

Intramuscular vascular malformations in pediatric patients: a retrospective study in a vascular anomalies clinic

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Abstract

Background: Intramuscular vascular malformations (IVMs) are rare developmental congenital structural abnormalities. Their clinical diagnosis is difficult, and imaging studies are essential to determine the type and extent of vessels involved. Treatment can be challenging and must be managed by a multidisciplinary team. **Methods:** A descriptive, observational, retrospective, longitudinal study of clinical records of patients diagnosed with IVMs who were evaluated at the vascular anomalies clinic from January 2011 to December 2021 was performed. Demographic, clinical, imaging, diagnosis, treatment, and response data were collected. **Results:** Seven patients (five females and two males) with a mean age of 13.66 years (standard deviation 5.82 years) were included in the study. In all cases, the clinical diagnosis was venous and lymphatic malformation. The radiological findings were dilated and tortuous vascular structures or multilobulated lesions with septa inside, with or without vascular flow; these findings allowed diagnosis in all cases. Treatment modalities included sclerotherapy in five patients, surgical resection in two, medical treatment with sirolimus in three, and surveillance in one. Subsequent clinical evolution was favorable in all patients, with decreased pain in six (partial in four and total in two) and size reduction in one patient. **Conclusion:** IVMs in our pediatric population most frequently affect the lower extremities. The main symptoms and signs were pain on exertion and volume increase. Treatment can be challenging given the extension and depth of the malformations, so a combination of therapeutic modalities may be necessary to obtain the best outcome.

Keywords: Vascular malformation. Sclerotherapy. Sirolimus.

Malformaciones vasculares intramusculares en pacientes pediátricos: un estudio retrospectivo de una clínica de anomalías vasculares

Resumen

Introducción: Las malformaciones vasculares intramusculares (MVI) son anomalías estructurales congénitas del desarrollo raras. Su diagnóstico clínico es difícil y los estudios de imagen son fundamentales para determinar su tipo y extensión. Su tratamiento puede ser un desafío y debe ser dirigido por un equipo multidisciplinario. **Métodos:** Se realizó un estudio descriptivo, observacional, retrospectivo y longitudinal de los expedientes clínicos de pacientes con diagnóstico de MVI que fueron valorados en la Clínica de Anomalías Vasculares desde enero 2011 a diciembre 2021. Se recolectaron datos demográficos, clínicos, imagenológicos, diagnóstico, tratamiento y respuesta al mismo. **Resultados:** Se incluyeron 7 pacientes

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(5 mujeres y 2 hombres) con una edad media de 13.66 años (DE 5.82 años). En todos, el diagnóstico clínico fue malformación venosa y/o linfática. Los hallazgos radiológicos mediante ultrasonido y/o resonancia magnética nuclear fueron estructuras vasculares dilatadas y tortuosas o lesiones multilobuladas con septos en su interior, con o sin flujo vascular; y en todos los casos permitieron hacer el diagnóstico. El tratamiento fue escleroterapia en 5 pacientes, resección quirúrgica en 2, tratamiento con Sirolimus en 3 y vigilancia en 1. La evolución clínica posterior fue favorable en todos, con disminución del dolor en 6 (parcial en 4 y total en 2) y reducción del tamaño en 1 paciente. **Conclusión:** Las MVI en nuestra población pediátrica, afectan con mayor frecuencia las extremidades inferiores. Los principales síntomas fueron dolor de esfuerzo y aumento de volumen. Su tratamiento puede ser un reto dada su extensión y profundidad, por lo que la combinación de modalidades terapéuticas puede ser necesarias para obtener el mejor desenlace.

Palabras clave: Malformación vascular. Escleroterapia. Sirolimus.

Introduction

Vascular malformations are congenital structural anomalies of development. They commonly affect the dermis and subcutaneous tissue (superficial) or infiltrate muscle and bone tissue (deep)¹. The latter are characterized by greater symptomatology, difficult diagnosis, and poor response to conventional therapy compared to their superficial counterparts^{2,3}.

