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ORIGINAL ARTICLE

Comprehensive review of fibroadipose vascular anomaly cases at a multidisciplinary vascular anomalies center

Revisión exhaustiva de los casos de anomalía vascular fibroadiposa en un centro multidisciplinario de anomalías vasculares

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Abstract

Background: *Fibroadipose vascular anomaly (FAVA), was first described in 2014 by Alomari. This is an intramuscular lesion predominantly affecting the lower extremities; and histologically, this is characterized by dense fibrous tissue, abundant adipose content, and dilated venous channels within muscle. We described our experience with these rare anomalies.* **Methods:** *This retrospective study reviewed 29 patients diagnosed between 2013 and 2023, including clinical, imaging, histopathological, and genetic assessments.* **Results:** *The cohort comprised 10 males and 19 females aged 6-45 years. Lower limb involvement occurred in 20 cases (13 gastrocnemius, seven thigh), upper limb in six, and trunk in three. No cutaneous involvement was observed, though all cases presented with limb or segmental enlargement; two showed phleboliths on MRI. Histopathology demonstrated fibroadipose tissue with dilated venous vessels.* **Conclusions:** *FAVA diagnosis is straightforward when clinical, radiologic, and histopathologic findings are integrated. Increased awareness may reduce misdiagnosis. Surgical resection remains an effective therapeutic option, providing pain relief and potential cure in selected cases.*

Keywords: *Fibro-adipose vascular anomaly. Vascular malformations/therapy. Vascular malformations/surgery. Vascular diseases/complications. Pain. Treatment outcome.*

Resumen

Antecedentes: *La anomalía vascular fibroadiposa (FAVA), descrita por primera vez en 2014 por Alomari. Esta es una lesión intramuscular que afecta predominantemente las extremidades inferiores. Histológicamente se caracteriza por tejido fibroso denso, abundante contenido adiposo y canales venosos dilatados dentro del músculo. Describimos nuestra experiencia con estas anomalías poco frecuentes.* **Métodos:** *Este estudio retrospectivo revisó a 29 pacientes diagnosticados entre 2013 y 2023, incluyendo evaluaciones clínicas, de imagen, histopatológicas y genéticas.* **Resultados:** *La cohorte incluyó 10 varones y 19 mujeres, de 6 a 45 años. La afectación de extremidades inferiores se observó en 20 casos (13 en gastrocnemio, siete en muslo), de extremidades superiores en seis y del tronco en tres. No se observó compromiso cutáneo, aunque todos presentaron aumento de volumen; dos casos mostraron flebolitos en resonancia magnética. El estudio histopatológico evidenció tejido fibroadiposo con vasos venosos dilatados.* **Conclusión:** *El diagnóstico de FAVA es claro al integrar hallazgos*

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clínicos, radiológicos e histopatológicos. Una mayor concienciación puede reducir errores diagnósticos. La resección quirúrgica es una opción terapéutica eficaz que proporciona alivio del dolor y puede ser curativa en casos seleccionados.

Palabras clave: *Anomalías vasculares. Malformaciones vasculares/cirugía. Malformaciones vasculares/terapia. Enfermedades vasculares/complicaciones. Dolor. Resultado del tratamiento.*

Introduction

The management, diagnosis, and treatment of vascular anomalies pose significant challenges in clinical practice. The overlapping clinical presentations, similar imaging findings, and the relatively small number of cases often complicate reaching accurate diagnoses. In 2014, Alomari et al. introduced the concept of fibroadipose vascular anomaly (FAVA)[1] after conducting a retrospective review of 16 patients. FAVA was characterized as an intramuscular anomaly exhibiting well-defined clinical, radiological, and histopathological features.

According to the classification of vascular anomalies by the International Society for the Study of Vascular Anomalies (ISSVA)[2], last reviewed in 2018, vascular anomalies are categorized into vascular tumors and vascular malformations, which can be simple, combined, involving major vessels, or associated with other anomalies. While FAVA is recognized as a distinct entity, it remains provisionally unclassified within this system.

FAVA constitutes a malformation characterized by intramuscular fibrofatty infiltration and slow-flowing malformations, predominantly venous but also lymphatic. This anomaly predominantly affects the extremities and is commonly observed in young patients. Imaging typically reveals a soft-tissue lesion with a muscular epicenter, frequently localized in the lower extremities. Patients often experience severe pain and contractures. Histologically, FAVA is characterized by dense fibrofatty tissue and lymphoplasmacytic infiltration of skeletal muscle, along with a variable number of venous channels. Alomari et al. noted that long-term symptom control in FAVA is challenging with non-operative management[1]. Sclerotherapy, typically the first-line therapy for other anomalies, is ineffective due to the fibrofatty component. Based on the hypothesis that FAVA may result from a somatic activating mutation in PIK-3CA, Erickson et al. reported successful treatment of two patients with sirolimus[3]. Cryoablation has also been reported as useful in 20 patients. However, Alomari et al. advocated for surgery as the optimal treatment choice. Wang et al. recently presented a retrospective series of 35 patients who underwent excision of lower-extremity FAVA, demonstrating that surgery can be curative in focal FAVAs contained within resectable muscles without neural involvement[4].

