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Research Article

Comparison of traditional and next-generation oral anticoagulants in the etiology of epistaxis

Traditional and novel anticoagulants in epistaxis

Süheyla Kandemir, Hüseyin Kandemir

159-162

Surveying dentistry students' perspectives on anatomy education: A questionnaire-based study

Survey of anatomy education among dentistry students

Nazire Kılıç Şafak, Hüseyin Erdem

163-167

Case Report

Genetic testing, a challenge to kidney biopsy? A case report

Genetic testing in persistent proteinuria

Behcet Simsek

168-171

Synovial hemangioma localized in the knee joint and diagnosed in adulthood: MRI findings and surgical treatment

Synovial hemangioma: MRI and surgery

Emrah Akay , Fatih Erdem , Bahar Yanık , Aziz Atik , Erdoğan Bülbül , Gülen Demirpolat

172-174

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Comparison of traditional and next-generation oral anticoagulants in the etiology of epistaxis

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Ethics Committee Approval
The study was approved by the Ethics Committee of Kırıkkale University Faculty of Medicine, decision dated March 29, 2023 and numbered 2023.03.04.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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No conflict of interest was declared by the authors.

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Abstract

Background/Aim: There is a dearth of studies addressing the effects of next-generation anticoagulants on epistaxis. The aim of this investigation was to determine whether there are any differences between traditional and next-generation anticoagulants in the etiology of epistaxis.
Methods: This retrospective cohort study focused on a total of 7,110 individuals (3,278 females (46.1%) and 3,832 males (53.9%)) diagnosed with epistaxis between 2018 and 2022; the mean age of the patients was 37.7 years. Patient data (age, gender, outpatient and inpatient treatments, relevant laboratory parameters, and treatment evidence) were retrospectively reviewed from a hospital database. The severity of epistaxis was assessed based on treatment notes. Patients with hypertension and those undergoing antiaggregant therapy were excluded from the study. International Classification of Diseases (ICD) codes from the automated system were examined retrospectively. The data were used to establish three patient groups: the first group consisted of individuals taking next-generation oral anticoagulants, the second group consisted of individuals taking traditional oral anticoagulants, and the third group consisted of healthy controls.
Results: We found statistically significant differences among the groups in terms of age, the severity of epistaxis, the treatment modality, and laboratory findings (P<0.001); no statistically significant difference was found in terms of gender (P=0.954). Group 2 contained the largest number of hospitalized patients and patients with severe active nosebleeds.
Conclusion: Next-generation anticoagulants are more reliable than traditional anticoagulants in terms of the severity of epistaxis, the need for hospitalization, and laboratory results.

Keywords: epistaxis, anticoagulants, warfarin, rivaroxaban, dabigatran

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Introduction

Epistaxis is a common otolaryngological problem that affects approximately 60% of the general population [1]. Medical treatment is required for about 6% of cases, and hospitalization is necessary for fewer than 0.2% of cases [2,3]. The majority of nosebleeds (90–95%) originate from the anterior region; the remaining cases derive from the posterior region [4]. While there are several risk factors for epistaxis, including allergic rhinitis, trauma, hypertension, anticoagulant use, bleeding disorders, seasonal factors, and sinonasal tumors, the most common cause (accounting for 38–40% of cases) is idiopathic (i.e., spontaneous bleeding without a clear trigger) [5-7]. Topical vasoconstrictors and nasal compression are usually effective at controlling most cases of epistaxis [8]. In severe cases, anterior or posterior nasal packing, electrical or medical cautery, or a balloon catheter may be used. In rare cases, surgical interventions such as embolization or endoscopic ligation may be necessary [9].

Patients with epistaxis who use anticoagulant drugs, particularly for associated cardiovascular diseases, often experience frequent nosebleeds due to their long-term treatment. The use of next-generation anticoagulants (NOAC) and traditional anticoagulants (COAC) is increasing in this patient population [8].

The aim of this study was to determine the demographic characteristics of patients with epistaxis, identify the risk factors for outpatient and inpatient treatment, assess the severity of epistaxis, systematically review laboratory parameters and treatment evidence, and compare the differences between NOAC and COAC.

Materials and methods

Participants and study design

This retrospective cohort study was conducted between 2018 and 2022 at Kırıkkale Yüksek İhtisas hospital. Patients diagnosed with epistaxis were identified via the hospital's automated system. We retrospectively analyzed the patients' clinical information, as determined by their physicians using International Classification of Diseases (ICD) codes. The hospital's information technology personnel assisted in amassing the relevant data, which were transferred to an Excel spreadsheet using specific filters. The ICD code R04 (epistaxis) was required. In addition to code R04, diagnostic codes I48 (atrial fibrillation and flutter) and Z95.2 (heart valve prosthesis) were used to identify patients using NOAC and COAC. Patients diagnosed with R04+I10 (hypertension) were excluded from the study. We defined three patient groups: the first group consisted of NOAC users, the second group consisted of COAC users, and the third group consisted of healthy controls. Demographic characteristics (age, gender) and outpatient and inpatient treatments, laboratory parameters (if available), and evidence regarding treatment were recorded. Patients who received antiplatelet treatment (such as acetylsalicylic acid, clopidogrel, or ticlopidine) and patients whose files could not be accessed were excluded from the study.

Anticoagulant treatments

Anticoagulant therapy is used to prevent thromboembolic events. Warfarin, a classic anticoagulant derived from vitamin K, requires regular blood tests to monitor international normalized ratios (INRs). Low INR levels increase the risk of thromboembolic events, and high INR levels can cause bleeding. Warfarin also has many interactions with other drugs and food. Therefore, NOAC, including direct thrombin inhibitors (e.g., dabigatran etexilate) and direct factor Xa inhibitors (e.g., rivaroxaban and apixaban), have been developed in recent years. These agents are increasingly replacing warfarin because they do not require laboratory monitoring and have shown equivalent or superior efficacy in preventing systemic embolism or stroke in high-risk populations [10-12]. Laboratory parameters (especially INR) were obtained from the hospital's automated records system; patients without laboratory parameters were excluded from the study.

Epistaxis severity

Patients were classified into one of three groups based on the severity of their epistaxis:

1. No active bleeding or only occasional bleeding.
2. Active bleeding that stopped with an intervention in the outpatient clinic.
3. Severe active bleeding requiring hospitalization and cauterization in an operating room.

To determine these groups, the patients were first divided into inpatient and outpatient groups based on hospital data. The nasal mucosa of hospitalized patients was cauterized, and the operation code was scanned to determine the patients belonging to group 3. The outpatient procedure code for cauterization of the nasal mucosa was scanned to determine patients belonging to group 2. Patients in group 1 included individuals who were seen in the outpatient clinic but did not undergo any procedures.

The study was approved by the Kırıkkale University Faculty of Medicine Ethics Committee (decision dated March 29, 2023, number 2023.03.04). Given that this study was a retrospective file review, written informed consent was not obtained from the patients. All procedures were conducted in accordance with ethical guidelines and the principles of the Declaration of Helsinki.

Statistical analysis

SPSS version 25.0 (IBM Corp., Armonk, NY, USA) was used for the statistical analysis. Frequencies (number, percentage) were provided for categorical variables, while descriptive statistics (mean [standard deviation]) were given for numerical variables. The normality of the data was assessed using normal distribution parameters and the Shapiro-Wilk test. Nominal categorical variables were compared using the chi-squared test and Fisher's exact test. Non-parametric variables were analyzed using the Mann-Whitney U test and the Kruskal-Wallis test. A significance level of $P < 0.05$ was used.

