	56	21.5%	0	0.0%	
Timing of the post	≤1 week after surgery	65	23.9%	62	23.8%	3	27.3%	0.791
	>1 week after surgery	182	66.9%	174	66.7%	8	72.7%	
	Anniversary of surgery	25	9.2%	25	9.6%	0	0.0%	
Tone of the post	Negative	60	22.1%	49	18.8%	11	100%	<0.001
	Positive	212	77.9%	212	81.2%	0	0.0%	
Post Content	RTS	54	18.1%	54	19%	0	0.0%	0.128
	RTW	12	4.0%	12	4.2%	0	0.0%	1.000
	ADL	67	22.4%	67	23.6%	0	0.0%	0.071
	Rehabilitation/PT	10	3.3%	10	3.5%	0	0.0%	1.000
	Incision site	62	20.8%	58	20.4%	4	26.6%	0.290
	Pain	58	19.4%	51	18%	7	46.6%	0.003
	X-ray/MRI	35	11.7%	31	10.9%	4	26.6%	0.043

ADL: activities of daily living, PT: physical therapy, RTS: return to sports, RTW: return to work. * Posts could have more than one post content. Significant p values are written in bold.

Discussion

Menendez et al. [9] highlighted the lack of clarity regarding the relationship between disability improvement, pain relief, and patient satisfaction after spinal surgery. They argue that traditional measures are insufficient to evaluate patient satisfaction as it is not solely dependent on the surgical outcome. They emphasize that patient satisfaction is influenced by seven key variables: pain levels, functional improvement, patient expectations and preferences, patient health characteristics, the interpersonal manner of the caregiver, efficacy and clinical outcomes of the treatment, and postoperative care and therapy. These factors together shape the overall patient experience and level of satisfaction.

Krauss et al. [10] stated that psychological factors may also be important. According to expectation-disconfirmation theory, the performance of a product (healthcare in this case) should be at least as much as a person's (the patient's) expectation. Otherwise, the person will have a negative view towards the product [11]. Scoring systems have been developed to evaluate patient satisfaction, such as the Press-Ganey system, but they are applied using stereotyped questions, so they cannot adequately reflect the insight of the patients, their perspective on the treatment, and their satisfaction [12].

Thus far, there has been no comprehensive disease-specific evaluation method that encompasses all aspects of patient satisfaction in the field of spine surgery. However, it is important to note that when patient satisfaction levels rise, several positive outcomes can be anticipated. These include increased treatment adherence, improved clinical outcomes, and a decrease in malpractice suits. The development of a robust evaluation approach that encompasses all dimensions of patient satisfaction in spine surgery is very important to enhance patient experiences and optimize overall healthcare outcomes.

Lumbar disc herniation is widely acknowledged as a prominent contributor to both low back pain and sciatica, representing a significant source of discomfort and impairment for individuals. Surgery should be considered in cases where conservative treatment has been applied for a certain period of time but is insufficient or there is a progressive neurological deficit. The surgical options include open, microendoscopic, and percutaneous endoscopic discectomy techniques, which have improved considerably in recent years [13]. Carragee et al. [14] reported that the failure rate in lumbar disc surgery varies between 20 and 40%, and low back pain, sciatica, and recurrent disc herniation were blamed as the causes of this failure. In our study, the causes of failure were pain and neurological deficits. Our observation that 22.1% of the analyzed posts exhibited a negative tone is consistent with the literature, providing additional support to our assertion that social media content can be a valuable resource for evaluating patient satisfaction.

Previous studies have utilized social media platforms to assess patient perceptions in various healthcare areas, including adult spine fusion, shoulder and elbow surgery, hip arthroscopy, anterior cruciate ligament surgery, pediatric scoliosis, cervical disc surgery, and total joint arthroplasty [15–20]. However, to our knowledge, no other study has focused on lumbar discectomy so far. In a study by Ramkumar et al. [17], 88% of the posts shared by patients who underwent anterior cruciate

ligament surgery had a positive tone, and the majority of them were related to rehabilitation and RTS. Another study on joint arthroplasties reported a prevalence of 93% for positive tone, and the posts generally focused on rehabilitation and ADL [16]. Similarly, in another study, 87% of the posts related to shoulder and elbow surgery had a positive tone, and return to play, surgical site, and ADL were the most shared topics [18].

