The Case of the Rare Malformation and Rare Variant: An Infant with a Self-Embolized Torcular Dural Sinus Malformation and a Concomitant Prothrombin Variant

Roxanne M Miller, PhD, OMS-IV1,2, Anthony Zarka, DO2, and Samiya F Ahmad, MD2,3

Abstract
Torcular dural sinus malformations (tDSMs) can occur in the brain during prenatal development. These rare vascular malformations occur in less than 1% of the population but can lead to a poor prognosis secondary to congestive heart failure and hydrocephalus. Many tDSM cases require surgical embolization or coiling to return normal cerebral blood flow and prevent mortality and morbidity. We describe the first case of spontaneous self-embolization of a large torcular dural sinus malformation, possibly due to hypercoagulability from a comorbid prothrombin gene variant. Despite a grim prognosis at birth, the child is alive and thriving at age 3, with only mild speech delay.

Keywords
dural sinus malformation, abnormality of prothrombin, arteriovenous malformation, thromboembolism

Received August 11, 2022. Received revised November 1, 2022. Accepted for publication November 3, 2022.

Introduction
Torcular dural sinus malformations (tDSMs) are rare, pathological venous anomalies of the brain within the larger category of pediatric dural arteriovenous shunts.1 The characteristic feature of tDSMs is a giant torcular pool replacing the confluence of sinuses that connects the superior sagittal, straight, occipital, and transverse sinuses. The overall mortality rate for tDSMs is approximately 22%, with a high prevalence of medical complications that significantly reduce quality of life, such as motor manifestations.2 A tDSM is rarer than a vein of Galen malformation (VGM); however, they present with similar symptoms and imaging results.3 Large cerebral vascular malformations can result in mortality due to high output heart failure, local compression, and herniation.1,2

The functional point mutation, F2 (NM_000506.5): c.*97G>A, colloquially termed prothrombin G20210A, leads to a variant in the factor II gene that may increase the risk for prothrombin thrombophilia and is inherited in an autosomal dominant manner. In asymmetric individuals of European descent, the prevalence of prothrombin G20210A is approximately 2%.4 A prothrombin G20210A variant is associated with cerebral venous thrombosis in adult patients, but no association has been found in pediatric patients.5

A review of the literature did not identify an association between any genetic anomalies and tDSM. Specifically, a search for the words “torcular dural sinus malformation AND prothrombin mutation/variation/variant” was conducted on the databases PubMed, Web of Science, and Science Direct and yielded zero results. Genetic anomalies have been noted in

1The Office of Research and Innovation, University of the Incarnate Word School of Osteopathic Medicine, San Antonio, TX, USA
2Department of Radiology, The Children’s Hospital of San Antonio, San Antonio, Texas, USA
3Departments of Radiology and Neurology, Baylor College of Medicine, San Antonio, Texas, USA

Corresponding Author:
Roxanne M Miller, PhD, OMS-IV, University of the Incarnate Word School of Osteopathic Medicine, San Antonio, TX, USA; Department of Radiology, The Children’s Hospital of San Antonio, San Antonio, Texas, USA
Email: roxannemm87@gmail.com

Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (https://creativecommons.org/licenses/by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access page (https://us.sagepub.com/en-us/nam/open-access-at-sage).
other vascular conditions related to cerebral vessel embryogenesis, like vein of Galen malformations.6

Case Presentation

History
A male infant with a prenatal diagnosis of a large dural venous sinus varix in the region of the vein of Galen was born at 35 and 5/7 weeks of gestation via induced vaginal delivery following partial placental abruption to a woman of European descent with a history of hypothyroidism. The pregnancy had been unremarkable until a 19-week anatomy scan indicated a small intracranial cyst. A follow up fetal MRI at 25 weeks of gestation demonstrated a partially thrombosed dural venous sinus malformation with mass effect on the adjacent cerebral/cerebellar parenchyma with noncommunicating hydrocephalus and effacement of the prepontine cistern (Figure 1A).

Imaging
The day of life 1 brain MRI showed a posterior, midline, extraxial structure measuring 5.8 cm anterior-posterior, 5 cm transverse, and 8.8 cm craniocaudal. The mass exhibited restricted diffusion. Hydrocephalus was noted without transependymal flow. The cerebellar tonsils were displaced 9 mm below the foramen magnum (Figure 1B).