Results

A retrospective search of Kırıkkale Yüksek İhtisas hospital database revealed 7,110 individuals with epistaxis. The mean age of the patients was 37.7 (24.3) years. Of those patients, 3,278 (46.1%) were female and 3,832 (53.9%) were male.

Group 1 consisted of 211 patients using NOAC (3.0% of the patient cohort), group 2 consisted of 303 patients using COAC (4.3% of the patient cohort), and group 3 (the control group) consisted of 6,596 patients not using anticoagulants (92.8% of the patient cohort).

Slightly more than half of the patients (4,473; 62.9%) did not have active bleeding when they were admitted to the hospital.

The mean age of those patients was 34.1 (23.1) years. On the other hand, 2,591 patients (36.4%) had active bleeding upon admission; the mean age of that cohort was 43.6 (24.9) years. Severe epistaxis was present in 46 patients upon admission (0.6%); that group had a mean age of 59.2 (28.2) years.

Nearly all of the patients (7,063; 99.3%) were treated as outpatients; 47 patients (0.7%) were treated as inpatients. The mean age of the outpatients was 37.6 (24.2) years; the mean age of the inpatients was 59.5 (28.0) years.

Laboratory parameters were not measured in 5,244 patients (73.8%); they were measured in 1,866 patients (26.2%). Among the patients for whom laboratory parameters were measured, 1,733 (24.4%) had values within the normal range; 133 (1.9%) had values outside the normal range.

Statistical analysis revealed a significant difference between the groups in terms of age, severity of epistaxis, treatment modality, and laboratory findings (P<0.001). However, no statistically significant difference was found in terms of gender (P=0.954) (Table 1). Severe active epistaxis was most common in group 2 (41.3% of patients), and patients with active bleeding upon admission more commonly belonged to group 2 rather than group 1 (Table 2). Inpatients were most frequently in group 2 (Table 3).

Table 1: Patient demographic and clinical features

Parameter	Group 1 (NOAC) (n=211)	Group 2 (COAC) (n=303)	Group 3 (Control) (n=6596)	*P*-value
Age, years, Mean (SD)	77.9 (5.3)	79.2 (7.1)	34.5 (22.2)	<0.001
Gender, female/male, n	99/112	138/165	3041/3555	0.954
Epistaxis severity, no active bleeding/there is active bleeding/active bleeding is severe, n	151/49/11	177/107/19	4145/2435/16	<0.001
Laboratory parameter, not checked/normal/ abnormal, n	154/38/19	188/93/22	4902/1602/92	<0.001
Treatment, outpatient/inpatient, n	200/11	283/20	7063/47	<0.001

Bold values indicate statistical significance. NOAC: New generation oral anticoagulant, COAC: Classical oral anticoagulant

Table 2: Epistaxis severity in groups

Epistaxis severity		Group 1 (NOAC)	Group 2 (COAC)	Group 3 (Control)	Total
No active bleeding	Count	151	177	4145	4473
	% within	3.4%	4.0%	92.7%	62.91%
There is active bleeding	Count	49	107	2435	2591
	% within	1.9%	4.1%	94.0%	36.44%
Active bleeding is severe	Count	11	19	16	46
	% within	23.9%	41.3%	34.8%	0.64%
Total	Count	211	303	6596	7110
	% within	3.0%	4.3%	92.8%	100.0%

NOAC: New generation oral anticoagulant, COAC: Classical oral anticoagulant

Table 3: Treatment in groups

Treatment		Group 1 (NOAC)	Group 2 (COAC)	Group 3 (Control)	Total
Outpatient	Count	200	283	6580	7063
	% within	2.8%	4.0%	93.2%	99.3%
Inpatient	Count	11	20	16	47
	% within	23.4%	42.6%	34.0%	0.66%
Total	Count	211	303	6596	7110
	% within	3.0%	4.3%	92.8%	100.0%

NOAC: New generation oral anticoagulant, COAC: Classical oral anticoagulant

Discussion

Epistaxis is a common emergency in otolaryngology that accounts for approximately 0.5% of total emergency admissions and 25–30% of ENT emergencies [13,14]. The condition can range from minor bleeding that can be stopped with simple interventions to life-threatening bleeding [15]. Previous studies have shown that epistaxis is more common in men than in women [16]. Our study found a similar distribution, with 53.9% of cases occurring in men and 46.1% occurring in women.

As life expectancy increases, the prevalence of chronic diseases, including prothrombotic conditions, also increases. There is a consequent uptick in the usage of antithrombotic drugs, particularly among older individuals [17,18]. The use of anticoagulants has been identified as a risk factor for epistaxis in numerous studies [19,20]. New oral anticoagulants, such as factor Xa inhibitors (e.g., rivaroxaban, apixaban) and direct thrombin inhibitors (e.g., dabigatran), have gained popularity due to their shorter half-lives and ease of discontinuation [21,22]. The introduction of a next generation of oral anticoagulants over the past decade has significantly increased awareness of the complexity of managing nosebleeds in antithrombotic therapy settings. In our study, patients had a history of using next-generation anticoagulants such as direct-factor Xa inhibitors (rivaroxaban and apixaban) and thrombin inhibitors (dabigatran). They also used warfarin as a classical anticoagulant. Up to 17% of all predicted epistaxis cases in the general population involve anticoagulant use [23,24]. In our study, we observed the use of both NOAC and COAC, with an overall rate of anticoagulant use of 7.2%.

Some studies have reported that anticoagulant use is both an etiological factor for epistaxis and something that increases its recurrence rate [25]. However, other studies have found no increased risk in patients using new oral anticoagulants compared with the general population [20]. Additionally, hospital stays have been found to be shorter for patients receiving NOAC therapy compared with patients receiving vitamin K-derived anticoagulation therapy [26]. In another study, Sauter et al. [27] showed that NOAC recipients actually had lower hospitalization rates. There is evidence suggesting that the risk of bleeding events, including epistaxis, is significantly lower in patients using NOAC compared with COAC [28,29]. While Send et al. [30] found similar bleeding severity and results with NOAC compared with COAC, Gökdoğan et al. [29] noted that it was more difficult to control bleeding in patients taking NOAC. Other studies have reported a lower rate of hospitalization in patients taking NOAC compared with patients taking COAC [26,27]. Yaniv et al. [31] determined that next-generation oral anticoagulants are safer than older anticoagulant/antiplatelet drugs in terms of severity of bleeding, the need for hospitalization and length of hospital stay. Our study found that severe active nosebleeds and inpatient treatment were most common in the group of patients using COAC.

Routine coagulation studies are not necessary for all patients presenting with epistaxis; the exception is children and individuals using warfarin [32-34]. However, patients using warfarin and patients whose nosebleeds do not respond to local treatment should have their INR levels checked [35,36]. In our study, laboratory parameters were evaluated in only 26.2% of patients, and the majority of these patients had normal values.

Overall, our study provides valuable insights into the characteristics and management of epistaxis. However, follow-on research is necessary to explore the specific effects of different anticoagulant therapies on the severity and outcomes of epistaxis.

Limitations

This study has several limitations. Firstly, the data collection was retrospective and only based on what was recorded in the hospital's automated system. Secondly, the data were collected from a single institution, which limits the generalizability of the findings. Thirdly, although the number of patients included in the study was sufficient, the control group constituted a significant portion of the study population. Therefore, future prospective studies should be conducted to validate our results.

Conclusion

Our findings indicate that NOAC are more reliable than COAC in terms of the severity of epistaxis, the need for hospitalization, and laboratory results. These results suggest that patients using NOAC have a lower hospitalization rate and can be managed with a more conservative approach.

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Surveying dentistry students' perspectives on anatomy education: A questionnaire-based study

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Ethics Committee Approval
The study was approved by the Çukurova University Non-Interventional Clinical Research Ethics Committee, February 23, 2024, 141. 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.