According to Haeberle et al. [21] did a study on hip arthroscopy and found that 52.9% of the related social media posts had a positive tone. They suggested that the lower rates of positive tone compared to other studies could be attributed to the specific recovery protocol implemented after hip arthroscopy. The most shared content was about rehabilitation. Rizkalla et al. [15] found a prevalence of 85% for positive tone as a result of the searches made with the hashtag “spine fusion”. The authors reported that there was no significant relationship between positive tone and ADL or between negative tone, pain, and ongoing neurological deficit.

In this study, posts with a positive tone constituted the vast majority (77.9%) and were found to be correlated with posts with ADL and RTS content. Negative posts comprised 22.1% of all posts and were associated with posts related to pain, neurological deficit, and X-ray/MRI. These data should encourage surgeons to proactively rehabilitate patients to return their previous activity level as early as possible. If there is no risk of complications in the early period after the surgery, the patient should be allowed to return to practicing sports in the short term.

Pain control should be provided on a long-term basis with appropriate medical treatment. Surgeons providing one-to-one explanation to patients regarding X-ray and MRI images could help to satisfy the patients’ curiosity and anxiety. It is necessary to take measures to prevent the development of neurological deficits, to maintain a high level of communication with the patient in case any deficits develop, and to patiently pay attention to the necessary surgical/rehabilitation treatments in coordination with the patient and at every stage.

According to a study conducted by Dominy et al. [22], Instagram exhibited the highest percentage of positive posts compared to other social media platforms. This may be due to Instagram’s more visual-focused posts and its special filters, which could increase the attractiveness of the posts. In our study, we observed that posts related to X-ray/MRI, which included visual content, had a negative tone and were associated with pain and neurological deficit. This finding suggests that users may have shared these posts to seek medical advice from their followers. The negative tone in these posts could reflect the users' concerns and the impact of their symptoms on their wellbeing.

In a social media study on Instagram, Holderread et al. [20] found a significant correlation between the incision site and patient satisfaction in cervical disc herniation operations. In contrast, our study did not find a significant relationship between the tone of the posts and the incision site. This discrepancy could be attributed to the visibility and attention drawn to the surgical incision in cervical disc surgeries, which is made in the frontal neck region. In contrast, the incision in lumbar surgeries is typically located in the waist region and is less visible, potentially leading to fewer mentions or discussions related to the incision site in social media posts.

In our study, the majority of the posts (66.9%) were shared after the first week following the surgical procedure. This suggests that patients tended to use Instagram less frequently in the early postoperative period (23.8%) but became more active in sharing their experiences and updates as time progressed. Users’ post-sharing times were found to be compatible with the literature. In a study by Ramkumar et al. [17], 21.8% of posts were shared in the first week after operation, and 71.5% were shared after the first week. This situation may be interpreted as patients avoiding social media in the first week after surgery.

In addition, negative tones were observed to be more common in the first week after surgery. This observation could be attributed to the pain and functional limitations experienced by patients during the early stages of the postoperative period. Additionally, it is noteworthy that posts shared on the anniversary of the surgery accounted for 9.1% of the total, and it is remarkable that all of these posts expressed a positive tone. The evaluation of satisfaction on the anniversary of the surgery among studies on post-operative satisfaction in social media has not been used in previous studies. Evaluation of satisfaction on the anniversary is important in terms of long-term follow-up result.

According to some studies, due to the increasing number of fake accounts, the number of likes per 1000 followers in reliable accounts has been estimated to be approximately 30-140 (3-14%) [23-25]. There is a perception that accounts with posts that are well above or below this rate are unreliable. In our study, the average Instagram like ratio was calculated as 11%. This ratio falls within the “safe limit,” which provides support for the reliability of the posts that were included in our study.

Limitations

One limitation of our study was the absence of information regarding the specific surgical technique employed, such as open, microendoscopic, or percutaneous endoscopic discectomy. Furthermore, the involvement of different operating surgeons introduces a potential factor that may impact the study results. The number of posts was also limited since only publicly accessible accounts were reviewed. Another limitation is the limited number of posts included as we focused on publicly available Instagram posts using a specific set of hashtags related to medical terminology, such as "discectomy" and "lumbar".

