

How to manage a congenital heart defect in a patient with thrombocytopenia-absent radius syndrome?

Hande İřtar, Buęra Harmandar

Department of Cardiovascular Surgery, Muęla Sıtkı Koęman University Medical Faculty, Muęla, Turkey

ORCID  of the author(s)

Hİ: <https://orcid.org/0000-0002-7150-0171>
BH: <https://orcid.org/0000-0002-7487-1779>

Abstract

Ventricular septal defect (VSD) can be repaired using cardiopulmonary bypass, resulting in a favorable postoperative outcome with minimal bleeding. Thrombocytopenia-absent radius (TAR) syndrome is rare, occurring in approximately 0.42 out of 100,000 live births. This syndrome is characterized by hypomegakaryocytic thrombocytopenia and bilateral absent radii. TAR syndrome can be life-threatening within the first 14 months of life due to severe bleeding. In this report, we present the case of a 4-month-old male patient diagnosed with both VSD and TAR syndrome. We describe the surgical management of the VSD as well as the perioperative treatment for hemorrhagic diathesis.

Keywords: thrombocytopenia-absent radius syndrome, TAR syndrome, ventricular septal defect, infant

Introduction

Thrombocytopenia-absent radius (TAR) syndrome is characterized by thrombocytopenia, along with specific skeletal abnormalities primarily affecting both upper limbs. It was initially described by Hall et al. [1] in 1969 as a condition characterized by thrombocytopenia, bilateral absence of the radius bones, and the presence of both thumbs. This exceedingly rare syndrome is associated with a high risk of severe hemorrhage due to significant thrombocytopenia, with a platelet count of less than $50 \times 10^9/L$ during the first year of life. Here, we present an uncommon association between TAR syndrome and congenital heart surgery, detailing our perioperative management of the patient.

Corresponding Author

Hande İřtar
Department of Cardiovascular Surgery, Muęla Sıtkı Koęman University Medical Faculty
Muęla, Turkey
E-mail: handeistar@yahoo.com

Informed Consent

The authors stated that the written consent was obtained from the parents of 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

2024 April 20

Copyright © 2024 The Author(s)



This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License 4.0 (CC BY-NC-ND 4.0) where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission.



Case presentation

A 4-month-old male patient weighing 4.3 kg, previously diagnosed with ventricular septal defect (VSD) and TAR syndrome, was referred to our clinic due to a cardiac murmur. During the physical examination, we observed syndactyly of digits 1–4 on both hands and low-set ears bilaterally. Furthermore, bilateral absence of the radii was noted, along with varus angulation of the metacarpal bones in relation to the ulna and diminutive second and third metacarpal bones on the left hand (Figure 1). The lower extremities appeared normal. A cardiac examination revealed a grade 2/6 murmur on the left parasternal side. The VSD was classified as perimembranous, and no additional heart defects were detected via a two-dimensional echocardiogram. The patient had previously received a TAR syndrome diagnosis based on physical findings and had been hospitalized every two weeks since birth for thrombocyte replacement due to a platelet count of less than $50 \times 10^9/L$. Upon admission, laboratory results showed a platelet count of $48,000/mm^3$ and a hemoglobin level of 9 g/dL. The size of the platelets appeared normal. Genetic analysis confirmed the diagnosis of TAR syndrome, revealing an interstitial microdeletion in 1q21.1 and a hypomorphic *RBM8A* allele. Informed consent was obtained from the patient's relatives.

Figure 1: Specific deformities on both hand and absence of radii in TAR syndrome.



VSD repair using cardiopulmonary bypass (CPB) is typically performed at the age of 4 months. However, considering the patient's fluctuating platelet count, we anticipated challenges in managing perioperative hemorrhage. Therefore, we opted to initially perform pulmonary banding to reduce pulmonary blood flow and delay the VSD repair until the platelet count increased. One hour before the operation, the patient received a 15 mL/kg platelet suspension through a peripheral catheter, resulting in a platelet count exceeding $100 \times 10^9/L$. Arterial and central venous catheters were inserted, and the procedure was performed via sternotomy following standard protocols. Postoperatively, an additional 15 mL/kg platelet suspension was administered at the 5th hour. The patient received a low dose of an inotropic agent and exhibited postoperative drainage of 30 mL on the first day. By the second postoperative day, the platelet count reached $65 \times 10^9/L$, and the total drainage was 40 cc. Consequently, the mediastinal tube was removed on this day. Routine thrombocyte infusions were administered to mitigate bleeding complications, and the

patient was successfully extubated on the third postoperative day, with a platelet count consistently above $50 \times 10^9/L$. Steroids were not required to improve the platelet count. Unfortunately, the patient developed catheter-related sepsis on the fifth postoperative day, leading to septicemia and subsequent demise on the eighth postoperative day.