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Abstract

Background/Aim: Anatomy plays a crucial role in medical and dental education, equipping students with vital knowledge for comprehending the human body and its clinical implications. The COVID-19 pandemic led to a significant transition to online learning, raising questions about the efficacy of virtual anatomy education. Additionally, recent natural disasters like earthquakes have disrupted traditional learning settings, highlighting the need for alternative methods such as online instruction. This study sought to investigate dentistry students' opinions on anatomy education, specifically comparing the perspectives of students affected by earthquakes with those who were not, to determine any disparities in their attitudes towards online anatomy courses.

Methods: A voluntary survey was conducted on 135 first-year students at Çukurova University Faculty of Dentistry during the 2023-2024 academic year. A 5-point Likert-type survey with 21 questions was used for data collection. Results were presented as percentages and analyzed. The Likert scale ranged from 1 = Strongly Disagree to 5 = Strongly Agree. Statistical analysis was performed using SPSS 20.0, including Kolmogorov-Smirnov and Shapiro-Wilk Tests for normal distribution assessment and the Mann-Whitney U-test for non-normally distributed scores comparison (P-value <0.05).

Results: Students directly affected by earthquakes showed a significant difference in their perception of online education compared to unaffected students, particularly in the question "Theoretical anatomy course can be followed online" (P=0.036).

Conclusion: This study provides insights for enhancing education planning and development based on student feedback.

Keywords: anatomy, online education, survey

Introduction

Dentistry education has a long history, initially integrated into medical education before evolving into a distinct discipline. Anatomy plays a crucial role in the foundational courses of the curriculum [1] and is universally recognized as a key component of medical education [2]. The study of anatomy, which explores the structure, function, and spatial relationships within the human body, forms the basis for clinical sciences, aiding in the accurate interpretation of patient symptoms and facilitating proper physical examinations in clinical settings [3,4]. A comprehensive understanding of anatomy is essential for diagnosing and treating diseases [5]. Effective learning methods are vital for grasping anatomy concepts thoroughly and accurately, with visualization and spatial ability playing key roles in understanding the intricate organization of the human body [6,7]. Traditional modalities such as didactic learning, cadaveric dissection, and the use of anatomical models are commonly employed in anatomy education [8]. Cadaveric dissection remains the most effective method due to its provision of real tissue information and depth perception [6]. However, the COVID-19 pandemic necessitated a shift to distance education in medical schools worldwide, impacting various areas, including anatomy education [9].

As the educational disruptions caused by the pandemic were beginning to subside, two powerful earthquakes struck on February 6, 2023, with magnitudes of 7.7 and 7.6 centered in Gaziantep Şehitkamil-Sofalarca and Kahramanmaraş Ekinözü, respectively [10]. Subsequently, a state of emergency was declared in the most affected cities to expedite search and rescue efforts [11], leading to the postponement of the spring term in universities [12]. Following this, students were granted the option of attending face-to-face classes alongside the ongoing distance education starting in April [13]. The earthquakes significantly disrupted anatomy education, traditionally reliant on methods like cadaveric dissection [14]. While distance education during the pandemic was challenging and concerning for both educators and students, it became a necessary adaptation for earthquake-affected students [15].

Feedback from students is crucial for improving education, fostering better communication between faculty and students, and addressing learning challenges [2]. This survey aims to explore dentistry students' perspectives on Anatomy education in the post-earthquake period and assess potential differences in opinions on online anatomy courses between students directly impacted by the earthquakes and those who were not.

Materials and methods

A survey was conducted on 135 first-year students at Çukurova University Faculty of Dentistry during the 2023-2024 academic year on a voluntary basis. The survey underwent a reliability analysis. Student identities and any information that could reveal their identities were not requested to ensure unbiased results. Approval was obtained from the Çukurova University Non-Interventional Clinical Research Ethics Committee on February 23, 2024 (Approval No. 141). The survey comprised 21 questions and did not include any influencing or guiding factors that could impact responses. The average completion time for the 5-point Likert-type survey, which included demographic information and opinions on anatomy, was approximately 6 minutes. The survey questions focused on anatomy education, online learning, and face-to-face instruction. Additionally, students were asked if they had experienced an earthquake in one of the 11 cities most affected by earthquakes.

The results of the survey, presented on a 5-point Likert scale, were analyzed and expressed as percentages. The responses were collected and analyzed as percentages due to the survey format. The frequency distribution of categorical responses and the scoring of answers were both included in the analysis. The 5-point Likert scale ranged from 1 = Strongly Disagree to 5 = Strongly Agree.

Statistical analysis

Data analysis was performed using IBM SPSS V20. Normal distribution was assessed using Kolmogorov-Smirnov and Shapiro-Wilk Tests. For non-normally distributed data, the Mann-Whitney U-test was utilized to compare between two groups, with a significance level set at $P < 0.05$.

The reliability of the survey questions was evaluated using Cronbach's Alpha Coefficient, yielding a value of 0.756, indicating good reliability.

A limitation of this study is the reliance on self-reported data from a single university cohort, resulting in a small sample size. Due to variations in educational practices during earthquakes across different universities, the questionnaire could not be administered to other institutions.

Results

A total of 135 dentistry faculty students participated in the study voluntarily, with 55 males (40.7%) and 80 females (59.3%). The mean age of the participants was 19.31 (0.94) years, ranging from 17 to 22 years.

Of the participants, 114 (84.4%) directly experienced the February 6, 2023 earthquakes in cities under a state of emergency, while 21 individuals (15.6%) did not. Following the earthquakes, 64.4% of the participants received face-to-face education, while 35.6% received online education. Among the students from earthquake-affected cities, 30.7% continued online education, and 69.3% continued face-to-face education.

On average, students spent 3.31 (2.83) hours per week studying anatomy, ranging from 0 to 20 hours. Men reported studying for 3.3 hours per day, while women studied for 3.28 hours per day. The majority of students (89.6%) chose to study dentistry voluntarily, while 10.4% did not (Table 1).

Table 1: Demographic characteristics of students and non-Likert questions

	Frequency (n)/Mean (SD)	Percentage (%)/median (min. - max.)
Sex		
Male	55	40.7
Female	80	59.3
Age	19.31 (0.94)	19 (17 - 22)
Experiencing the February 6 earthquakes		
Yes	114	84.4
No	21	15.6
Did you choose to follow classes online or face-to-face in the Spring Semester after the earthquakes?		
Online	48	35.6
Face-to-face	87	64.4
Anatomy study time per week (Hours)	3.31 (2.83)	3 (0 - 20)
Choosing the faculty on your own will		
Yes	121	89.6
No	14	10.4