This approach may have resulted in the exclusion of a significant number of posts and patients who did not use these specific hashtags or did not use medical jargon in their posts. Consequently, the study sample size was small, which could affect the generalizability of the findings. However, this approach allowed us to obtain a relatively homogeneous group of patients with similar experiences, which could provide valuable insights within the scope of our study objectives. Another limitation is the high tendency of sharing posts with positive tones on Instagram, which may have affected the results. Analyzing social media is a difficult task as users may not regularly post or may post several differing accounts over the course of recovery.

In addition, a certain standardization could be achieved by adding more analysis criteria, such as the interpersonal

manner of the caregiver, the patient's health characteristics, the patient's expectations/preferences, etc. A tool could also be developed to evaluate the patients' satisfaction with specific regard to the spine surgery after passing tests for reliability and validity.

Conclusion

In summary, our study has offered a distinct viewpoint on the satisfaction and experiences of patients who have undergone lumbar discectomy. The majority of the analyzed posts conveyed a positive tone, highlighting a generally positive outlook among patients. However, negative posts were associated with pain and neurological deficit, indicating areas of concern for patient outcomes. The use of social media as a means of evaluating patient perceptions and identifying factors contributing to postoperative dissatisfaction proved to be valuable in our study. This approach sheds light on the potential of social media as a tool for gaining insights into patient experiences and improving surgical care.

References

1. Carr CT, Hayes RA. Social Media: Defining, Developing, and Divining Social Media: Defining, Developing, and Divining. Atl J Commun. 2015;(March):37–41.
2. McLawhorn AS, De Martino I, Fehring KA, Sculco PK. Social media and your practice: navigating the surgeon-patient relationship. Curr Rev Musculoskelet Med [Internet]. 2016;9(4):487–95. Doi: 10.1007/s12178-016-9376-1
3. Baker JF, Devitt BM, Kiely PD, Green J, Mulhall KJ, Synnott KA, et al. Prevalence of Internet use amongst an elective spinal surgery outpatient population. Eur Spine J. 2010;1776–9.
4. Kemp S. Digital 2020 global digital overview. Available at: https://wearesocial.com/blog/2020/01/digital-2020-3-8-billion-people-use-social-media. Accessed March 13, 2021.
5. Alhabash S, Ma M. A Tale of Four Platforms: Motivations and Uses of Facebook, Twitter, Instagram, and Snapchat Among College Students ? Soc Media+Society. 2017;1–13.
6. Griffis HM, Kilaru AS, Werner RM, Asch DA, Hershey JC, Hill S, et al. Use of social media across US hospitals: Descriptive analysis of adoption and utilization. J Med Internet Res. 2014;16(11):1–11.
7. Yan L, Kai Z. Using social media for telemedicine during the COVID-19 epidemic. Am J Emerg Med. 2021;(46):667–8.
8. Erdem MN, Karaca S. Evaluating the accuracy and quality of the information in kyphosis videos shared on youtube. Spine (Phila Pa 1976). 2018;43(22):E1334–9.
9. Menendez JY, Omar NB, Chagoya G, Tabibian BE, Elsayed GA, Walters BC, et al. Patient satisfaction in spine surgery: A systematic review of the literature. Asian Spine J. 2019;13(6):1047–57.