Discussion

TAR syndrome is an extremely rare genetic disorder characterized by hypo-megakaryocytic thrombocytopenia and radial aplasia or hypoplasia in both thumbs, as described by Hall et al. [1]. This condition impairs the maturation of megakaryocyte progenitor cells in the bone marrow, resulting in hypo-megakaryocytic thrombocytopenia. Various biological and molecular studies conducted on TAR syndrome have indicated elevated levels of the cytokine thrombopoietin (TPO) and suboptimal differentiation of megakaryocyte progenitor cells in response to TPO *in vitro*, suggesting a potential defect in the TPO signaling pathway [2]. Most TAR syndrome patients develop thrombocytopenia within the first week of life, with approximately 95% of cases being diagnosed within the initial 4 months of life and exhibiting platelet counts typically below $50 \times 10^9/L$ [2]. Initially, thrombocytopenia tends to be severe (less than $30 \times 10^9/L$), but the platelet count gradually increases over time and reaches near-normal levels by 1–2 years of age [3]. The severity of thrombocytopenia correlates with symptoms such as petechial rash and bleeding. Severe spontaneous hemorrhagic events, most commonly in the brain, gastrointestinal tract, or other organs, are the leading cause of mortality in these patients. However, major hemorrhages are predominantly observed during the first 2 years of life [4].

Patients diagnosed with TAR syndrome may exhibit facial dysmorphism, macrocephaly, renal malformations, and skeletal abnormalities. It is important to investigate the presence of additional cardiac defects, such as atrial septal defect, VSD, tetralogy of Fallot, patent ductus arteriosus, and atrioventricular septal defect [4,5]. While there are limited case reports discussing TAR syndrome in conjunction with heart surgery, Kumar et al. [4] described a rare association between TAR syndrome and tetralogy of Fallot. They reported a successful surgical repair in a 3-month-old male patient in their study. However, the authors did not provide detailed information regarding postoperative drainage in the case report.

Conclusion

During heart surgery, the use of cardiopulmonary bypass (CPB) and heparin can lead to thrombocyte dysfunction and increased bleeding tendency in the general population. However, there is limited information in the literature regarding managing congenital heart defects in patients with TAR syndrome [4]. Given our understanding of TAR syndrome and its associated complications, we anticipated that performing VSD repair under CPB could result in higher-than-expected postoperative bleeding due to thrombocyte dysfunction. Therefore, we opted for a palliative procedure, specifically pulmonary banding, which involves a sternotomy but not a complete repair under CPB with heparin. This approach was chosen to minimize bleeding risks. Despite the unfortunate outcome of sepsis in our patient, we believe that adopting a conservative procedure offers maximum

safety in terms of bleeding for patients with congenital heart defects and TAR syndrome who undergo surgery within their first 1.5 years of life.

References

1. Cowan J, Parikh T, Waghela R, Mora R. Thrombocytopenia with absent radii (TAR) syndrome without significant thrombocytopenia. *Cureus*. 2020;12:e10557. doi: 10.7759/cureus.10557.
2. Roberts I, Stanworth S, Murray NA. Thrombocytopenia in the neonate. *Blood Rev*. 2008;22:173-86.
3. Lambert MP. Inherited platelet disorders: a modern approach to evaluation and treatment. *Hematol Oncol Clin North Am*. 2019;33:471-87.
4. Kumar C, Sharma D, Pandita A, Bhalerao S. Thrombocytopenia absent radius syndrome with tetralogy of Fallot: a rare association. *Int Med Case Rep J*. 2015;8:81-5.
5. Greenhalgh KL, Howell RT, Bottani A, Ancliff PJ, Brunner HG, Verschuuren-Bemelmans CC, et al. Thrombocytopenia-absent radius syndrome: a clinical genetic study. *J Med Genet*. 2002;39:876-81.

Disclaimer/Publisher's Note: The statements, opinions, and data presented in all publications are exclusively those of the individual author(s) and contributor(s), and do not necessarily reflect the views of JOSAM, SelSistem and/or the editor(s). JOSAM, SelSistem and/or the editor(s) hereby disclaim any liability for any harm to individuals or damage to property that may arise from the implementation of any ideas, methods, instructions, or products referenced within the content.