SD: Standard deviation, min: minimum, max: maximum

Table 2: Descriptive statistics of survey question responses

	I totally disagree		I disagree		I am undecided		I agree		I totally agree		Mean (SD)	Median (min.-max.)
	n	%	n	%	n	%	n	%	n	%		
Theoretical anatomy course can be followed online.	25	18.5	30	22.2	24	17.8	43	31.9	13	9.6	2.92 (1.29)	3.00 (1.00-5.00)
Anatomy practical course can be followed online.	37	27.4	45	33.3	18	13.3	18	13.3	17	12.6	2.50 (1.35)	2.00 (1.00-5.00)
Online education may be an option in cases of necessity.	8	5.9	9	6.7	18	13.3	70	51.9	30	22.2	3.78 (1.06)	4.00 (1.00-5.00)
If online education was an option, I would choose it.	23	17.0	34	25.2	32	23.7	32	23.7	14	10.4	2.85 (1.25)	3.00 (1.00-5.00)
Online education can be useful for us not to waste time.	17	12.6	26	19.3	28	20.7	45	33.3	19	14.1	3.17 (1.26)	3.00 (1.00-5.00)
Anatomy is very important for medical education.	8	5.9	0	0.0	4	3.0	50	37.0	73	54.1	4.33 (1.00)	5.00 (1.00-5.00)
I enjoy studying anatomy.	6	4.4	12	8.9	48	35.6	50	37.0	19	14.1	3.47 (0.99)	4.00 (1.00-5.00)
I have a hard time studying anatomy.	5	3.7	10	7.4	33	24.4	53	39.3	34	25.2	3.75 (1.03)	4.00 (1.00-5.00)
Theoretical anatomy courses interest me.	7	5.2	20	14.8	38	28.1	54	40.0	16	11.9	3.39 (1.04)	4.00 (1.00-5.00)
Anatomy practical lessons interest me.	9	6.7	11	8.1	36	26.7	60	44.4	19	14.1	3.51 (1.05)	4.00 (1.00-5.00)
The number and duration of theoretical lessons are sufficient.	7	5.2	18	13.3	29	21.5	54	40.0	27	20.0	3.56 (1.11)	4.00 (1.00-5.00)
The number and duration of practical lessons are sufficient.	14	10.4	22	16.3	33	24.4	43	31.9	23	17.0	3.29 (1.23)	3.00 (1.00-5.00)
Cadaver training is required.	6	4.4	7	5.2	15	11.1	41	30.4	66	48.9	4.14 (1.09)	4.00 (1.00-5.00)
Educational videos are useful.	5	3.7	3	2.2	18	13.3	60	44.4	49	36.3	4.07 (0.96)	4.00 (1.00-5.00)
Anatomy models (dummies) are useful.	7	5.2	7	5.2	9	6.7	57	42.5	54	40.3	4.07 (1.07)	4.00 (1.00-5.00)
I use social media while studying anatomy.	5	3.7	6	4.5	23	17.2	61	45.5	39	29.1	3.92 (0.99)	4.00 (1.00-5.00)
I can easily reach my instructors to ask questions.	8	6.0	13	9.7	46	34.3	42	31.3	25	18.7	3.47 (1.09)	3.50 (1.00-5.00)
I study anatomy by myself.	5	3.7	15	11.2	23	17.2	57	42.5	34	25.4	3.75 (1.07)	4.00 (1.00-5.00)
I study anatomy with my friends.	14	10.5	12	9.0	20	15.0	54	40.6	33	24.8	3.60 (1.25)	4.00 (1.00-5.00)

SD: Standard deviation, min: minimum, max: maximum; Cronbach's alpha coefficient=0.756

Table 3: Comparison results based on earthquake experience

	Experiencing the February 6 earthquakes				Test statistics	*P*-value
	Yes		No			
	Mean (SD)	Median (min.-max.)	Mean (SD)	Median (min.-max.)		
Theoretical anatomy courses can be followed online.	3.02 (1.28)	3.00 (1.00-5.00)	2.38 (1.24)	2.00 (1.00-5.00)	861.000	**0.036**
Practical anatomy courses can be followed online	2.54 (1.37)	2.00 (1.00-5.00)	2.29 (1.27)	2.00 (1.00-5.00)	1079.000	0.459
Online education may be an option in cases of necessity.	3.80 (1.02)	4.00 (1.00-5.00)	3.67 (1.24)	4.00 (1.00-5.00)	1164.500	0.830
If online education was an option, I would choose it.	2.88 (1.26)	3.00 (1.00-5.00)	2.71 (1.23)	3.00 (1.00-5.00)	1107.500	0.577
Online education can be useful for us not to waste time.	3.23 (1.24)	3.00 (1.00-5.00)	2.86 (1.31)	3.00 (1.00-5.00)	1003.500	0.226
Anatomy is very important for medical education	4.31 (1.01)	5.00 (1.00-5.00)	4.48 (0.98)	5.00 (1.00-5.00)	1036.500	0.273
I enjoy studying anatomy.	3.44 (1.00)	3.00 (1.00-5.00)	3.67 (0.97)	4.00 (2.00-5.00)	1047.500	0.339
I have a hard time studying anatomy.	3.74 (1.06)	4.00 (1.00-5.00)	3.81 (0.93)	4.00 (2.00-5.00)	1196.500	0.997
Theoretical anatomy courses interest me.	3.40 (1.03)	4.00 (1.00-5.00)	3.29 (1.15)	3.00 (1.00-5.00)	1123.000	0.637
Anatomy practical lessons interest me.	3.47 (1.06)	4.00 (1.00-5.00)	3.71 (1.01)	4.00 (1.00-5.00)	1043.500	0.323
The number and duration of theoretical lessons are sufficient.	3.57 (1.14)	4.00 (1.00-5.00)	3.52 (0.98)	4.00 (2.00-5.00)	1134.500	0.692
The number and duration of practical lessons are sufficient.	3.25 (1.26)	3.00 (1.00-5.00)	3.48 (1.03)	4.00 (2.00-5.00)	1094.500	0.522
Cadaver training is required.	4.16 (1.11)	4.50 (1.00-5.00)	4.05 (1.02)	4.00 (2.00-5.00)	1089.500	0.480
Educational videos are useful.	4.02 (0.98)	4.00 (1.00-5.00)	4.38 (0.80)	5.00 (2.00-5.00)	927.500	0.078
Anatomy models (dummies) are useful.	4.03 (1.10)	4.00 (1.00-5.00)	4.33 (0.91)	5.00 (2.00-5.00)	983.500	0.180
I use social media while studying anatomy.	3.86 (1.03)	4.00 (1.00-5.00)	4.24 (0.62)	4.00 (3.00-5.00)	973.000	0.163
I can easily reach my instructors to ask questions.	3.4 (1.06)	3.00 (1.00-5.00)	3.38 (1.24)	4.00 (1.00-5.00)	1153.000	0.831
I study anatomy by myself.	3.73 (1.04)	4.00 (1.00-5.00)	3.81 (1.25)	4.00 (1.00-5.00)	1094.000	0.551
I study anatomy with my friends.	3.67 (1.22)	4.00 (1.00-5.00)	3.24 (1.37)	3.00 (1.00-5.00)	947.500	0.140

SD: Standard deviation, min: minimum, max: maximum; *Mann-Whitney U-test

The survey responses regarding anatomy education were analyzed using a 5-point Likert scale, with the frequency distribution and mean values presented in Table 2.

A significant difference was found in the opinion that "Theoretical anatomy course can be followed online" between students who experienced the earthquakes and those who did not (*P*=0.036). The median score for students who experienced the earthquakes was 3.00, compared to 2.00 for those who did not. No other significant differences were observed in the responses. Detailed information on P-values can be found in Table 3.

The comparison of responses between students who experienced the earthquakes and those who did not is detailed in Table 3, showing a significant difference in the perception of online education, particularly for the question "Theoretical anatomy course can be followed online" (*P*=0.036).

Discussion

The significant earthquakes that occurred on February 6, 2023, had a profound impact on various sectors, including education. The educational process was disrupted due to housing issues and inadequate learning conditions in the earthquake-affected cities [17]. Distance education, which gained prominence during the COVID-19 pandemic, revealed certain limitations in global studies assessing its outcomes [15]. The concept of social distancing in education dates back to the early 20th century when open-air classrooms were introduced to prevent the spread of infections during the tuberculosis epidemic. The first application of distance education through correspondence occurred in 1918 during the Spanish flu pandemic, followed by radio lecture broadcasts at Pennsylvania State College in 1922 [18]. Countries affected by previous epidemics like SARS and MERS had also experimented with web-based education [19,20]. Turkey initiated online education in medical training during the COVID-19 crisis [21]. Subsequently, in response to the consecutive earthquakes on February 6, 2023, online education was regionally implemented in our country, leading to the transition of the 2023 spring semester to online platforms [10,12].