10. Krauss P, Sonnleitner C, Reinartz F, Meyer B, Meyer HS. Patient-Reported Expectations, Outcome and Satisfaction in Thoracic and Lumbar Spine Stabilization Surgery: A Prospective Study. Surgeries. 2020;1(2):63–76.
11. Oliver RL. Effect of expectation and disconfirmation on postexposure product evaluations: An alternative interpretation. J Appl Psychol. 1976;62(4):480–6.
12. Mistry JB, Chughtai M, Elmallah RK, Le S, Bonutti PM, Delanois RE, et al. What Influences How Patients Rate Their Hospital After Total Hip Arthroplasty? J Arthroplasty [Internet]. 2016;31(11):2422–5. Doi: 10.1016/j.arth.2016.03.060
13. Park J, Park J, Ham D, Kwon B, Park S, Kim H, et al. Minimally Invasive Spine Surgery: Techniques, Technologies, and Indications. Asian Spine J. 2020;14(5):694–701.
14. Carragee EJ, Han MY, Suen PW, Kim D. Clinical outcomes after lumbar discectomy for sciatica: The effects of fragment type and anular competence. J Bone Jt Surg. 2003;85(1):102–8.
15. Rizkalla JM, Holderread B, Hotchkiss W, Clavenna A, Dossett A, Ogola G, et al. Instagram and Spine Fusion: An Analysis of Social Media and Its Relationship to Patient Perception of Surgery. Glob Spine J [Internet]. 2021; Available from: https://journals.sagepub.com/doi/pdf/10.1177/21925682211001814
16. Ramkumar PN, Navarro SM, Haeberle HS, Chughtai M, Flynn ME, Mont MA. Social Media and Total Joint Arthroplasty: An Analysis of Patient Utilization on Instagram. J Arthroplasty [Internet]. 2017;32(9):2694–700. Doi: 10.1016/j.arth.2017.03.067
17. Ramkumar PN, La T, Fisch E, Fabricant PD, White AE, Jones KJ, et al. Integrating Social Media and Anterior Cruciate Ligament Surgery: An Analysis of Patient, Surgeon, and Hospital Use. Arthrosc - J Arthrosc Relat Surg [Internet]. 2017;33(3):579–85. Doi: 10.1016/j.arthro.2016.08.021
18. Ramkumar PN, Navarro SM, Cornaghie MM, Haeberle HS, Hameed H, Schickendantz MS, et al. Social Media in Shoulder & Elbow Surgery: An Analysis of Twitter and Instagram. Int J Sports Med. 2018;39(7):564–70.
19. Ng JP, Tarazi N, Byrne DP, Baker JF, Mccabe JP. Scoliosis and the Social Media : Facebook as a Means of Information Exchange. Spine Deform [Internet]. 2017;5(2):102–8. Doi: 10.1016/j.jspd.2016.11.003
20. Holderread B, Botros D, Orozco E, Liu J, Syed IY, Rizkalla J. Instagram and Anterior Cervical Discectomy and Fusion Surgery: An Analysis of Social Media and Its Relationship to Patient Perception of Surgery. Int J Spine Surg. 2022;16(3):581–4.
21. Haeberle HS, Bartschat NI, Navarro SM, Rooney PW, Rosneck J, Westermann RW, et al. Hip Arthroscopy: A Social Media Analysis of Patient Perception. Orthop J Sport Med. 2019;7(6):1–5.
22. Dominy CL, Arvind V, Tang JE, Bellaire CP, Diana S, Jun P, et al. Scoliosis surgery in social media : a natural language processing approach to analyzing the online patient perspective. Spine Deform [Internet]. 2021;(0123456789). Available from: doi: 10.1007/s43390-021-00433-0
23. Eline L. E. De Vries. When more likes is not better: the consequences of high and low likes-to-followers ratios for perceived account credibility and social media marketing effectiveness. Mark Lett. 2019;30(3–4):275–91.
24. De Vries L, Gensler S, Leeflang PSH. Popularity of Brand Posts on Brand Fan Pages: An Investigation of the Effects of Social Media Marketing. J Interact Mark. 2012;26(2):83–91.
25. Erkan I. Electronic Word of Mouth on Instagram: Customers' Engagements with Brands in Different Sectors. Int J Manag Account Econ. 2015;2(12):1435–44.

