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Case Report

Surgical Managment of a Forearm Arteriovenous Fistula in a Child with Noonan Syndrome: A Case Report

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ABSTRACT

Peripheral arteriovenous fistulas (AVFs) are rare vascular anomalies in children and typically result from trauma or iatrogenic injury. To the best of our knowledge, we report the first case of a peripheral AVF associated with genetically confirmed CBL syndrome (Noonan syndrome-like disorder). A 5-year-old boy with CBL syndrome presented with a two-week history of progressive swelling, prominent superficial veins, and a palpable thrill in the right forearm. He had no known history of trauma or invasive procedures involving the affected extremity. Genetic testing had revealed a heterozygous pathogenic variant in the *CBL* gene (c.1100A>C, p.Gln367Pro). Physical examination revealed marked swelling in the antecubital region, dilated tortuous veins, a strong continuous thrill over the antecubital fossa, and an audible vascular bruit. Distal pulses were intact with no signs of ischemia. Computed tomography angiography demonstrated a direct abnormal connection between the brachial artery and basilic vein at the antecubital level. Color Doppler ultrasonography confirmed arterialized venous flow patterns. Comprehensive preoperative coagulation studies were within the normal limits. Under general anesthesia, surgical exploration identified a 5 mm wide fistulous connection between the brachial artery and basilic vein. The fistula was primarily repaired with 7-0 polypropylene sutures. Postoperatively, the thrill disappeared with preserved distal pulses. Postoperative Doppler ultrasonography confirmed complete fistula closure. At one-year follow-up, the patient remained asymptomatic with excellent extremity perfusion and no evidence of recurrence. Cranial magnetic resonance imaging and thoracic computed tomography revealed no evidence of intracranial or intrathoracic vascular malformations on available imaging. This case expands the vascular phenotype of RASopathies and suggests a link between RAS-MAPK dysregulation and peripheral AVF development. Clinicians should maintain heightened awareness for peripheral vascular anomalies in syndromic patients, even without a trauma history.

Keywords: Arteriovenous fistula, CBL syndrome, Noonan syndrome-like disorder, brachial artery, RAS-MAPK pathway

Introduction

Arteriovenous fistulas (AVFs) bypass the normal capillary bed, connecting arteries and veins. In childhood, they are exceptionally rare and most commonly result from trauma or iatrogenic procedures (1). Congenital or spontaneous AVFs, particularly involving the brachial artery, are uncommon, with only a few pediatric cases reported (2-4).

Noonan syndrome (NS) is an autosomal dominant disorder caused by mutations in the genes of the RAS-MAPK signaling pathway. This syndrome is characterized by distinctive facial features, congenital heart defects, short stature, and skeletal abnormalities (5,6). Although cardiovascular anomalies are well documented in NS, peripheral vascular anomalies such as AVFs have not been previously reported.

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The RAS-MAPK pathway is critical for vascular development and endothelial cell function. Dysregulation of this pathway has been implicated in various vascular malformations in related genetic conditions (7). Despite this biological plausibility, no cases of peripheral AVF associated with NS or related RASopathies have been documented in the English-language medical literature (PubMed and Scopus databases were searched throughout May 2026 using the terms "arteriovenous fistula", "Noonan syndrome", "CBL syndrome", and "RASopathy").

Here, we present a 5-year-old boy with genetically confirmed CBL syndrome (NS-like disorder) who had developed a large AVF between the brachial artery and basilic vein without any history of trauma. This case expands the recognized vascular phenotype of RASopathies and highlights the importance of vascular anomalies in syndromic patients.

Case Report

A 5-year-old boy with genetically confirmed CBL syndrome presented with a two-week history of swelling and prominent veins in the right forearm. His parents had noticed the progressive enlargement of superficial veins. The patient had no history of trauma, venipuncture, or invasive procedures involving the affected extremity.

His medical history included developmental delay and cryptorchidism, for which he had undergone right orchiopexy at age 3 years (two years prior to the diagnosis of the AVF). Although perioperative peripheral venous access was inevitably obtained during this procedure, the specific extremity used for intravenous cannulation could not be ascertained from the available anesthesia records. However, the family did not observe any noticeable changes in the right upper extremity following the surgery. Genetic testing performed at age 2 years had revealed a heterozygous pathogenic variant in the *CBL* gene (c.1100A>C, p.Gln367Pro), confirming CBL syndrome.