Intramuscular vascular malformations (IVMs) have for many years been erroneously termed “intramuscular hemangiomas,” “cavernous hemangiomas,” or “angiomas,” terms which due to their suffix “oma” incorrectly suggest a true neoplasm. This inadequate nomenclature can lead to erroneous study, diagnosis, and treatment. Since 1996, the International Society for the Study of Vascular Anomalies has classified IVMs as true malformations, distinct from hemangiomas, and tumors with undetermined proliferative potential^{4,5}.

IVMs are quite rare; the true incidence and prevalence are unknown, but they are believed to be < 1% of all vascular malformations. Females are more affected, with a ratio of up to 2:1⁶⁻⁸. Clinically, only 8%-15% can be diagnosed⁹, which is why imaging studies are fundamental in determining the type and extent of the malformation. Treatment can be challenging and should be directed by a multidisciplinary team¹.

This study aims to describe pediatric patients with IVMs, including clinical manifestations, radiological characteristics, evolution, treatment, and therapeutic response.

Methods

A descriptive, observational, retrospective, and longitudinal clinical study was conducted on all clinical records of patients diagnosed with IVMs who were evaluated and registered in our hospital's vascular anomalies clinic (VAC) database from January 2011 to

December 2021. Demographic, clinical, and imaging data, as well as diagnosis, treatment, and response to treatment, were collected. Patient records lacking the clinical variables to be studied were excluded/eliminated.

Descriptive statistics were used with frequency distribution and measures of central tendency.

Results

Seven patients (five females and two males) with a mean age of 13.66 years (standard deviation \pm 5.82) were included in the study. The reason for consultation was the presence of swelling or a palpable mass (Figs. 1-3) following trauma (three patients) and associated with limb pain (four patients). The clinical diagnosis was venous or lymphatic malformation (LMs) in all cases. Radiological findings in all cases allowed the diagnosis of IVM and were described as dilated and tortuous vascular structures (in four patients) or multilobulated/multi-compartmentalized lesions (Figs. 4-6) with internal septa (in three patients), with or without vascular flow. The affected muscles were the triceps (Fig. 4), quadriceps (Fig. 5), and gluteus maximus. Treatment consisted of sclerotherapy in five patients, surgical resection in two, medical treatment with Sirolimus in three, and surveillance in one patient. The clinical evolution after treatment was favorable in all cases, with pain reduction (partial in four and total in two) and size reduction in one patient. One patient was lost during follow-up. The individual characteristics of each patient are shown in table 1.

Discussion

IVMs are benign lesions⁸ secondary to congenital errors in vascular morphogenesis¹⁰ that infiltrate the muscle thickness¹¹. There are few reports on the epidemiology of vascular malformations in general, but



Figure 1. Discrete increase in volume in the distal third of the left thigh.

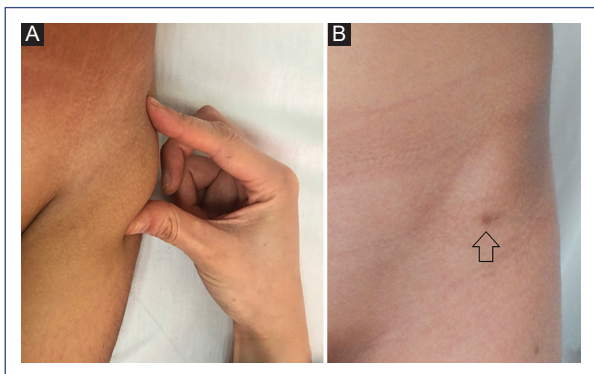


Figure 2. A: increase in volume observed on the lateral aspect of the left hip before sclerotherapy. **B:** after treatment with sclerotherapy, only a post-inflammatory hyperpigmented spot is observed at the puncture site.

they are estimated to have an incidence of 1.2%¹²; IVMs are estimated to comprise 0.8%- < 1% of all vascular malformations^{13,14}. In our institute, they accounted for 1.43% of all cases of vascular malformations during the study period, likely attributed to our status as a referral center with a specialized clinic in vascular malformations, which facilitated their diagnosis.

