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CASE REPORT

Familial Arteriovenous Malformation in Extremity: A Case Report

Malformación Arteriovenosa Familiar en Extremidad: Reporte de un Caso

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ABSTRACT

Arteriovenous malformation (AVM) is a genetic vascular anomaly that can significantly affect daily activities. Its occurrence varies by race and gender, being more common in women. This report examines AVM in two siblings, aged 12 and 14. Clinical, radiological, and pathological evaluations revealed differing tumor sizes, expansions, and causes of vascular enlargement. Consequently, the siblings received different treatments: one underwent embolization, while the other had a wide excision. Both approaches resulted in favorable outcomes. AVM is a vascular neoplasm that may present at birth or be discovered later, often during routine check-ups or after trauma. The familial nature of AVM in this case emphasizes the variability in presentation and treatment response. Established diagnostic and therapeutic guidelines may not always be applicable, necessitating individualized treatment plans. This case highlights the importance of tailored treatment approaches for familial AVM, demonstrating successful outcomes with both embolization and wide excision.

Keywords: Arteriovenous Malformation; Inherited Disease; Genetic Disease; Embolization; Wide Resection.

RESUMEN

La malformación arteriovenosa es un problema vascular que surge genéticamente y puede causar alteraciones en la actividad diaria del paciente. Este artículo analiza la malformación arteriovenosa como una enfermedad familiar/hereditaria entre hermanos de 12 y 14 años. Ambos fueron evaluados con discusión clínica, radiológica y patológica y se decidió tratarlos de manera diferente debido a las diferencias en el tamaño del tumor, la expansión tumoral y la causa principal del agrandamiento vascular. La malformación arteriovenosa es una neoplasia vascular en lugar de un defecto vascular. Su manifestación puede aparecer tan pronto como nace un bebé o puede encontrarse inesperadamente durante un chequeo médico o empeorar debido a algún trauma. Su incidencia varía de manera diferente entre razas, y su proporción es mayor en mujeres que en hombres. Por lo tanto, las pautas establecidas para diagnosticar y tratar este tumor pueden no ser apropiadas en la práctica en todos los casos. Este caso muestra cómo se encontró una sospecha de enfermedad hereditaria familiar de malformación arteriovenosa dentro de un hermano con dos años de diferencia de edad y se trató de manera diferente. El tratamiento de estos pacientes puede ser diferente, pero tanto la embolización como la escisión amplia del tumor muestran un buen resultado en el tratamiento de la malformación arteriovenosa.

Palabras clave: Malformación Arteriovenosa; Enfermedad Hereditaria; Enfermedad Genética; Embolización; Resección Amplia.

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INTRODUCTION

Instead of a vascular defect, the arteriovenous malformation is more of an endothelium neoplasm. Current theories are mainly concerned with the derangement of angiogenesis, mutations in the cytokine regulating gene, placental involvement, progenitor cells, and developmental field pathway with abnormalities.

The incidence ranges from 1,1 to 2,6 % in the general newborn population, but by the age of one year, it can reach up to 12 %. Infantile AVM is detected in about 30 % of newborns, and in the first four weeks of life, it affects 70–90 % of children. The majority of arteriovenous malformations are sporadic, but it has been noted that IH can run in families.

Mostly, AVM sporadically appear as part of a pleiotropic syndrome. However, some researchers identified some research within families that stated autosomal dominant segregation of arteriovenous malformation and/or vascular defect. This study presents a perspective on AVM cases by showing the AVM case in a sibling, and both have been treated differently yet showing a good outcome. Written informed consent was acquired on both patient for their data to be reported for case report

CASE REPORT

This article discusses the unique case of infantile AVM within the same familial tree. Ms. A, 12 years old, and Mr. B, 14 years old, were siblings in the same family. Ms. A came to the outpatient ward with the chief complaint of an ingrowing mass on her right thigh in 2014 (5 years before she came to the hospital). This bulging mass felt painful when she moved/climbed the stair. Whenever she stays still or rests, the pain will be gone. She had a history of falling from certain heights in August 2014. No associated complaint was related to the bulging mass on his left thigh.

