Complex dural arteriovenous fistula in Bannayan-Riley-Ruvalcaba syndrome

Case report

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In this paper the authors report the case of a complex dural arteriovenous fistula (dAVF) with high-risk features in a 14-year-old girl with Bannayan-Riley-Ruvalcaba syndrome (BRRS), a phosphatase and tensin homolog–associated syndrome, presenting with signs and symptoms of increased intracranial pressure (ICP) that had previously been attributed to pseudotumor cerebri. This fistula was obliterated following 2 stages of embolization, and the patient experienced immediate symptomatic improvement. At the 2-month follow-up evaluation, the fistula remained angiographically occluded, and her symptoms continue to improve. This is the third reported case of an intracranial dAVF in a patient with BRRS. Because high-risk dAVFs can result in devastating morbidity, early detection with vascular imaging is crucial for patients with BRRS presenting with signs of increased ICP. Goals of treatment should include complete fistula obliteration whenever possible. (http://thejns.org/doi/abs/10.3171/2013.3.PEDS12551)

**KEY WORDS** • dural arteriovenous fistula • Bannayan-Riley-Ruvalcaba syndrome • phosphatase and tensin homolog • embolization • vascular disorders

Dural arteriovenous fistulas in pediatric patients can present with high-output cardiac failure, macrocephaly, developmental delay, seizures, and signs of high ICP; high-risk lesions can progress to hemorrhagic complications with or without venous stenosis/occlusion.\(^{11}\) Bannayan-Riley-Ruvalcaba syndrome is a rare autosomal dominant disorder that belongs to a family of hamartomatous polyposis syndromes, including Cowden syndrome. The syndrome typically involves macrocephaly, pseudopapilledema, and extracranial vascular malformations. Bannayan-Riley-Ruvalcaba syndrome has not traditionally been described to include intracranial pathologies, although a recent radiological study found intracranial developmental venous anomalies in 89% of patients in a small series.\(^{30}\) Regardless, monitoring for intracranial vascular lesions is not considered standard testing or workup for these patients.

This represents the third report of a dAVF in a child with BRRS. Srinivasa and Burrows described a case in 2006,\(^7\) and Palencia and Ardua reported a case in 1986 in a Spanish journal.\(^7\) We present the case of a child with BRRS who had previously been diagnosed with pseudotumor cerebri and subsequently treated with CSF diversion before the discovery of a complex and high-risk dAVF, which required 2 stages of embolization.

**Case Report**

**History and Examination.** This patient was a 14-year-old girl, the result of a twin pregnancy of 37 weeks’ gestation, complicated by preterm labor, preeclampsia, and toxemia. She was delivered by caesarean section and was noted to be macrocephalic. Her early childhood was significant for global developmental delay (motor, language, and cognitive delays) and autism. Her height, weight, and head circumference were noted to be consistently in the 95th percentile, while neither her twin nor other siblings were noted to have any developmental anomalies. Bannayan-Riley-Ruvalcaba syndrome was diagnosed when the patient was 9 years old, after she underwent positive genetic testing for a PTEN mutation. Her parents and twin tested negative for the same mutation. Her parents and twin tested negative for the same mutation. She underwent a complete thyroidecotomy and partial parathyriecotomy the same year for a thyroid nodule and was noted to have several colon polyps and a lymph node hemangioma dur-
ing her childhood. Her ophthalmological history included papilledema and diplopia.

At the age of 12 she was diagnosed with pseudotumor cerebri after undergoing 4 serial lumbar punctures with opening pressures ranging from 36 cm to 42 cm of water over a period of 5 months. A venogram was performed to measure cerebral venous pressures with selective catheterizations of the sagittal, transverse, and sigmoid sinuses, and jugular bulbs. This study did not demonstrate any evidence of venous sinus stenosis or abnormal drainage patterns, but in retrospect did demonstrate some subtle abnormalities of arterial channels in unsubtracted views of the skull that were not believed to be significant at the time (Fig. 1). She first underwent placement of a lumboperitoneal shunt and right frontal reservoir after an unsuccessful trial of acetazolamide, the former requiring multiple revisions followed by conversion to a ventriculoperitoneal shunt. Magnetic resonance imaging at this time also revealed ventriculomegaly and a Chiari malformation, for which she underwent a posterior fossa decompression without improvement in her symptomaticity. Follow-up MRI and MR angiography at the age of 14 revealed transverse sinus dilation, prompting angiography (Fig. 2).