The most frequent sex was female (71.4%), as described in the literature^{4,7,8}. Although vascular

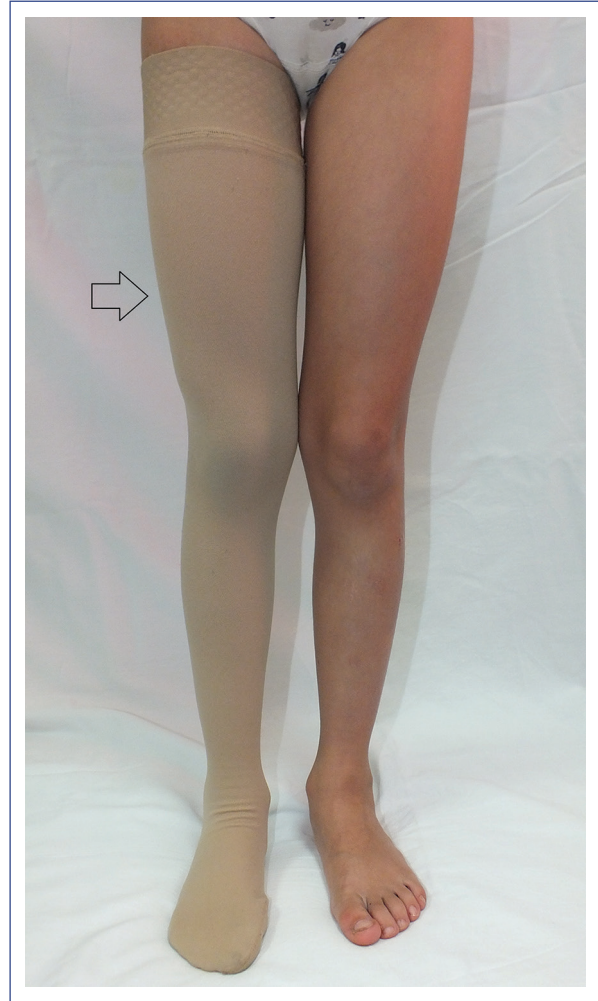


Figure 3. Discrete increase in volume in the distal third of the right thigh. A custom compression stocking is visible as part of the home treatment.

anomalies are present at birth, only 25% are evident at that time^{15,16}; in our series, only 1 (14.3%) case is presented at birth. The remaining 75% manifest between the first and third decades of life^{15,16}; however, in our study, the mean age of disease onset was 5.28 years. It is reported in the literature that clinical presentation starts during adolescence or early adulthood^{6,17} due to increase in volume secondary to the effect of hormonal factors on blood vessels¹⁰. However, IVMs can also appear after trauma, as in three of the patients in our series, or after an infection¹⁰.

IVMs typically present with pain as the initial or distinctive symptom or with swelling; they can be significant enough to limit physical activity^{17,18}. In all our patients, the reason for consultation was swelling, which can be secondary to vascular congestion due to

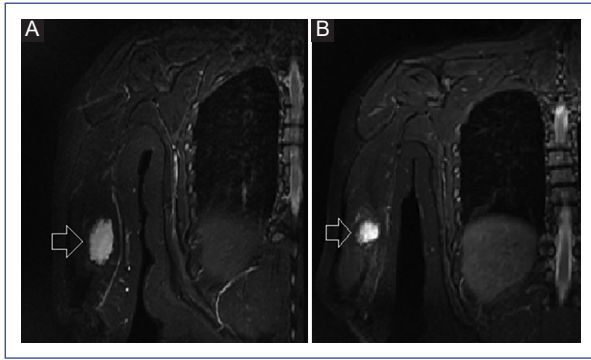


Figure 4. Magnetic resonance images in short-TI inversion recovery sequence. **A:** coronal view of the right arm showing an ovoid image with lobulated edges and hyperintense signal on T2 at the level of the triceps muscle. **B:** comparative study after sclerotherapy showing a significant decrease in size.