The patient was followed by pediatric cardiology. Echocardiography at age 5 years revealed normal cardiac chamber sizes, intact interatrial and interventricular septa, no patent ductus arteriosus or coarctation, preserved systolic function (ejection fraction 72%), minimal mitral regurgitation, trace aortic regurgitation, and dilated coronary arteries (left main coronary artery 3.8 mm, right coronary artery 4.0 mm), findings consistent with NS. Cranial magnetic resonance imaging performed at 10 months of age revealed no evidence of intracranial vascular malformations, moyamoya disease, or structural brain abnormalities; diffusion-weighted imaging showed no restricted diffusion. Thoracic computed tomography performed during the diagnostic workup demonstrated focal pulmonary consolidation without evidence of pulmonary vascular malformations or arteriovenous shunting on the available non-contrast images. There was no family history of vascular anomalies or bleeding disorders.

On physical examination, the patient exhibited typical NS features including triangular face and low-set ears. Cardiovascular examination was normal. Examination of the right upper extremity revealed marked swelling in the antecubital region with dilated, tortuous superficial veins. A strong, continuous thrill was palpable over the antecubital fossa, and a loud vascular bruit was audible. There were no signs of distal ischemia. Capillary refill time was normal. These findings suggested an AVF.

Given the high prevalence of bleeding diathesis in NS, which can reach up to 40% (8), comprehensive preoperative laboratory evaluation was performed (Table I). Prothrombin time (11.7 sec), activated partial thromboplastin time (25.2 sec), international normalized ratio (1.0), bleeding time (3.0

Table I. Patient's preoperative laboratory findings

Laboratory parameter	Value	Reference range/ interpretation
Hemoglobin	12.47 g/dL	Normal
Hematocrit	38.95%	Normal
White blood cell count	12.39x10^9/L	Slightly elevated
Platelet count	346x10^9/L	Normal
Prothrombin time	11.70 sec	Normal
PT%	100.70%	Normal
INR	1.00	Normal
APTT	25.20 sec	Normal
Bleeding time	3.00 min	Normal
Clotting time	5.50 min	Normal
ALT	17 U/L	Normal
AST	37 U/L	Normal
Creatinine	0.38 mg/dL	Low (age-appropriate)
BUN	12.85 mg/dL	Normal
Glucose (fasting)	94 mg/dL	Normal
CRP	2 mg/L	Normal
ESR	4 mm/hour	Normal

PT: Prothrombin time, INR: International normalized ratio, APTT: Activated partial thromboplastin time, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, BUN: Blood urea nitrogen, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate

min), clotting time (5.5 min), and platelet count (346×10^9/L) were all within the normal limits.

Color Doppler ultrasonography demonstrated arterialized flow in the basilic vein with turbulent, high-velocity flow at the antecubital level, confirming an arteriovenous communication. Computed tomography angiography revealed prominent axillary and brachial arteries with a clear abnormal connection between the brachial artery and the basilic vein (Figure 1). The distal vessels appeared smaller in caliber. These findings were consistent with an AVF rather than a complex arteriovenous malformation.

Surgical intervention was planned with the cardiovascular surgery team. Under general anesthesia, a longitudinal incision was made over the antecubital fossa. Using ultrasound guidance, careful dissection exposed the brachial artery and basilic vein. After systemic heparinization, vascular clamps were applied proximal and distal to the fistula.

Upon direct visualization, a 5 mm wide fistulous connection between the brachial artery and the basilic vein was identified (Figure 2). The fistula tract was carefully dissected circumferentially and directly divided, separating the arterial and venous components. The resulting defects in both the brachial artery and the basilic vein were primarily repaired using 7-0 polypropylene sutures with an interrupted technique, ensuring the preservation of vessel continuity and luminal patency. After clamp removal and hemostasis confirmation, normal blood flow was verified. The palpable thrill immediately disappeared, and distal pulses remained easily palpable. The wound was irrigated and closed in layers.

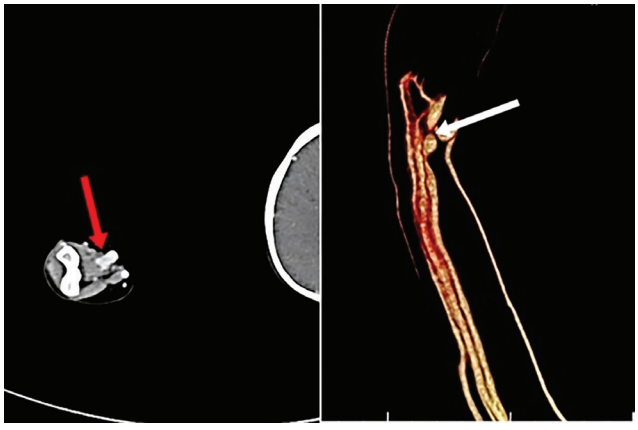


Figure 1. Computed tomography angiography demonstrating an abnormal connection between the brachial artery and the basilic vein at the right antecubital region (red arrow), with dilatation of the proximal venous segment (white arrow), consistent with an arteriovenous fistula



Figure 2. Intraoperative photograph showing the fistulous connection (approximately 5 mm in diameter) between the brachial artery and the vein at the antecubital level (white arrow). Vessel loops are placed around the brachial artery and the basilic vein for vascular control

The postoperative course was uneventful. On postoperative Day 1, Doppler ultrasonography confirmed complete fistula closure with patent arterial and venous flow. The patient was discharged on postoperative Day 2.