Operative Course. Digital subtraction angiography revealed an extensive dAVF of the SSS, supplied by multiple branches of the ECA, tentorial branches of the ICA, and pial branches of the ACAs, middle cerebral arteries, and posterior cerebral arteries. The fistulous point was identified as a large venous pouch parallel and adjacent to the SSS (arrow). B: A-plane projection of left ECA injection, demonstrating a similar pattern of feeding arteries to the fistula. C: B-plane projection of right ECA injection, demonstrating the fistulous pouch (arrows), as well as large aneurysmal dilations of the MMA feeders to the fistula. D: B-plane projection of left ECA injection, demonstrating additional aneurysmal dilations of feeding MMA branches.
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have dramatically grown in size over the interval 2-year period (Fig. 5). Retrograde drainage was evident through the straight sinus and frontal cortical veins, along with a point of venous sinus stenosis (Fig. 6).

The first stage of embolization was performed through a transarterial route with transvenous balloon occlusion of the ostium draining from the fistulous pouch into the SSS. Arterial access into the distal MMA was achieved through the aneurysmal dilations using a 6-Fr Neuron guide catheter (Penumbra, Inc.), with an Echelon microcatheter (ev3, Inc.) advanced over a Synchro-2 microwire (Boston Scientific) into the venous pouch. Venous access was achieved using a 6-Fr Envoy guide catheter (Codman & Shurtleff, Inc.), with a 7 × 7 mm Hyperperform balloon (ev3) advanced into the SSS. The balloon was inflated to protect the venous outflow, and Onyx (ev3) embolization was performed through the arterial microcatheter, casting the distal pseudoaneurysms of the MMA as well as a portion of the venous pouch (Fig. 7).

The second stage of embolization, performed 2 days later, included transarterial access to the fistulous pouch followed by deployment of 4 detachable coils (Target 360, Stryker Corp.) to bolster additional Onyx delivered transarterially through MMA branches (Fig. 8). Postembolization angiography revealed obliteration of the fistula (Figs. 1 and 9).

**Postoperative Course and Follow-Up.** The patient was noted to have significantly improved headaches within 24 hours. Unfortunately, due to her radiation dose area product of 1,659,643 mGy × cm², she suffered from radiation-induced alopecia, a potential complication that was disclosed in detail prior to the procedure. Two-month follow-up angiography revealed continued obliteration of the fistula (Fig. 10). Additionally, 7-month follow-up angiography revealed stable occlusion. She continues to do well, with only mild headaches and continuing improvement in her cognitive performance.

**Discussion**

Dural AVFs are rare vascular lesions that may cause venous hypertension leading to increased ICP in high-risk
cases involving retrograde flow into the sinuses and cortical veins. Although the origin of dAVFs remains unclear, they are commonly associated with venous hypertension, often in the setting of venous sinus thrombosis. Lasjaunias et al. described 3 types of pediatric dAVFs: dural sinus malformations, infantile-type dural arteriovenous shunts, and adult-type dural arteriovenous shunts. The patient in this report falls into the third category, with high-risk features such as retrograde drainage through the straight sinus and cortical veins. Furthermore, she rapidly developed large dysplastic aneurysmal dilations of feeding arteries, which included parasitized pial feeders from the ACA, middle cerebral artery, and posterior cerebral artery branches. Our treatment strategy for this lesion included transvenous balloon occlusion for protection of critical venous outflow and structural support during Onyx casting.