Physical examination showed a diffuse mass with localized pain. The radiological evaluation shows calcification of soft tissue projected on the left thigh with soft tissue bulging surrounding it (figure 1).

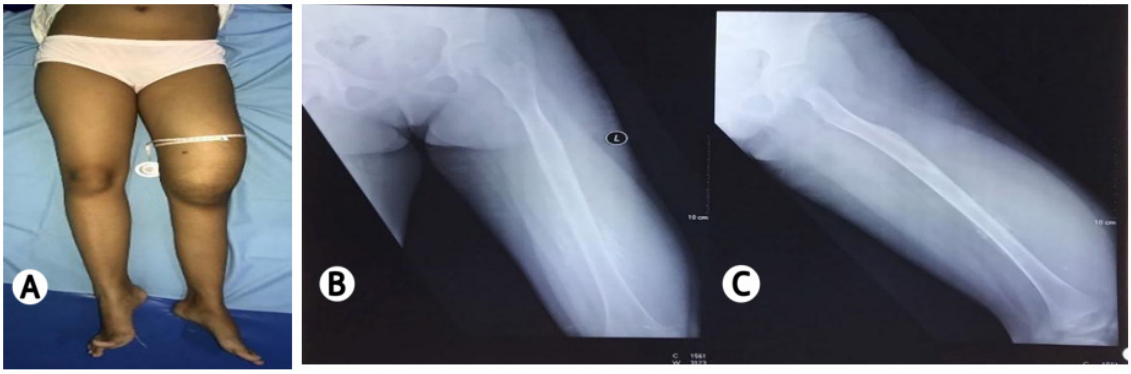

Figure 1. Clinical Photo (A) and Femoral Xray Anteroposterior (B) and Lateral (C) of Ms

MRI evaluation of the left thigh found a solid mass of the left anterior (figure 2). It spreads into the lateromedial side, which involves vastus medial, vastus intermedius, and vastus lateral muscles with the size of 10,4 x 8,14 x 27,3 cm. The mass obtained feeding vascularization from the femoral artery and had associated bone marrow changes at the level of the diaphysis of the left femur, which is suspected as a malignant mass. The FNAB (Fine Needle Aspiration Biopsy) evaluation of the patient shows a non-specific inflammation, which cannot deliberately remove soft tissue or osteogenic tumor from suspicion.

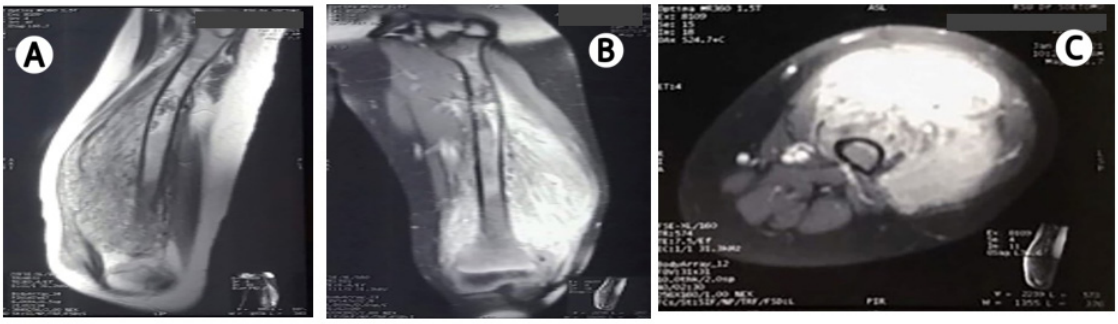

Figure 2. Femoral MRI of Ms. Az. (A) Sagittal view. (B) Coronal view. (C) Axial view at the level of middle third

Arteriography and embolization were done one month after her first visit. There were several findings of the large vascular lesion with the superficial femoral artery that have several feeder arteries, from the medial

side into the distal side and the branches of the left deep femoral artery. Embolization was done with PVC (Percutaneous Venous Catheter) 355-500 and continued with gel foam of three large branches of both deep and superficial left femoral artery. MRI evaluation post-embolization was repeated two months later, finding a decrease in lesion size compared with the previous MRI. After embolization, wide excision, biopsy, and ORIF plating on the femur was done (figure 3).