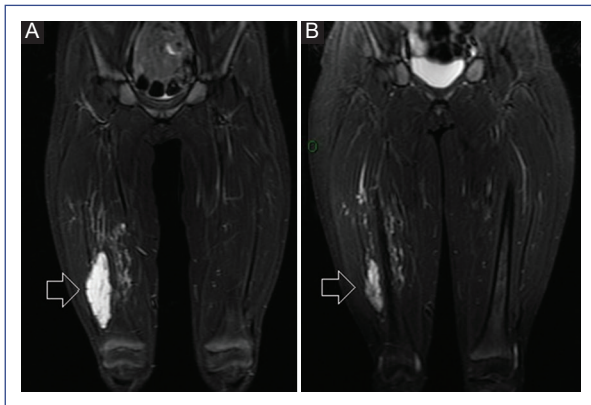


Figure 5. Magnetic resonance images in short-TI inversion recovery sequence. **A:** coronal view of the left thigh showing a fusiform image with lobulated edges and hyperintense signal at the level of the vastus lateralis and intermedius muscles. **B:** comparative study after sclerotherapy showing a significant decrease in size.

movement^{3,13}. About 57.1% presented with pain, a symptom that has been reported in the literature in up to 50-80% of patients^{8,17}, as a consequence of microthrombus formation at rest^{4,19} and due to the diffuse and infiltrative growth of IVMs along the longitudinal axis of the muscle that follows and compresses neurovascular bundles¹⁷. Moreover, the pain can be even more intense if found in long and narrow muscles, as in all our patients, and even if they are relatively small, they can cause intense pain¹³.

The most frequent type of malformation in the presented patients was venous, representing 42.8% of

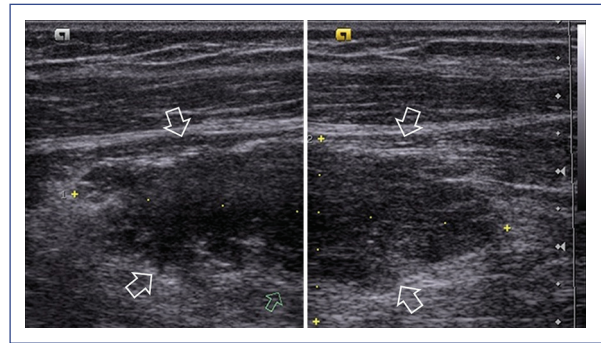


Figure 6. Gray scale ultrasound image of the muscular plane of the right arm showing an ovoid image with markedly lobulated edges and hypoechoic appearance.

cases, similar to the 40% reported in the literature^{15,17}. The most frequently affected topography was the lower extremities, of which the thigh was the most common region, as in the case series reported by Scorletti et al.⁷, and differs from what was reported by Wieck et al., where the lower portion of the leg was the most affected¹⁷.

In 71.4% of patients, the initial suspicion coincided with the final diagnosis, while in other reports, only 8-15% coincided¹⁴. This higher concordance may be due to the fact that in our institute, we have the multidisciplinary VAC composed of Dermatology, Interventional Radiology, and Oncological Surgery services (among others), with whom doctors from different subspecialties have contact, increasing their knowledge, and improving their diagnostic skills.

The first study requested in 71.4% of cases was ultrasound, which is recommended to identify the location (superficial or deep), nature (cystic or solid), and flow (null, low, or high) of IVMs^{4,8}, and it should always be complemented with a contrast-enhanced magnetic resonance imaging (MRI) for precise characterization of its extension and relationship with other adjacent vital structures, such as the neurovascular bundle^{4,18,20}.