Clinical Course and Development
Given the sizeable lesion and herniation, the family was counseled on the possibility of palliative care after delivery. At birth, the infant was weak, minimally responsive, and macrocephalic, but he had appropriate weight for gestation. He was hemodynamically stable, able to feed by mouth, and breathe room air. Decision was thus made to discharge the infant home. Contrary to initial expectations, the infant continued to thrive and at his three months visit was meeting most of his developmental milestones when corrected for

Figure 1. Sagittal and axial HASTE fetal MR Images (A) at 25 weeks gestation shows a giant venous lake located at the torcular herophili and posterior superior sagittal sinus (arrows). There is two-intensity (inner hyperintense and outer hypointense) thrombus posteriorly and inferiorly (arrowheads). Sagittal and axial T2W postnatal MR images (B) at birth shows that the posterior collection compresses the cerebellum, resulting in herniated tonsils and brainstem (arrow). There is increased volume of stratified/concentric thrombus (arrowhead) which now occupies the entire volume of the torcular dural sinus malformation (tDSM). Also noted is hydrocephalus (arrow).
gestational age. As the infant showed vigor and appropriate growth, a decision was made to pursue a cerebral angiogram and venogram with plans for embolization. However, the neurovascular imaging showed that the malformation had spontaneously thrombosed and involuted (Figure 2A).

Following the arterial catheterization for the diagnostic angiogram/venogram, the patient developed thrombosis of his left superficial femoral artery, prompting a thrombophilia evaluation and determination of a prothrombin II pathogenic variant. ARUP Laboratory (Salt Lake City, UT) testing revealed a maternally inherited heterozygous prothrombin F2 (NM_000506.5): c.*97G>A (G20210A) pathogenic variant. In addition to the genetic testing, other labs were also performed. Prothrombin time (PT), international normalized ratio (INR), thrombin time (TT), functional protein S, antithrombin III activated, and factor V Leiden PCR were all within normal limits. Partial thromboplastin time (PTT) was high at 45.7 s (range is 20-32.2 s). Fibrinogen was low at 200 mg/dL (range 211-448 mg/dL). Functional protein C was high at 103% (range 28-80%). Given the association of tDSMs and cardiac anomalies, an electrocardiogram was performed which demonstrated possible left ventricular hypertrophy. An echocardiogram showed normal cardiac structure and function with a patent foramen ovale and no evidence of coarctation.

Enoxaparin therapy was initiated and continued for several months until the resolution of the femoral clot at twelve months of age. Even though the child inherited the gene variant from his mother, she did not have any reported history of increased clotting. Having this variant does not guarantee that the person will develop abnormal clotting. Usually, the person has other hypercoagulable risk factors in addition to the gene variant before abnormal clotting occurs. The child had a known hypercoagulable risk factor with the tDSM since these can cause stasis of blood movement due to pooling of blood.

During a follow-up visit at 32 months of age, the patient had his blood drawn and tests performed to see if any changes had occurred to his clotting abilities. His INR, PTT, and TT were within normal limits. His fibrinogen level was still slightly low, but stable compared to his previous fibrinogen level. A thromboelastographic (TEG) analysis panel had the following results: reaction time (R), kinetics (K), maximum amplitude (MA), amplitude at 30 min (LY30), and clot lysis time (CLT) were all within normal limits, but he had a low alpha angle

---

**Figure 2.** (A) Postnatal MR venogram shows absent flow within the collection (arrow) and subsequent catheter directed cerebral venogram at 3 months of age confirms spontaneous thrombosis of the torcular lake (arrow). (B) Axial T2W MRI at 3 months (left), 12 months (middle), and 30 months (right) of age shows progressive spontaneous involution of the thrombosed torcular lake with venous system remodeling (arrows). Evidence of a brain injury is present with ventriculomegaly and mild to moderate cerebral periventricular white matter and mild cerebellar volume loss (not shown).
(slope of line between R and K) of 41.6 degrees (reference range 53–72 degrees), which indicates low levels of fibrinogen and platelets. These blood studies signify that his prothrombin variant continued to affect his clotting capabilities.

At 36 months of age, the patient had mild communication and gross motor delays but otherwise age appropriate problem solving, social, and fine motor skills. He continues to have macrocephaly with a >99th percentile head circumference for his age.

Discussion/Conclusion

Our case is not the first to report a patient with spontaneous thrombosis of a brain arteriovenous malformation, but it is a rare occurrence. Most malformations are treated with surgical embolization or coiling, even if initially managed conservatively, in order to normalize the pressure, blood flow, and size of the vasculatures in the brain. Appaduray et al. reported three cases of pediatric dural arteriovenous malformations, two of which spontaneously thrombosed, and were without a known variant in thrombotic factors. However, all three eventually underwent endovascular embolization. It is particularly unusual that our patient avoided any surgical management of his tDSM, since other case reports have indicated a need for surgical embolization even after an initial spontaneous thrombosis. In 2020, Liby et al. proposed a 4-grade classification system for tDSMs (table 3 in the Liby et al paper), using timing of diagnosis, thrombosis of the tDSM pouch, brain damage, arterial feeders/arteriovenous shunts, crowded posterior fossa, and hydrocephalus. Based on this classification system, we propose that our patient had a grade IV tDSM since the tDSM was diagnosed antenatally, had a thrombosed pouch, lacked feeders, and was associated with brain damage and a crowded posterior fossa. Our patient also had hydrocephalus, so he demonstrated features of both a grade IVa and IVb proposed in the Liby et al 2020 paper. We suggest that the proposed grading system be slightly altered by not splitting grade IV into “a” and “b” subtypes since our patient is probably not the only person that had exhibited features of both grade IV subtypes. Grade IV is thought to carry the highest mortality at a rate of 75%, although recent reports indicate that the mortality rate for tDSMs may not be as high as originally suspected.