Distance education offers advantages such as flexibility in time and space, easy access to course content, and cost-effectiveness due to the absence of physical classroom requirements. However, it also presents challenges like the lack of direct supervision for students struggling with discipline and the inability to provide immediate face-to-face responses to queries [22]. Practical anatomy education, in particular, necessitates physical settings for students to observe and interact with anatomical structures on cadavers and models, fostering active learning through discussions with peers in a physical environment [23]. The impact of distance education extends beyond academic realms, affecting socialization and stakeholder analysis, which require long-term evaluation. Furthermore, the enduring effects of remote anatomy education on professional and academic development warrant thorough investigation through surveys to establish a feedback mechanism [24].

Studies conducted with medical students have highlighted the inadequacy of online theoretical and practical anatomy courses for medical training [25]. Student feedback on distance anatomy education has indicated lower efficiency compared to traditional methods, emphasizing the need for curriculum enhancements to optimize distance learning outcomes [23]. While distance education offers benefits such as flexibility and time savings, a significant proportion of students still prefer face-to-face instruction, underscoring the importance of tailored curricula based on student feedback [26]. Instructors have also expressed concerns about the efficacy of distance education compared to traditional methods, particularly in practical anatomy education [24]. Student surveys have revealed mixed opinions on the effectiveness of distance education for anatomy courses, with a consensus emerging on the necessity of face-to-face instruction for practical components and professional skill development [27].

The ongoing debate between online and traditional education methods underscores the importance of adapting educational approaches to evolving circumstances. While traditional methods like dissections and models provide visual orientation for anatomy learning, the COVID-19 pandemic has necessitated the integration of online education, prompting calls for its enhancement and development [14]. Comparative studies have shown varying outcomes between face-to-face and blended learning methods, with blended learning demonstrating higher course success rates attributed to improved online course delivery and self-directed study opportunities [28]. The optimal approach to anatomy education involves a blend of traditional and remote methods, leveraging synchronous and asynchronous online tools to enhance learning outcomes [29].

Student perspectives on online education during the pandemic have highlighted challenges such as technical issues and lack of self-motivation, underscoring the need for continuous improvement in digital learning platforms [30]. Studies have also indicated a decrease in anatomy study time among students during the pandemic, emphasizing the importance of maintaining engagement and motivation in remote learning environments [31]. Student feedback has been instrumental in shaping the future of anatomy education, with calls for a balanced approach that combines traditional and online methods to maximize learning outcomes [32].

Conclusion

In conclusion, the integration of online education in response to natural disasters and disruptions underscores the need for continuous improvement and adaptation in educational practices. Student feedback plays a crucial role in shaping the evolution of anatomy education, guiding curriculum enhancements and technological advancements. While online education presents challenges for practical anatomy courses, it remains a valuable resource in emergency situations. By leveraging technological innovations such as 3D technologies and augmented virtual reality, anatomy education can be further enhanced to provide a comprehensive and engaging learning experience. Continuous evaluation and refinement of online education platforms based on student input are essential for ensuring the effectiveness and relevance of anatomy education in the digital age.

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Genetic testing, a challenge to kidney biopsy? A case report

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Abstract

The field of genetic testing has experienced significant growth in medical practice since 1956, when the first genetic analysis was introduced. Persistent proteinuria has long been considered a strong risk factor for the progression of chronic renal failure, though, paradoxically, it can also be a benign process, as seen in individuals with mutations in the cubilin (CUBN) protein, specifically the C-terminal. CUBN is a peripheral protein that plays a crucial role in the receptor-mediated endocytotic reabsorption of albumin in the proximal tubule. In the past, there have been misinterpretations of CUBN variants with isolated proteinuria as glomerular injury, leading to unnecessary kidney biopsies and ineffective treatments. This paper discusses two siblings with a homozygous variant of (p.Tyr3018Ser) in the C-terminal of the CUBN protein, inherited from both heterozygous carrier parents. This case presents an opportunity to question our typical approach to proteinuria in an effort to avoid unnecessary kidney biopsies and the subsequent side effects of treatments, particularly for those with proteinuria.

Keywords: cubilin, proteinuria, albuminuria, p.Tyr3018Ser, genetic testing, kidney biopsy, children

Introduction

Genetic analysis in the field of cytogenetics began when Tjio and Levan reported the correct number of human chromosomes in 1956. From this point onwards, genetic testing has grown at a rapid pace in medical practice. Currently, genetic testing is available for over 2000 genetic conditions, including kidney diseases, at affordable prices [1-3].

Persistent proteinuria, especially albuminuria, is known to be a significant risk factor for the progression of chronic kidney disease (CKD) [4]. The main cause of proteinuria is a defect in the glomerular filtration barrier, possibly combined with dysfunction in proximal tubular protein reabsorption. As such, kidney biopsies have long been recommended, primarily to exclude glomerular diseases in children with persistent proteinuria before initiating a proteinuria-lowering treatment [5].

However, recent publications suggest that not all forms of proteinuria may be destructive, particularly in cases exhibiting albuminuria due to the diminished function of cubilin (CUBN) [5-7]. Follow-up studies on such cases show that isolated proteinuria, caused by mutations in the CUBN gene, is benign and does not negatively impact the long-term prognosis of kidney function [5-7].

CUBN, encoded by the CUBN gene, is a 460 kDa peripheral protein that forms the uptake receptor complex in the proximal tubule. This complex is constituted of transmembrane proteins, megalin, and amnionless, with an N-terminal of 110 amino acids, eight EGF-like domains, and 27 CUB domains [5]. A limited amount of albumin, filtered from the glomerulus, is physiologically reabsorbed via receptor-mediated endocytosis, a process dependent on CUBN in the proximal tubule [5,6].

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

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Uncovering genetic risk factors through prompt genetic analysis may encourage clinicians to revise traditional strategies used for diagnosing and treating underlying disorders of proteinuria. Could genetic analysis be a viable challenge in questioning the need for a kidney biopsy and the initiation of empirical immune-suppressive treatment in chronic proteinuria?

In this context, we present two siblings with a homozygous variant (p.Tyr3018Ser) on the 22nd domain of the CUBN's C-terminal. These siblings come from a nuclear family in which both parents are heterozygous carriers, although there is no consanguinity. The aim is to instigate a debate about the classical approach to proteinuria.

Case presentation

Admittedly, we obtained written parental consent in advance to share the medical history of her sons in a medical article or any medical discussion context.

Initial presentation

Patient A, a boy who recently turned 13, was consulted for incidentally detected 2+ proteinuria during a urine analysis. There was neither a family history of proteinuria nor any kidney disease, nor was there any consanguinity between his parents. Upon the initial check, no clinical manifestations were observed. Additionally, both ophthalmologic and hearing examinations showed no significant abnormalities.

Laboratory results

Kidney function was normal, with a serum creatinine of 0.55 mg/dl. Plasma albumin level was 4.6 g/dl. Urinary protein was 0.54 g/24 h. Complete blood count (CBC), immunologic data (Complement 3 (C3), 1.77 g/L (N: 0.86–1.82 g/L) and complement 4 (C4), 0.35 g/L (N: 0.17–0.51 g/L), ANA (-), anti-dsDNA-10.33 IU/ml (N:<100 IU/ml)). However, CRP was 3.4 mg/L (N: 0.0–5.0 mg/L). Urine protein electrophoresis revealed that albumin-64.38% (N: 55.8–66.1%), α1-%4.27 (N: 2.9–4.9%), α2-8.95% (N: 7.1–11.8%), β1-5.92% (N: 4.7–7.2%), β2- 3.43% (N: 3.2–6.5%),γ-13.04% (N: 11.1–18.8%). A urinary ultrasound examination showed normal kidneys and a normal urinary system.