The characteristic radiological findings on ultrasound are well-defined, fusiform or oval masses, lobulated or septated, of variable echogenicity, arranged along the muscle fibers, thus having a hypoechoic appearance, and whose flow in Doppler mode depends on their etiology⁴. Regarding MRI, they are described as well-defined intramuscular masses, oval-shaped, multiseptated, as they are composed of vascular channels oriented longitudinally to the muscle fibers, markedly hyperintense on T2, and with Gadolinium administration, in the late phases, the enhancement becomes more intense and

Table 1. Main demographic, clinical, radiological characteristics and response to treatment of reported cases

Case no.	Age (years, months)	Sex	Reason for consultation (age at onset)	Topography	Symptoms	Diagnosis		Imaging study	Radiological finding	Affected muscle(s)	Affected vessel	Treatment (quantity of procedure)	Response to treatment
						Initial (Service that made the diagnosis)	Final at VAC (age at diagnosis)						
1	9y 1m	M	Increased volume (7d)	Right thigh distal third	Asymptomatic	Intramuscular hemangioma (Oncologic Surgery)	VM (4 m)	US, contrast MRI	Dilated and tortuous vascular structures	Rectus anterior and vastus lateralis of quadriceps	Vein	Surveillance	No progression ^a
2	16y 10m	M	Increased volume (9y 3m)	Right thigh distal third	Pain when walking	Prob. Synoviooma vs VM (Orthopedics)	VM (11y 2 m)	Contrast CT	Multiple dilated tortuous veins with abnormal paths that cause a significant increase in volume	Vastus lateralis of quadriceps	Vein	Sclerotherapies with polidocanol 3% (6)	Partial pain reduction
3	18 y	F	Increased volume post-trauma (11y)	Right arm, distal third	Pain, paresthesias	Lipoma vs Myositis ossificans (Orthopedics)	VM (15y 3m)	US, contrast MRI	Multifoliated lesion of 43 x 11 mm, hyperintense on T2	Triceps (N/S)	Vein	Surgical resection (2) Sclerotherapy with polidocanol 3% (1), aspirin and rehabilitation	Total pain reduction
4	15y 3m	M	Increased volume, post-trauma (6y)	Left thigh distal third	Pain	Prob. VM (Dermatology)	VLM (8y 8m)	US, contrast MRI	Anechoic areas with tortuous appearance showing vascular flow	Vastus internus of quadriceps	Vein and lymphatic	Sclerotherapies with polidocanol 3% (6), aspirin, rehabilitation	Size reduction (100%), partial pain improvement
5	8y 8 m	F	Palpable tumor (1y 11m)	Right thigh, distal third	Asymptomatic	Prob. LM (Oncology)	VLM (3y)	US	Fusiform image of 3.8 x 1.2 cm, with fine and coarse echoes inside suggesting the presence of septa and without vascular flow	Vastus medialis of quadriceps	Vein and lymphatic	Sclerotherapy with polidocanol (4), Sirolimus ^b , Sclerotherapy with bleomycin (4)	Partial improvement of pain, resolution of CIL
6	17 y 9m	M	Increased volume (0y 0m)	Left buttock and thigh	Asymptomatic	LM in gluteus (Oncological Surgery)	LM (14y 4m)	Contrast MRI	Heterogeneous multicompartmental lesion, with cystic areas and reticular component of soft tissues, with intense and heterogeneous enhancement with Gadolinium	Gluteus maximus and vastus lateralis of quadriceps	Lymphatic	Surgical resection ^c , Sirolimus	100% pain reduction
7	15 y 2 m	M	Increased volume, post-trauma (12y)	Left thigh, distal third	Intermittent pain	Prob. LM (Dermatology)	LM (13y 8m)	US, contrast MRI	Serpiginous hypoechoic lesion that does not affect bone	Vastus intermedius and lateralis of quadriceps	Lymphatic	Sclerotherapy with bleomycin (3), Sirolimus	Partial improvement of pain

^aLost to follow-up.
^bSirolimus was suspended due to adverse effects.
^cPerformed before being known in the Vascular Anomalies Clinic.
y: years; m: months; d: days; M: male; F: female; Prob: probable; LM: lymphatic malformation; VM: venous malformation; VLM: venolymphatic malformation; VAC: vascular anomalies clinic; US: ultrasonography; MRI: magnetic resonance imaging; CT: computed tomography; N/S: not specified.

homogeneous⁴. This is an important clue for diagnosis, as this phenomenon is explained by the relative isolation from systemic venous circulation, which limits the passage of contrast to these low-flow lesions⁴. All our patients presented some or several of the findings described above.