J Surg Med. 2023;7(12):765-767.
DOI: 10.28982/josam.7451

Journal of Surgery and Medicine
e-ISSN: 2602-2079
https://jsurgmed.com/

Neuropathic arthropathy of the shoulder associated with chronic inflammatory demyelinating polyneuropathy: A case report

Burcu Ortanca, Onur Armağan, Mazlum Doğan Bilici

Department of Physical Medicine and Rehabilitation, Eskişehir Osmangazi University School of Medicine, Eskişehir, Turkey

ORCID ID of the author(s)

BO: 0000-0001-5421-0116
OA: 0000-0002-5917-5839
MDB: 0000-0003-4351-4434

Abstract

Neuropathic arthropathy is a chronic degenerative arthropathy that results from a neurosensory deficit of the affected joint. According to neurovascular theory, the loss of sensation of the joint is responsible for its formation. Chronic inflammatory demyelination polyneuropathy (CIDP) is a rare disease with sensorimotor involvement in which demyelination and axonal damage occur in the peripheral nerves as a result of an abnormal immune response. A case is presented of a 64-year-old male patient with a diagnosis of CIDP who had Charcot arthropathy of the right shoulder.

Keywords: Charcot arthropathy, shoulder, polyneuropathy

Introduction

Neuropathic arthropathy or Charcot joint is a form of chronic degenerative arthropathy that results from neurosensory deficits of the involved joint. Although upper extremity involvement is rare in neuropathic arthropathy, the shoulder joint is usually affected [1]. Shoulder involvement (often called Charcot shoulder) has been reported in 5-6% of all neuropathic arthropathies [2]. Neuropathic arthropathy is often caused by syringomyelia, but other causes include diabetes mellitus, tabes dorsalis, leprosy, peripheral neuropathy, multiple sclerosis, chronic alcoholism, intra-articular steroid injections, gigantism, end-stage renal disease, congenital insensitivity to pain, amyloidosis, meningomyelocele, and myelodysplasia [3,4].

Chronic inflammatory demyelinating polyneuropathy (CIDP) is a rare disease in which an abnormal immune response causes demyelination and axonal damage of peripheral nerves. It characteristically shows slow progressive symmetrical sensorimotor involvement. The exact etiology of CIDP is unknown [5]. Patients with CIDP experience progressive weakness, sensory and motor dysfunction in the legs and arms, decreased deep tendon reflexes (areflexia), and fatigue [6]. The most accepted diagnostic criteria in recent clinical studies are based on clinical history, examination, electrodiagnostic criteria, and exclusion of other causes [7].

Although chronic fatigue, depression, sleep disorders, and respiratory failure related to CIDP have been reported in the literature, no development of neuropathic arthropathy has been found [8]. This report presents a case with neuropathic arthropathy in the shoulder joint due to CIDP. This case is important because it is the first report of Charcot shoulder to develop due to CIDP in the literature.

Corresponding Author
Burcu Ortanca
Department of Physical Medicine and Rehabilitation, Eskişehir Osmangazi University School of Medicine, Odunpazarı, Eskişehir, 26040, Turkey
E-mail: burcu-ayik@hotmail.com

Informed Consent
The authors stated that the written consent was obtained from the patient presented with images in the study.

Conflict of Interest
No conflict of interest was declared by the authors.

Financial Disclosure
The authors declared that this study has received no financial support.

Published
2023 December 16

How to cite: Ortanca B, Armağan O, Bilici MD. Neuropathic arthropathy of the shoulder associated with chronic inflammatory demyelinating polyneuropathy: A case report. J Surg Med. 2023;7(12):765-767.

Case presentation

A 69-year-old male patient was admitted to our clinic due to difficulty in walking, loss of strength in his arms and legs, neuropathic pain, and swelling in the right shoulder that had recurred intermittently since 1 month prior, and restricted movement. The patient was diagnosed with CIDP in 2016. He had a history of coronary artery disease and myocardial infarction. The patient's right shoulder developed bruising and swelling for the first time in January 2019 without pain or trauma. When he visited the orthopedic clinic with this complaint, X-rays indicated that he had a dislocated shoulder (Figure 1 and 2).

The patient had used a shoulder splint for a while and had experienced swelling, bruising, and redness in the right shoulder from time to time without pain, even after the splint was removed. Due to these complaints, the patient visited the orthopedic clinic in February 2021. No malignant cells were found in the histochemical staining of a fluid sample from the right shoulder-joint. Blood analysis was performed, and PET-CT images were taken for a paraneoplastic study. The results showed no pathology suggestive of neoplasm.

Magnetic resonance imaging (MRI) of the shoulder showed humeral head dislocation, areas with significant destruction, and complete rupture of the rotator cuff tendons. A preliminary diagnosis of Charcot arthropathy was considered by the radiologist. Cerebral cervical, thoracic, and lumbar MRIs were performed in February 2021 to examine the etiology of Charcot shoulder but revealed no syrinx cavity, discopathy, or spondylosis findings. The patient was referred to the rheumatology clinic in January 2022 for inflammatory arthritis and vasculitis, but no pathology was found in this regard. The results of a Brucella tube agglutination test were also negative.

In the examination of the patient, the muscle strength was 2/5 in the right shoulder group globally, 2/5 in the hip extensor and abductor, 3/5 in the bilateral hip rotators, 3/5 in the bilateral knee flexors, and 3/5 in the toe group. The strength in other muscles was 4/5. His right shoulder flexion was 80°, abduction was 75°, and internal and external rotations were limited. The patient's deep sense was decreased in all 4 extremities. The patient described bilateral hypoesthesia from the C4 dermatome area. The deep tendon reflex (DTR) was hypoactive in both upper extremities, but DTR could not be obtained in the bilateral lower extremities.