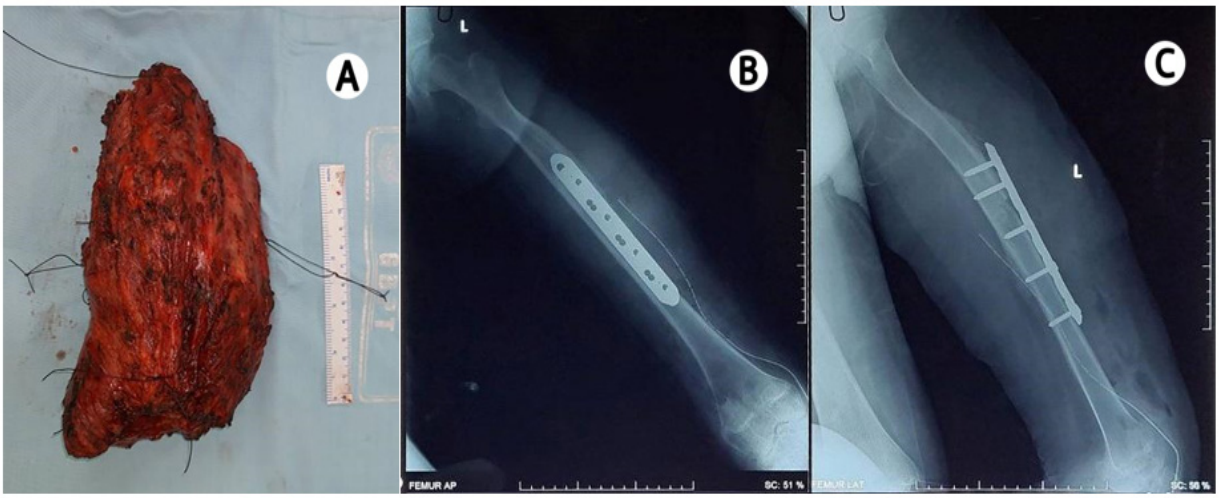

Figure 3. Surgery result (A) and Femoral Anteroposterior (B) and Lateral Radiograph Post Surgery of Ms

The biopsy of the left femur shows no signs of malignancy, and it is similar to a benign mesenchymal lesion like myolipoma (figure 4).

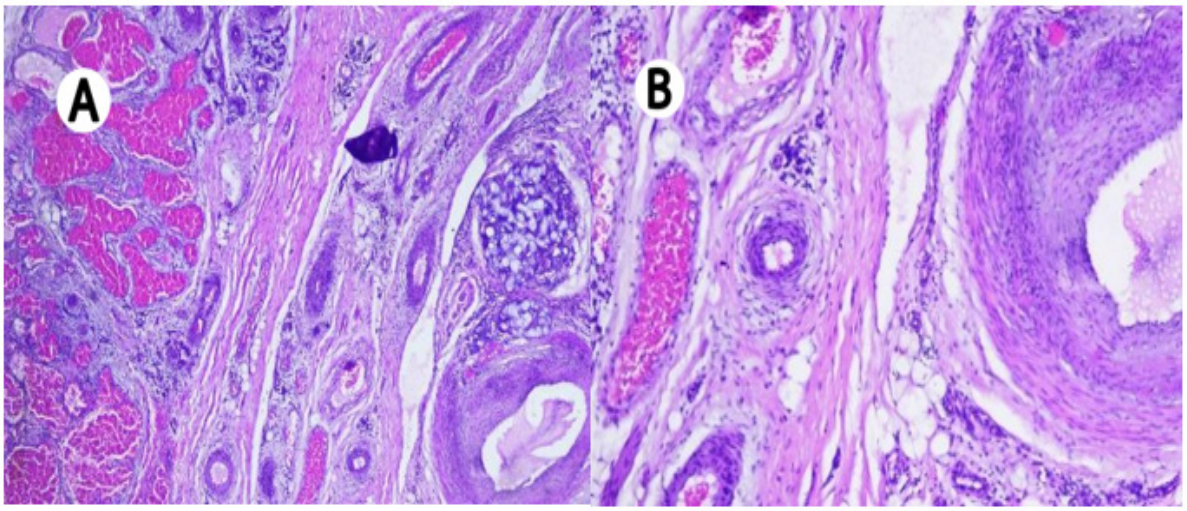

Figure 4. Histological Examination of the AVM of Ms. A. (A) 40x magnification. (B) 100x magnification