Clinical course

In the subsequent 3 months, urinary protein excretions varied between 0.5 and 4 g/day (Table 1). A renal biopsy was performed when the patient presented with severe proteinuria over the nephrotic range (>4 g/day) and mild hypoalbuminemia, exhibiting a serum albumin of 3.1 g/dl, in addition to mild to moderate general edema. The pathological examination of the kidney specimen disclosed minor changes in glomeruli with prominent podocytes, with no immunological staining observed. Electron microscopy demonstrated minimal irregularities in the basal membrane and a slight increase in the mesangial matrix; the epithelium and capillary walls were intact (Figure 1). Given the severe proteinuria, the possibility of Minimal Change Disease was excluded. Consequently, immune-suppressive treatment with prednisone and the renin-angiotensin-aldosterone system blocker Ramipril was initiated while waiting for the biopsy results. Over a 10-week period, there was no response to the treatment. The clinical presentation indicated a steroid-resistant process, which was bolstered by the recent discovery of ++ proteinuria without hypoalbuminemia in the patient's younger sibling. The immune-suppressive treatment was then discontinued, while Ramipril was continued in consideration of a potentially genetically transmitted disorder. The elevated level of proteinuria was expected to decrease spontaneously over time. Currently, the boy is 16 years old and has lived for 3 years post-diagnosis. The most recent tests showed urine protein, creatinine, and serum albumin levels of 0.35 g/day, 0.47 mg/dl, and 4.1 g/dl, respectively.

Patient B, the younger brother, was first diagnosed with 2+ proteinuria at the age of 5 during a family examination. Despite the diagnosis, he had no complaints or significant abnormalities in his blood biochemical data or clinical findings. A kidney biopsy was not considered necessary. Thus, no treatment was initiated. At the time of writing this report, his latest serum albumin level was noted to be 4.4 g/dl, with his serum creatinine at 0.39 mg/dl and urine protein at 0.15 g/d.

Following the detection of proteinuria (++ level) in a younger boy during family screening, genetic testing was conducted for both siblings and their parents. No pathologic variant was identified in the COL4A3, COL4A4, or COL4A5 genes using Next Generation Sequencing (NGS) to analyze for Alport syndrome in the boys. However, the homozygous variant "NM_001081.4(CUBN):c.9053A>C (p.Tyr3018Ser)" was found upon performing Sanger sequencing in both patients, with each parent exhibiting a heterozygous variant.

Figure 1: Minor irregularities in basal membrane and a mild increase in mesangial matrix with intact epithelium and capillary walls.

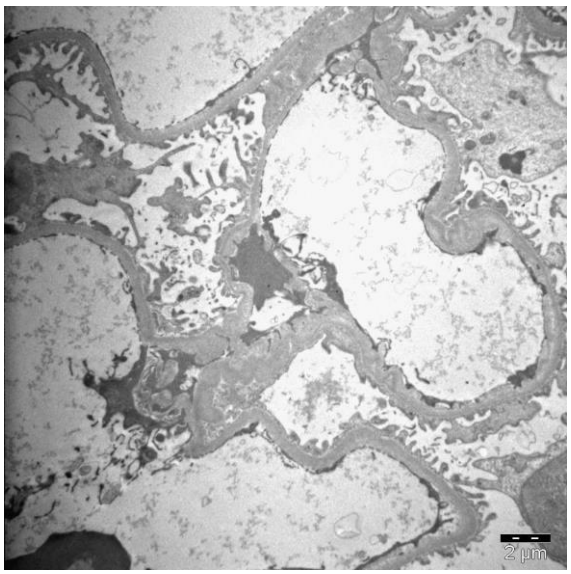

Table 1: Summary of the chronologic clinical record of the family.

	Patient A	Patient B	Mother	Father
1st admission-3months	(++) proteinuria Upr=0.5-4 g/d N serum Alb N RF	(+/++) proteinuria N serum Alb N RF	Clinically N No proteinuria	Clinically N No proteinuria
3months-1st year	(++++) proteinuria Upr=4g/d Serum Alb=3.1g/dl N RF Biopsy (minor changes)	(+/++) proteinuria Nserum Alb N RF	Clinically N No proteinuria	Clinically N No proteinuria
1st-2nd year	(+/++) proteinuria N serum Alb N RF	(+/++) proteinuria N serum Alb N RF	Clinically N No proteinuria	Clinically N No proteinuria
2nd-3rd year	(+/++) proteinuria N serum Alb N RF	(+/++) proteinuria N serum Alb NRF	Clinically N No proteinuria	Clinically N No proteinuria
3rd year-	(+/++) proteinuria N serum Alb N RF	(+/++) proteinuria N serum Alb N RF	Clinically N No proteinuria	Clinically N No proteinuria

Upr: Urine Protein, N: Normal, Alb: Albumin, RF: Renal function

Discussion

Proteinuria has long been recognized as a clinical sign of kidney injury, which can alert clinicians to a potential risk of progression to chronic kidney disease. However, there is limited information on whether all forms of proteinuria are harmful to patients. The primary cause of proteinuria involves disorders of the glomerular filtration barrier, in conjunction with a newfound possibility for harmless effects stemming from defects in proximal tubular protein reabsorption [5,8].

Plasma proteins, chiefly albumin, undergo size-selective glomerular filtration, followed by tubular reabsorption in the proximal tubule through receptor-mediated endocytosis, allowing normal urine to be protein-free. The concentration of albumin in the glomerular ultrafiltrate is reported to be 1 to 50 g/ml, and it is reabsorbed in the initial proximal tubule regardless of the amount under physiological conditions [8]. The uptake receptor complex comprises transmembrane proteins, namely megalin (LRP2) and amnionless (AMN), and a peripheral protein, CUBN, which could be the main albumin receptor in the proximal tubules [5,9,10]. Each CUBN protomer has 8 EGF domains and 27 CUB (complement C1r/C1s, UEGF [EGF-related sea urchin protein] and bone morphogenic protein 1) domains [5]. Unlike mutations mostly in the N-terminal and those in the Vitamin B12/intrinsic factor-binding (IF-binding) CUB domains 5–8, which cause Imerslund-Gräsbeck syndrome (IGS), the variants after the Vitamin B12/intrinsic factor-binding domain result in albuminuria, highlighting that C-terminal CUB domains are crucial for tubular protein reabsorption, without impairing renal filtration function [5,10]. The cases presented here possessed a homozygous p.Tyr3018Ser mutation on the 22nd domain, which is located in the C-terminal, similar to previous cases with isolated proteinuria due to CUBN variants in published cohorts [5–7,11].

Yet, there have been reports claiming that proteinuria was not associated with an unfavorable prognosis, thus preventing chronic kidney disease [5,6,9]. Bedin et al. [5] revealed that high urinary albumin was often misinterpreted as glomerular injury in patients in their cohort, leading to unnecessary kidney biopsies and subsequent protein-lowering treatments despite the presence of clinically benign CUBN variants. Accordingly, they argued that detecting CUBN variants could help avoid inefficient therapies and invasive procedures, particularly when diagnosing cases with subnephrotic proteinuria [5]. We concur with Bedin's claim, considering the favorable prognosis observed in the two siblings with minor changes in kidney biopsy presented here after a three-year follow-up. Likewise, we recommend that genetic testing be considered well before a biopsy in children with persistent proteinuria to avoid both unnecessary procedures and ineffective treatments.