At follow-up visits at 1 week, 1 month, 6 months, and 1 year postoperatively, the surgical incision was well healed with no complications. Physical examination revealed no recurrence of swelling, thrill, or bruit. Distal pulses were symmetric and easily palpable. Follow-up Doppler ultrasonography at 1 year confirmed sustained fistula closure with normal vascular anatomy.

Discussion

To the best of our knowledge, this case represents the first reported peripheral AVF in a patient with genetically confirmed CBL syndrome, a NS-like RASopathy. While congenital AVFs are rare in childhood, their occurrence in a patient with a RASopathy raises important questions about potential mechanistic links between constitutive RAS-MAPK pathway activation and vascular development abnormalities.

Peripheral AVFs in children are predominantly caused by trauma or iatrogenic injury (1). Congenital AVFs without trauma are exceedingly rare. In the upper extremity, large fistulas involving the brachial artery have been reported in only a handful of pediatric cases (2-4). Our patient's presentation fits the profile of a congenital or spontaneous AVF.

One distinctive aspect of this case is the coexistence of AVF with CBL syndrome. The *CBL* gene encodes an E3 ubiquitin ligase which negatively regulates RAS signaling. Heterozygous CBL mutations result in constitutive RAS-MAPK activation, leading to a Noonan-like phenotype with a predisposition to juvenile myelomonocytic leukemia and autoimmune disorders (9). CBL syndrome has been associated with vasculopathies, including Takayasu arteritis suggesting that dysregulated RAS-MAPK signaling can affect vascular wall integrity across multiple vascular beds (9,10).

However, the mechanistic link between constitutive RAS-MAPK activation and peripheral AVFs remains speculative and warrants confirmation through additional case reports and systematic vascular screening studies in RASopathy cohorts.

Regarding iatrogenic etiology, although perioperative intravenous access during orchiopexy cannot be entirely excluded, several factors argue against this: (1) routine peripheral IV cannulation uses small-gauge catheters (20-24G), making brachial artery injury unlikely; (2) the 5 mm fistula size is disproportionately large for cannulation-related injury; (3) iatrogenic AVFs typically present acutely, whereas the symptoms appeared two years later in this case; and (4) the family reported no post-procedural changes.

Regarding additional vascular anomalies, the patient was evaluated for both intracranial and intrathoracic vascular pathology. Cranial magnetic resonance imaging (MRI) performed at 10 months of age revealed no intracranial vascular malformations, effectively excluding clinically significant intracranial vascular pathology. Thoracic computed tomography demonstrated only focal pulmonary consolidation with no evidence of pulmonary arteriovenous malformations, abnormal vascular communications, or other intrathoracic vascular anomalies on the available non-contrast images. Echocardiography findings (including dilated coronary arteries) were consistent with NS and did not suggest additional hemodynamically significant vascular abnormalities. Collectively, these evaluations support the suspicion that the AVF described here represents an isolated peripheral vascular anomaly rather than a manifestation of a broader systemic vasculopathy.

Limitations: First, as a single case report, definitive causation cannot be established. Second, although cranial MRI and thoracic computed tomography (CT) were performed and showed no evidence of intracranial or intrathoracic vascular malformations, dedicated pulmonary vascular imaging (e.g., CT pulmonary angiography) was not performed due to the absence of clinical indications. The available non-contrast thoracic CT demonstrated only focal pulmonary consolidation, which did not warrant further vascular imaging. Therefore, subclinical pulmonary vascular lesions cannot be entirely excluded, and we acknowledge this as a limitation of this report. Third, a remote iatrogenic contribution remains theoretically possible.

Conclusion

This case expands the phenotypic spectrum of RASopathies and suggests that constitutive RAS-MAPK pathway dysregulation may play a role in peripheral AVF development. Clinicians should maintain high suspicion for vascular anomalies in syndromic patients, even in those with no trauma history.

Ethics

Informed Consent: Written informed consent was obtained from the patient's parents for the publication of this case report and its accompanying images.

Footnotes

Authorship Contributions

Surgical and Medical Practices: G.B., A.İ.D., Concept: G.B., Design: G.B., Data Collection or Processing: G.B., Analysis or Interpretation: G.B., Literature Search: G.B., Writing: G.B., A.İ.D.

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