The PTEN gene encodes a tumor suppressor protein that regulates pathways involved in cell-cycle regulation, angiogenesis, and cellular proliferation; its major substrate is phosphatidylinositol-3,4,5-triphosphate. Phosphatidylinositol-3,4,5-triphosphate activates numerous downstream targets, including the serine-threonine kinase PKB/Akt, which is involved in antiapoptosis and onco genesis. Germline heterozygous mutations of PTEN cause BRRS and Cowden syndrome. Riley and Smith first described 5 family members with macrocephaly, pseudopapilledema, and multiple hemangiomas in 1960. Intellect and vision were unimpaired in these patients. Bannayan later described the triad of macrocephaly, lipomatosis, and angiomatosis in a child observed at autopsy in 1971. Other common characteristics of this syndrome include autism and hamartomatous intestinal polypos. Our patient was noted to have several of these features, including a lymph node hemangioma. Although vascular anomalies such as arteriovenous malformations or fistulas have been traditionally described as extracranial in location (musculoskeletal or visceral), associations with other vascular lesions of the CNS have been suggested, such as cavernous malformations in Cowden syndrome. This represents the third report of a dAVF in a child with BRRS.

It is important to note that these patients may present initially with signs of increased ICP and no obvious abnormality on MRI or MR angiography, but rapidly develop a high-risk lesion. Our patient, in particular, was noted to have papilledema in the setting of normal MRI. She was diagnosed with pseudotumor cerebri at an outside hospital, prompting a venogram to be obtained, which
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was interpreted as normal. She later presented to us with a dilated transverse sinus on follow-up MRI, which prompted formal angiography, but only after 2 years of treatment by CSF diversion. Comparison of her skull images at this time revealed rapid development of a high-risk lesion within this interval 2-year course. Admittedly, retrospective review of unsubtracted views of the skull from the prior venogram demonstrates subtle prominence of feeding MMA branches, which likely represented an underlying low-risk fistula that was not diagnosed at the time (Fig. 5). Given that her twin brother tested negative for the mutation and did not exhibit any similar symptoms, he was not screened using MRI or formal angiography.

In the setting of our patient’s congenital syndrome, there are 2 fundamental questions that must be addressed. The first question relates to the origin of pseudopapilledema or papilledema in many of these patients. While early reports of this syndrome may have attributed this finding to pseudopapilledema, some of these patients may have true papilledema resulting from increased ICP, potentially related to occult dAVF or venous sinus anomalies. In our patient, the chronological development of symptoms of increased ICP suggests that perhaps an underlying dAVF or venous sinus stenosis resulted in a high-risk lesion and subsequent intracranial hypertension. Therefore, many patients with BRRS may actually have true papilledema as part of the syndrome. Secondly, it is unclear if she developed her dAVF secondary to a venous sinus stenosis or as an accelerated result of molecular pathways leading to increased angiogenesis in the setting of her PTEN mutation. It remains possible that she had a prior low-grade dAVF that later developed multiple high-risk features prior to definitive diagnosis.

Many patients with this syndrome may be predisposed to indolent low-grade dAVFs and, thus, are underdiagnosed. The same may even apply to patients with other PTEN-associated syndromes such as Cowden syndrome, although there are no formal reports in the literature at this time. Given the apparent association between BRRS and a dAVF, we recommend cerebral angiography as a definitive screening tool in patients with evidence of elevated ICP. Moreover, pediatric patients with newly diagnosed dAVFs should undergo genetic screening and hypercoagulable workup, especially in the setting of other vascular anomalies or lesions.

Conclusions

Bannayan-Riley-Ruvalcaba syndrome is a PTEN-associated disorder that can include intracranial dAVFs. Dural AVFs can account for many aspects of the spectrum of symptoms observed in BRRS, including signs and symptoms of elevated ICP. High-risk fistulas can develop rapidly and diagnostic cerebral angiography should be considered as standard screening in patients with this presentation. Goals of therapy should include complete obliteration of the dAVF whenever possible. Further research is indicated to determine the mechanisms by which these lesions form within the context of these congenital syndromes, and to identify patients at highest risk.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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