The second patient is Mr. B. He is the older brother of Ms. A. He is 14 years old. He comes to our outpatient ward with the main complaint of a lump on the inferior thigh. The lump is static without any increasing size of the lump for a year. The patient feels pain whenever the lump is palpated. It showed no abnormalities with the X-ray. Extremity MRI showed an enhancing solid of soft tissue mass with a void flow inside the lateral vastus muscle that suspected a haemangioma (figure 5).

In the left lateral vastus muscle, musculoskeletal USG revealed a hypervascular mass with an anechoic portion filled with a doppler signal suspected of haemangioma. We planned to do the further examination with a biopsy. We performed FNAB with a conclusion of benign vascular lesions.

The excision biopsy showed similar results with a conclusion of arteriovenous malformation (figure 6). We did a haemangioma-wide excision as concluded in our hospital clinicopathological conference. The surgery was done by a senior orthopaedic oncologist in our center and no complication occurred due to the surgery. Upon examination, we evaluated that the result was no different from her sister's. There was no more expanding mass, no recurrence occurred after 3 and 6 months of follow-up, the patient felt the pain subsided and there

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is no particular complain.

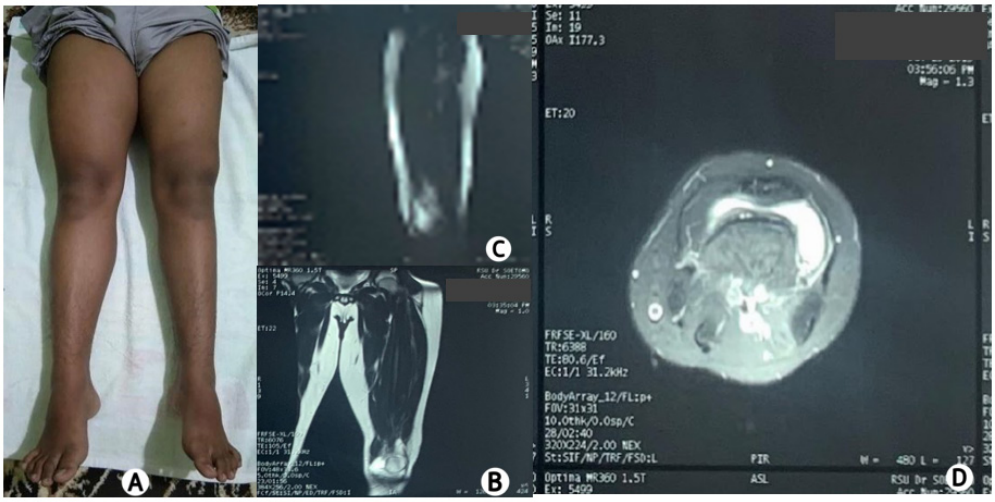

Figure 5. Clinical Photo (A), Femoral MRI of Mr. B with Coronal view (B) and Sagital View (C) and Axial View (D)