Since Ovunc et al. [7] first reported two patients with proteinuria due to mutations in the CUBN genes, over 60 cases have been reported worldwide, with c.9053A>C being the most frequently mutated locus, as in the family presented here. Diagnoses of CUBN-mediated proteinuria typically occur in childhood, with an average age of 4 to 10.9 years at clinical diagnosis in different cohorts [5,11]. The male-female ratio was 3:2 [6]. Consistent with previous data, the patients presented herein were both males, ages 13 and 5.

The CUBN domains provide ligand binding sites for various proteins, particularly for the intrinsic factor-vitamin B12 complex and albumin, thereby facilitating their intestinal and renal absorption. The albumin binding site is exclusively the C-terminal structural domain, located subsequent to CUBN domains 5-8, where the intrinsic factor-vitamin B12 complexes bind [5,6]. In the cases presented herein, the mutation occurs in the C-terminal, with no corresponding vitamin B12 deficiency or loss of renal function, consistent with findings already documented in the literature.

While proteinuria due to mutations in CUBN genes is usually subnephrotic, Ovunc et al. [7] reported two cases with intermittent nephrotic-range proteinuria. In cohorts where albuminuria is caused by C-terminal variants in the *CUBN* gene, kidney function has been reported to be preserved for over 7 years or until adulthood [5,11]. A common thread in diverse cohorts with persistent proteinuria due to CUBN mutations has been a benign course with normal kidney biopsy results and preserved kidney function over time despite a lack of response to treatment. In the siblings presented here, renal function has been individually maintained for over 3 years despite ongoing mild proteinuria and no response to Angiotensin-converting enzyme inhibitors (ACE) inhibitors and steroids.

The use of genetic testing has become more common recently, especially in patients with unexplained proteinuria, revealing more information about etiology and prognosis prediction [5,11]. Sanger sequencing is used to classify variants in the CUBN gene, following guidelines from the American College of Medical Genetics and Genomics and the Association for Molecular Pathology (ACMG/AMP) [12]. In cohorts of proteinuria secondary to CUBN gene mutations, the diagnostic power of a renal biopsy was negligible compared to genetic testing. In these cases, the results were either normal or showed minimal lesions, as was the case presented here [5,7,11].

In this regard, I argue that not all forms of isolated proteinuria are originally damaging to the glomeruli but might be benign, similar to cases with CUBN variants. Hence, the initial detection of CUBN variants through genetic testing can prevent unnecessary renal punctures and ineffective therapies, which may bring side effects besides leading to a diagnosis. I strongly propose that the typical approach of nephrologists to isolate proteinuria needs to be reevaluated for potential updates. Considering genetic testing as an initial step before contemplating a renal biopsy or starting treatment in patients with isolated subnephrotic proteinuria could be a more judicious approach unless there are atypical clinical scenarios such as nephrotic syndrome or deteriorating kidney function.

Patient perspective

The family has always been cooperative and eager to receive a proper diagnosis. They have formed a positive relationship with the clinician in charge of their care throughout the follow-up period.

Conclusion

In conclusion, isolated persistent proteinuria may not always indicate a glomerular disorder with a high risk for a poor prognosis, which would justify a kidney biopsy. Instead, it could potentially have a benign nature. Genetic testing, such as Sanger sequencing, challenges the traditional approach to persistent

proteinuria. It argues for its prioritized use before considering a biopsy because it promises to prevent unnecessary procedures and pointless treatments that could have potential side effects.

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Synovial hemangioma localized in the knee joint and diagnosed in adulthood: MRI findings and surgical treatment

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Abstract

Synovial hemangioma is a rare vascular issue that can lead to persistent knee swelling and bleeding within the joint. It is typically seen in children and young adults but can also affect those in older age groups. Because the symptoms and x-ray results are not specific, it is often diagnosed late. Magnetic Resonance Imaging (MRI) is the best process for identifying and understanding the characteristics of synovial hemangioma. The recommended treatments are surgical removal and partial synovectomy, both of which offer good outcomes and minimal chance of recurrence. We discuss a case of a 48-year-old man with synovial hemangioma in the knee joint. His symptoms included swelling, pain, and restricted movement. His medical history included regular drainage of persistent knee swelling. An MRI highlighted typical features of synovial hemangioma, such as enlarged veins, looped or linear patterns, and greater visibility under gadolinium. He underwent a successful open surgery with partial synovectomy and mass removal. The pathology report confirmed the diagnosis of synovial hemangioma. Post-surgery, the patient had no complications and showed significant symptom reduction and better movement range 6 months later.

Keywords: synovial hemangioma, knee joint, recurrent effusion, hemarthrosis, MRI, surgical excision

Introduction

Synovial hemangioma, a kind of vascular malformation, is often identified in early childhood. It can be an uncommon cause of recurring knee effusions. Though it rarely affects the joint, it is relatively common in the limbs. Most people with this condition are young and commonly experience symptoms such as restricted mobility, discomfort, localized pain, and hemarthrosis. Diagnosing this condition can be challenging, as many clinical, laboratory, and radiographic tests often yield imprecise results, leading to prolonged diagnostic uncertainty [1]. In the past, various preoperative diagnostic methods, including computed tomography (CT) scans, angiography, ultrasonography, and plain-film radiography, have had varying success rates. Lately, however, MRI has become the preferred method for analyzing hemangiomas and determining their extent [2]. Here, we present a case of a delayed diagnosis of synovial hemangioma in an adult patient.

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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.

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Case presentation

A 48-year-old male patient came to the orthopedic and traumatology clinic, reporting pain, swelling, a sense of fullness, and limited movement in his left knee. He had received frequent treatments for recurrent knee fluid build-up. The physical exam revealed enlarged superficial veins in his left lower leg, as well as swelling and decreased mobility in his left knee. Despite these symptoms, his knee x-ray did not show any significant findings. To better understand the issue, he was sent to the radiology department for an MRI.

The MRI indicated an ovoid mass, approximately 40 × 15 × 16 mm in size, located at the medial suprapatellar recess. This mass, filled with enlarged venous structures, was consistent with a synovial hemangioma (Figure 1). It appeared to be connected to the enlarged superficial veins, which suggested drainage veins. Other than this, the MRI showed the patient's knee ligaments, menisci, and cartilages were normal.

Subsequently, the patient had open surgery featuring a partial synovectomy to remove the vascular formation. Using a parapatellar external approach, the surgeon made a skin incision medial to the patellar tendon. The lesion was excised broadly to prevent any chance of recurrence (Figure 2). The final pathology report confirmed the diagnosis of synovial hemangioma.

Post-surgery, an MRI showed no remaining lesion (Figure 3). There were signs of enhancement along the synovium due to surgery-related trauma, and the presence of surgical materials led to paramagnetic artifacts. The patient's postoperative period was without complications. It was advised that he begin moving as soon as possible after surgery, with the aim of fully bearing weight within 30 days.

Over the following 6 months, the patient's symptoms noticeably improved thanks to the surgery and physiotherapy. He regained nearly full range of movement in his knee. Written consent for the procedures was obtained from the patient.

Figure 1: In the fat-suppressed T1-weighted sagittal image (a), fat-suppressed postcontrast T1-weighted coronal image (b), fat-suppressed proton density sagittal image (c), and fat-suppressed T2-weighted coronal image (d), synovial hemangioma (arrows) consisting of dilated venous structures with medium-high signal in T1WI, high signal in T2WI, showing contrast enhancement is seen in the suprapatellar fat pad.