During the patient's hospitalization in our clinic, his blood glucose, biochemistry, hemogram, and acute-phase reactants were normal. The infectious diseases department was consulted for evaluation for infectious causes of the patient's Charcot shoulder, such as tabes dorsalis or Lyme disease). The patient also consulted the neurology department to undergo lumbar puncture (LP), and electromyography (EMG) was planned.

ARB, Gram staining, direct microscopy, cerebrospinal fluid (CSF) biochemistry, syphilis VDRL, and Lyme PCR analyses were performed. No pathology was detected in the results. The anti-HIV test came back negative. Infectious pathology was not considered according to the anamnesis and examination results of the patient. The results were reexamined by the infectious diseases department. EMG showed axonal type sensorimotor polyneuropathy with prominent diffuse sensory and motor involvement in the lower extremity, and the result supported the diagnosis of CIDP. A physical therapy program including electrotherapy and strengthening exercises was provided to the patient. Information was given about protective measures for the shoulder joint. Informed consent form was obtained from the patient for presentation.

Figure 1: X-ray image of the shoulder

Figure 2: X-ray image of the shoulder

Discussion

Neuropathic arthropathy of the shoulder is rarely seen, and the etiology can include peripheral neuropathies that result from pathologies such as syringomyelia, syphilis, diabetes, chronic alcoholism, and leprosy [9]. The neuropathic joint undergoes 3 phases. In the destructive phase, the joint is hyperemic and swollen, and there is osteoclastic bone resorption associated with repetitive trauma. The reparative phase continues with the formation of dense fibrous tissue and coalescence of debris. Finally, the silent phase is characterized by decreased vascularity and bone sclerosis [10].

The pathogenesis is not fully understood, but two different theories have been proposed: neurovascular and

neurotraumatic theories. According to the neurovascular theory, loss of sensation at the joint level impairs normal neurovascular reflexes. This results in osteoclast activation, which causes hyperemia and bone resorption. According to the neurotraumatic theory, the loss of somatic muscle reflexes that maintain the range of motion of the joint causes repetitive traumas. As a result, joint destruction occurs [4,11].

The most common initial symptoms of neuropathic shoulder arthropathy are swelling, redness, decreased range of motion, and loss of function. Considering the symptoms, septic arthritis, synovial chondromatosis, idiopathic osteolysis, tumoral calcinosis, and neoplasia (soft tissue sarcoma) should also be considered in the differential diagnosis [12,13]. In the present case, shoulder joint biopsy had been performed previously in the orthopedic clinic to aid in differential diagnosis, and no neoplasm or synovial chondromatosis was detected.

Radiological findings in neuropathic arthropathy include sclerosis, joint destruction, new bone formation, bone fragmentation, subluxation, osteophytes, osseous debris, effusion, heterotopic ossification, and periarticular soft-tissue swelling in the involved joint [14]. Radiographically specific findings for Charcot shoulder include superomedial flattening of the humeral head, periarticular soft tissue calcification, and glenoid sclerosis [15]. In the present case, radiological findings were consistent with neuropathic arthropathy in the shoulder X-ray. Despite the significant joint destruction, the absence of pain and sensory deficit in neurological examination, normal follow-up of acute phase reactants and white blood cell count, advanced stage destructive arthropathy findings in radiological imaging, and sensorimotor polyneuropathy detected in EMG were compatible with neuropathic arthropathy.

Cervical syringomyelia is the cause of 75% of neuropathic arthropathies in the shoulder [13]. Cases have been reported in which Charcot shoulder developed due to diabetes, chronic alcoholism, intra-articular steroid injection, and congenital painlessness syndrome [4]. In the present case, no syrinx cavity was found in cervical MRI, and there was no history of diabetes, alcoholism, or steroid injections. The literature showed no case of neuropathic arthropathy of the shoulder developing with CIDP etiology as in our case.

Physical therapy, effusion aspiration, nonsteroidal anti-inflammatory drugs, immobilization, and a shoulder sling can be applied as conservative treatments for neuropathic arthropathy of the shoulder [9,12]. If there is no response to conservative treatments, shoulder hemiarthroplasty, total shoulder arthroplasty, glenohumeral arthrodesis, arthroscopic irrigation, and debridement can be applied as surgical treatments [12]. In our clinic, electrotherapy, exercises to protect the range of motion, and isometric strengthening exercises were used to treat the patient's shoulder.