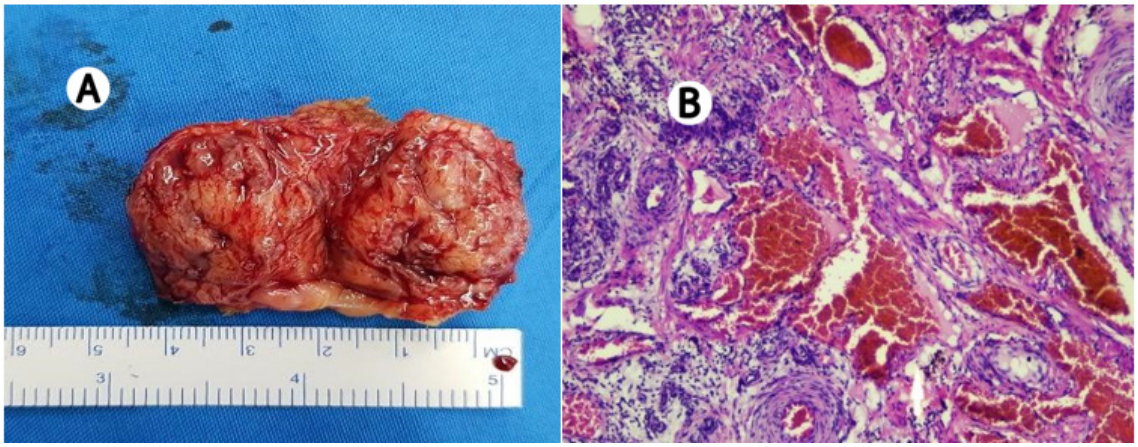

Figure 6. Surgery result (A) Gross morphology and (B) Histological Section of AVM of Mr. B with HE staining

DISCUSSION

Tumors and malformations are the two main classifications of vascular abnormalities. These clinical entities are different but often confused. Vascular malformations, such as infantile AVM, are more frequently misdiagnosed as benign vascular tumors than vascular malignancies themselves. Increased endothelial and other vascular cell proliferation rates characterize vascular tumors, which are neoplastic. It is important to remember that they differ histologically depending on clinical behavior and cellular composition. Vascular deformities are congenital abnormalities with normal epithelial turnover, as opposed to AVM, which are neoplasms with endothelial hyperplasia.

The most probable explanation is that hypoxic stress increases GLUT 1 and VEGF expression, which mobilizes endothelial progenitor cells. CD133 and CD31 are present in the progenitor cells. Around 4 % to 5 % of neonates have infantile AVM, the most prevalent benign vascular tumor of infancy.

Infantile AVM characteristics between familial and sporadic cases were similar in terms of perinatal risk factors, site, subtypes, complications, and therapies, according to a cohort study. 28 genes have been identified in another meta-analysis study whose mutations have been linked to vascular abnormalities. This study demonstrates that there are six mutations related to AVMs (3q26.1, 5q14.3, 5q31, 7p14, 9q34, 12q13), 4 are related to vascular malformations and glomerulovenous malformations (1p22, 4p, 9p21, 16q24.3), and five different loci are connected with arteriovenous malformations (2p13, 2q23, 4q12, 5q31, 7q33, and 15q26; and other loci were associated with vascular malformation and vascular tumor as well.

A previous study showed AVM suspected to be associated with familial inheritance/genetic disease. With physical examination, sharply bordered, raspberry-red skin spots of increasing size can be made certain by ultrasound (US) and magnetic resonance imaging (MRI). High diastolic velocities and high vessel density are present in the venous and arterial waveforms, and a Doppler shift greater than 2 kHz can be seen with Doppler US. Infantile arteriovenous malformations appear as solid, homogenous masses with sharp margins on MRI and

are iso- to intermediately intense on T1w and intermediate-to-bright on T2w and PDw sequences.

American Association of Pediatric (AAP) Guideline for Infantile Arteriovenous malformation should always be taken into consideration in a multidisciplinary environment and may involve medication therapy, surgery, or occasionally interventional methods. For complicated infantile AVM, propranolol has become the medication of choice. Bleomycin image-guided intralesional medication injections can have serious complications and should only be used in exceptional circumstances. In the early stages of a disease, surgical approaches—either open or laser—are used; prompt treatment success is essential to prevent complications (e.g., orbital or hepatic arteriovenous malformations). Given the evident therapeutic benefits of propranolol, embolization therapy should not be utilized as the first-line treatment for infantile AVM. Still, it can be used to reduce the perioperative bleeding rate. Transarterial embolization has been reported to be safe and effective in treating infant arteriovenous malformations resilient to propranolol, cardiac failure with high output brought on by massive flow of shunt, intraoral and intranasal arteriovenous malformations, arteriovenous malformations with the lesion in challenging locations, symptomatic and seriously damaged hepatic congenital arteriovenous malformations, and ulcerated arteriovenous malformations with life-threatening bleeding.

CONCLUSIONS

Arteriovenous malformation is an inherited disease that causes harm both due to pain and complications that have occurred. Infantile AVM within the same family, which is treated differently, may still show a good outcome, depending on the indication and the patient's condition

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest

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