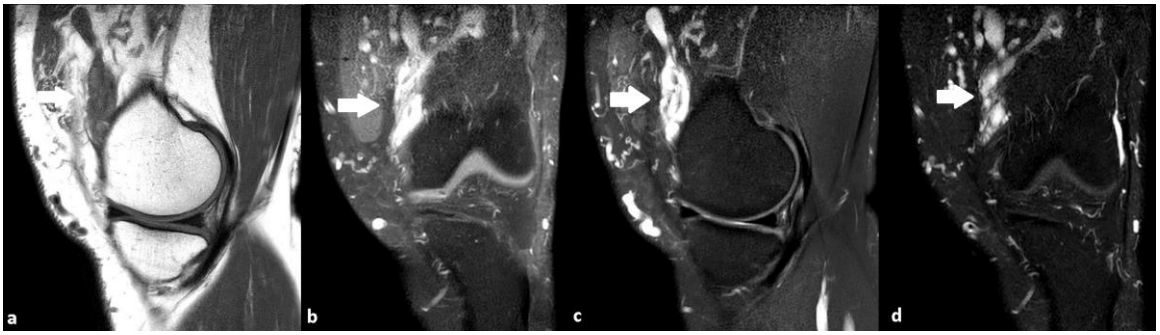


Figure 2: Synovial hemangioma excision and partial synovectomy operation after parapatellar incision.

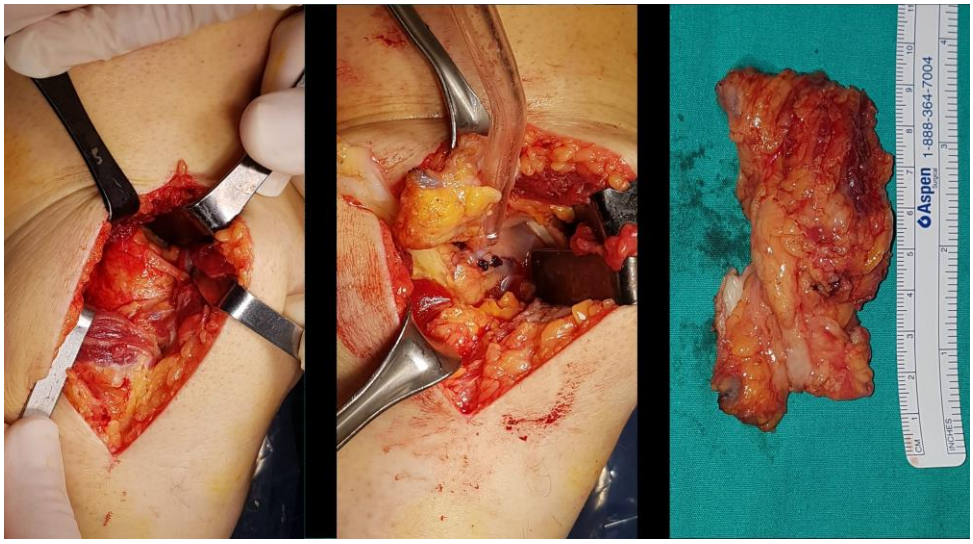
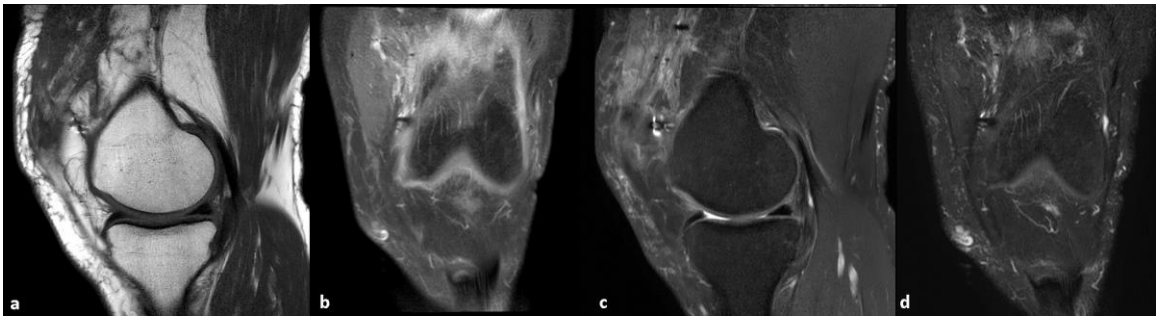


Figure 3: In postoperative fat-suppressed T1-weighted sagittal image (a), fat-suppressed postcontrast T1 weighted coronal image (b), fat-suppressed proton density sagittal image (c), and fat-suppressed T2-weighted coronal image (d), postoperative changes are seen. Residual tumor was not seen.



Discussion

Diagnosing a knee joint hemangioma is difficult despite its distinctive symptoms. It commonly affects teenagers or young adults and may be responsible for recurrent spontaneous knee joint hemarthrosis [1]. Typically, a patient with this condition may have experienced painful, recurring, non-traumatic bloody knee effusions since childhood. When there are recurrent spontaneous hemarthroses in the knee joint and normal coagulation markers, a synovial hemangioma should be considered as a potential diagnosis. However, many instances present nonspecific symptoms, leading to years passing before an accurate diagnosis is made [3]. Regarding our case, the patient had a history of recurrent effusions, but it was unclear if these effusions were bloody.

The diagnostic significance of patients' radiographs is often diminished, given that more than half are normal. However, under specific conditions, they could reveal a soft tissue density, suggesting a joint effusion or tumor. These radiographs might also display phleboliths or amorphous calcifications, seen as definitive indicators of disease. A small fraction of patients – less than 5% – showcase early epiphyses maturation, osteoporosis, periosteal reaction, disproportioned leg length, or even hemophilia-like arthropathy [3,4].

To evaluate the size and range of a soft tissue lesion, MRI is more effective than CT due to its increased tissue contrast. It is now predominantly used to detect synovial lesions and devise treatment plans [4]. On T1-weighted imaging, synovial hemangiomas typically present intermediate to high signal intensity due to the presence of intra-tumoral fat or blood products. The lesion appears brighter on T2-weighted imaging than fat, a sign of stagnant blood in vascular spaces [4,5]. Because of the histological nature of synovial hemangioma, both T1 and T2-weighted images usually display lace-like or linear patterns [3,6].

Post intravenous gadolinium administration, the signal intensity escalates, aiding in differentiating them from muscle. These characteristic MRI features of a synovial hemangioma were also evident in our case's lesion. If there is associated joint effusion, it is advisable to use a contrast medium to distinguish the hemangioma from the unenhanced intra-articular fluid. The differential diagnosis should primarily include synovial sarcoma, pigmented villonodular synovitis and other arthropathies such as juvenile chronic arthritis, rheumatoid arthritis, synovial osteochondromatosis, hemophilic arthropathy or lipoma arborescence, typically identified via clinical MRI [3].

These lesions cannot be classified as varicose vessels or aneurysms due to the absence of typical histologic layers found in actual vessel walls. More likely, they are hamartomas rather than true tumors. Past treatment methods have ranged from radiation and synovectomy to mass excision, the use of sclerosing agents, cautery, freezing, and hot water. Surgical excision and partial synovectomy have shown consistently positive results when removal can be effectively confirmed [1,3]. Radiation therapy should be reserved for cases where surgical excision is not feasible. For contained lesions, total excision is suggested, while for widespread ones, a combination of radiation therapy and synovectomy seems most beneficial [1]. To reduce the risk of cartilage damage, immediate treatment is preferable [3]. In this study, the patient showed improvements in range of motion, less knee joint discomfort, and no signs of cartilage loss 6 months after surgery.

Conclusion

Synovial hemangioma is a rare condition primarily diagnosed in children and young adults, typically affecting the knee joint. Its uncommon nature and vague symptoms can lead to delayed diagnosis. For prompt and accurate diagnosis, MRI is recommended. The optimal treatment depends on the size of the lesion and the feasibility of complete removal.

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