Conclusion

Sensory nerve damage in CIDP may predispose patients to the development of neuropathic arthropathy. The reason is that sensory deficit in the related joint causes the development of neuropathic arthropathy by disrupting the neurovascular reflex according to neurovascular theory. Although neuropathic shoulder arthropathy is a rare disease, it should not be ignored as it may develop in patients with a diagnosis of CIDP. We think that careful evaluation of patients' joints is important for early diagnosis and treatment.

References

1. Jones EA, Manaster BJ, May DA, Disler DG. Neuropathic osteoarthropathy: diagnostic dilemmas and differential diagnosis. Radiographics. 2000 Oct;20 Spec No:S279-93. doi: 10.1148/radiographics.20.suppl_1.g00oc22s279.
2. Xu DY, Cao LB, Liu C, Zhan AL, Feng WH. Neuroarthropathy. Clinico-radiologic analysis of 115 cases. Chin Med J (Engl). 1992 Oct;105(10):860-5.
3. Alpert SW, Koval KJ, Zuckerman JD. Neuropathic Arthropathy: Review of Current Knowledge. J Am Acad Orthop Surg. 1996 Mar;4(2):100-8. doi: 10.5435/00124635-199603000-00005.
4. Yanik B, Tuncer S, Seçkin B. Neuropathic arthropathy caused by Arnold-Chiari malformation with syringomyelia. Rheumatol Int. 2004 Jul;24(4):238-41. doi: 10.1007/s00296-003-0389-x.
5. Mathey EK, Park SB, Hughes RA, Pollard JD, Armati PJ, Barnett MH, Taylor BV, Dyck PJ, Kiernan MC, Lin CS. Chronic inflammatory demyelinating polyradiculoneuropathy: from pathology to phenotype. J Neurol Neurosurg Psychiatry. 2015 Sep;86(9):973-85. doi: 10.1136/jnnp-2014-309697.
6. Broers MC, Bunschoten C, Nieboer D, Lingsma HF, Jacobs BC. Incidence and Prevalence of Chronic Inflammatory Demyelinating Polyradiculoneuropathy: A Systematic Review and Meta-Analysis. Neuroepidemiology. 2019;52(3-4):161-72. doi: 10.1159/000494291.
7. Van den Bergh PY, Hadden RD, Bouche P, Cornblath DR, Hahn A, Illa I, et al. European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society-first revision. Eur J Neurol. 2010 Mar;17(3):356-63. doi: 10.1111/j.1468-1331.2009.02930.x.
8. Bromberg MB. What is in the Literature. J Clin Neuromuscul Dis. 2021 Jun 1;22(4):200-8. doi: 10.1097/CND.0000000000000371.
9. Snoddy MC, Lee DH, Kuhn JE. Charcot shoulder and elbow: a review of the literature and update on treatment. J Shoulder Elbow Surg. 2017 Mar;26(3):544-52. doi: 10.1016/j.jse.2016.10.015.
10. Eichenholtz SN. Charcot joints. Springfield, IL: Charles C Thomas; 1966.
11. Brower AC, Allman RM. Pathogenesis of the neurotrophic joint: neurotraumatic vs. neurovascular. Radiology. 1981 May;139(2):349-54. doi: 10.1148/radiology.139.2.7220879.
12. Rickert MM, Cannon JG, Kirkpatrick JS. Neuropathic Arthropathy of the Shoulder: A Systematic Review of Classifications and Treatments. JBJS Rev. 2019 Oct;7(10):e1. doi: 10.2106/JBJS.RVW.18.00155.
13. Kenan S, Lewis MM, Main WK, Hermann G, Abdelwahab IF. Neuropathic arthropathy of the shoulder mimicking soft tissue sarcoma. Orthopedics. 1993 Oct;16(10):1133-6. doi: 10.3928/0147-7447-19931001-09.
14. Norman A, Robbins H, Milgram JE. The acute neuropathic arthropathy--a rapid, severely disorganizing form of arthritis. Radiology. 1968 Jun;90(6):1159-64. doi: 10.1148/90.6.1159.
15. Sackellares JC, Swift TR. Shoulder enlargement as the presenting sign in syringomyelia. Report of two cases and review of the literature. JAMA. 1976 Dec 20;236(25):2878-9.