Other congenital vascular abnormalities, like vein of Galen malformations, can look similar to tDSMs on prenatal imaging, leading to challenges in early diagnosis. The differential diagnoses of prenatal brain abnormalities may also include subdural fluid collections, pial malformations, tumors, and cysts. Our case report adds to a small but growing body of literature that we anticipate will raise awareness and help expedite the proper diagnosis, management, and prognostication of cerebral vascular malformations.

Our patient’s heterozygous prothrombin variant may have contributed to his survival and favorable neurodevelopment without the need for surgical embolization. Based on the low level of fibrinogen reported above, his prothrombin variant may have been depleting fibrinogen by generating small clots. While these small clots may not necessarily cause symptoms, many of these clots could have aggregated in his cerebral vasculature, leading to an embolism that, over time, thrombosed his large venous malformation (Figure 2B). While it cannot be stated with certainty that this patient’s genetic variant is the reason for the spontaneous thrombosis, this case highlights a positive outcome for a rare condition that could have resulted in considerable morbidity and mortality.

Acknowledgments

Thank you to Jackie Dipaola, RN for helping us acquire the images; to Patricia A. Clarke, DNP for being a consultant on the hematological aspect of this case; to Rebecca Okashah Littlejohn, MS, CGC for helping us obtain the genetics information related to this case; and to Patricia Mancuso, MD for providing the neurosurgical guidance on this case.

Author Contributions

RMM, AZ, and SFM drafted the manuscript. AZ edited the images for the figures. All authors contributed to conception and design; contributed to acquisition, analysis, and interpretation; critically revised the manuscript; gave final approval; and agrees to be accountable for all aspects of work ensuring integrity and accuracy.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Ethical Approval

Contents of this case report were discussed with the CHRISTUS IRB who confirmed that case reports involving less than three patients are exempt from IRB approval. HIPAA compliance was maintained throughout the process of composing this case report. This case report and review of the related literature follows the recommendations set forth by the Children’s Hospital of San Antonio, the Baylor College of Medicine, and the University of the Incarnate Word School of Osteopathic Medicine for the conduct, reporting, editing, and publication of scholarly work in medical journals. Written consent from the patient’s mother was given to us to present this case.

ORCID iD

Roxanne M Miller https://orcid.org/0000-0002-3174-0605

References

1. Lasjaunias P, Magufis G, Goulao A, et al. Anatomoclinical aspects of dural arteriovenous shunts in children: review of 29 cases. Interv Neuroradiol. 1996;2(3):179-191. doi:10.1177/159101999600200303.
2. Liby P, Lomachinsky V, Petrab K, Kyncl M, Montarroyos UR, Tichy M. Torcular dural sinus malformations: a grading system proposal. Childs Nerv Syst. 2020;36(11):2707-2716. doi:10.1007/s00381-020-04569-8.
3. Barbosa M, Mahadevan J, Weon YC, et al. Dural Sinus malformations (DSM) with giant lakes, in neonates and infants. Review of 30 consecutive cases. Interv Neuroradiol. 2003;9(4):407-424. doi:10.1177/159101990300900413.
4. Varga EA, Moll S. Cardiology patient pages. Prothrombin 20210 mutation (factor II mutation). *Circulation*. 2004;110(3):e15-e18. doi:10.1161/01.CIR.0000135582.53444.87.

5. Beye A, Pindur G. Clinical significance of factor V Leiden and prothrombin G20210A-mutations in cerebral venous thrombosis – comparison with arterial ischemic stroke. *Clin Hemorheol Microcirc*. 2017;67(3-4):261-266. doi:10.3233/CH-179207.

6. Duran D, Karschnia P, Gaillard JR, et al. Human genetics and molecular mechanisms of vein of Galen malformation. *J Neurosurg Pediatr*. 2018;21(4):367-374. doi:10.3171/2017.9.Peds17365.

7. Appaduray SP, King JA, Wray A, Lo P, Maixner W. Pediatric dural arteriovenous malformations. *J Neurosurg Pediatr*. 2014;14(1):16-22. doi:10.3171/2014.4.Peds13695.

8. Ochiai D, Miyakoshi K, Miwa T, et al. Prenatal diagnosis of thrombosed dural sinus malformation with periorbital hemangioma: a case report. *Eur J Obstet Gynecol Reprod Biol*. 2016;198:157-159. doi:10.1016/j.ejogrb.2015.09.035.

9. Ku JC, Hanak B, Muthusami P, et al. Improving long-term outcomes in pediatric torcular dural sinus malformations with embolization and anticoagulation: a retrospective review of The Hospital for Sick Children experience. *J Neurosurg Pediatr*. 2021;28(4):469-475. doi:10.3171/2021.3.Peds20921.