There is no precise algorithm for choosing the treatment of IVMs¹⁷; it depends on the location, size, extent, and associated symptomatology^{17,21}. Treating vascular malformations, in general, can be challenging and should be approached by a multidisciplinary team^{20,22}. Regarding the treatment of our patients, two had an initial surgical resection with partial clinical improvement. Some authors report that these patients with IVM frequently undergo multiple surgical procedures that generally result in little improvement or even worsening of symptoms by damaging functional muscles^{20,23}. However, it has also been reported that surgery can be effective in combination with medical treatment or sclerotherapy¹⁷. In well-defined malformations that measure < 5 cm or that only affect a single muscle, surgery, even as monotherapy, can improve movement, quality of life, and radiological image more effectively than isolated sclerotherapy^{21,24}.

The rest of the patients were referred to the VAC to offer them the best therapeutic option agreed upon by an experienced team, thus reducing morbidity and improving quality of life. Sclerotherapy is considered the first-line treatment, and an average of 2-6 sessions may be required^{7,15,17}. However, in our series, only one patient required up to 8 sessions due to the appearance of an IVM in the same affected segment. 82-94% success rate has been reported¹⁴, especially in reducing pain. In our study, 57.1% had partial improvement, and 28.6% had total pain resolution, similar to those found by Crawford et al. (57.9% and 21.1%, respectively)^{21,25}. However, in other studies, such as Bianchini et al., pain improvement of up to 88.9% was reported, although most were large venous malformations, which generally have a better response¹⁵.

Regarding medical treatment²⁶, it has been reported that sirolimus directly inhibits mTOR (mammalian target of Rapamycin), a serine/threonine protein kinase, part of the PI3K/Akt/mTOR pathway, which acts as a master switch in numerous cellular processes, such as cell proliferation and growth, as well as angiogenesis and lymphangiogenesis^{27,28}. Up to 92% of patients treated with sirolimus show a decrease in size, especially in LMs, and improvement in pain, particularly in mixed malformations, as well as a decrease in bleeding and improvement in their quality of life^{28,29}. In general, the

response is evident after 2 months of treatment, and as such, the optimal duration of treatment has not been established²⁹. The suggested dose is 0.8 mg/m²/dose twice daily³⁰. In our case series, four of our patients were treated with sirolimus, either because they were not candidates for initial surgical treatment or sclerotherapy (patient 6) or because they persisted with pain or swelling despite having had surgical treatment or sclerotherapy (patients 4, 5 and 7). All patients showed improvement in pain and continued treatment for up to 2 years, except for patient 5, whose treatment was suspended due to hypertriglyceridemia and recurrent infections, which have been described as the most frequent adverse effects²⁶.

Possible limitations of this study include referral bias, as ours is the only clinic of its kind in the country, and those limitations inherent to a retrospective study. However, studying the clinical manifestations, radiological characteristics, evolution, treatment, and therapeutic response of this group of seven patients with such a rare condition allows for the generation of valuable knowledge for the medical community caring for the pediatric population.

Conclusion

In our pediatric population with IVM, lower limb involvement was found more frequently, and the main symptoms were exertional pain and swelling. Diagnosis can be difficult; it is important not only to suspect them but also to identify and characterize them with the support of imaging studies. Treatment is challenging given the extent and depth of the lesions; a multidisciplinary team should carry out their care and follow-up, and the combination of therapeutic modalities (surgery and sclerotherapy) may be necessary to obtain the best outcome for patients.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author has this document.

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Conflicts of interest

The authors declare no conflicts of interest.

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