The aim of this study is to present a series of patients diagnosed with FAVA at a Spanish vascular anomalies' unit, delineating their diagnostic features and treatment approaches.

Methods

We present a retrospective series comprising 29 patients diagnosed with FAVA at a specialized vascular anomalies unit between 2013 and 2023.

The unit operates under a multidisciplinary framework, established by the Departments of Angiology and Vascular Surgery and Pediatric Surgery. These departments oversee patient selection, management, and follow-up. Weekly meetings are held to discuss and determine the optimal approach for each patient. In addition, other Departments, including Vascular and Interventional Radiology, Genetics, and Pathology, contribute to the diagnostic and treatment processes as needed.

During the study period, FAVA accounted for 6% of all diagnosed anomalies within the unit. Patients were often referred with a range of preliminary diagnoses, such as angioma, hemangioma, or venous malformation (VM).

Medical records, radiological imaging, histopathological studies, surgical interventions, and patient outcomes were reviewed comprehensively. Diagnosis relied on clinical evaluation, magnetic resonance imaging (MRI), and ultrasound imaging, complemented by operative and histopathological findings.

Inclusion criteria encompassed: (1) Diagnosis of FAVA by the interdisciplinary team of the vascular anomalies unit, adhering to the description outlined by Alomari et al. (2) Availability of clinical tests, radiological data, histopathological, and genetics reports for follow-up assessment.

Results

Clinical characteristics

Among the 29 patients, there were 10 males and 19 females, with ages ranging from 6 to 45 years at the time of diagnosis (median: 21 years). The majority of patients (n = 22) were under 30 years old. Most patients had no significant medical history (n = 26), although one patient had Poland Syndrome presenting with

agenesis of the left pectoralis major and pectus excavatum, and two others were obese (Table 1).

Lower limb involvement was predominant, with 20 cases observed, including 12 in the gastrocnemius, one in the soleus, and seven in the thigh. In addition, there were six cases involving the upper limbs and three cases affecting the body trunk (Table 2).

Pain was the most common symptom, with six patients requiring analgesic treatment from the second and third steps of the World Health Organization analgesic ladder, and one patient was using a neuro stimulator to reduce the pain. Significantly increased limb girth was noted in all cases (Fig. 1), and limited mobility was observed in four patients. Skin was not involved in any of the cases (Table 3).

Ten patients had undergone prior treatments such as sclerotherapy or embolization, with one patient having undergone internal saphenectomy for varicose veins in the same extremity affected by the anomaly. Most of these patients had been treated several times.

Pre-operative analysis revealed increased D-dimer levels in eight out of fourteen patients.

Table 1. Patient demographics

Variables	Patients (n = 29)	Percentage
Sex Female	19	65.52%
Age	6-45 years	Median 21 years
Poland syndrome	1	3.4%
Obesity	2	6.89%

Table 2. Patient affectation distribution

Localization	Patients (n = 29)	Percentage
Lower extremity	20	68.97
Leg	13	44.83
Thigh	7	24.14
Upper extremity	6	20.69
Forearm	3	10.34
Arm	3	10.34
Trunk	3	10.34

FAVA: fibroadipose vascular anomaly.

Imaging findings

Diagnosis was primarily established through MRI and ultrasonography. The size of the anomaly varied widely, ranging from 35 to 170 mm, and no correlation was identified between size and the severity of pain.

During the initial patient visit (18), ultrasonography revealed a hyperechoic intramuscular solid mass with heterogeneous echogenic changes in the fibrillary pattern of the muscle. Large and small veins were observed within the mass, with phleboliths identified in two patients. Color Doppler imaging demonstrated low vascular density in most anomalies (14/18), occasionally enhanced by distal compression. Smaller malformations (4/18) exhibited no intralesional vascularity (Fig. 2). Spectral Doppler analysis typically indicated venous flow, although some anomalies showed absence of flow. MRI was the primary pre-operative imaging modality utilized, with multiple muscle involvement observed in seven patients. Fatty tissue was noted within the intrafascial or intramuscular compartments, occasionally extending into the subcutaneous layer. Affected muscles exhibited high signal intensity on both T1- and T2-weighted images, indicative of adipose tissue, with a higher signal intensity observed on short tau inversion recovery weighted images, suggesting a vascular component (Fig. 3). Osseous changes, including cortical irregularities, were identified in only two patients. Phleboliths were detected in lesions involving the gastrocnemius in two cases.

Operative findings

Surgical resection was the treatment of choice, with 18 patients undergoing the procedure. The remaining patients either had previous treatments, chose alternative therapies, or were asymptomatic/mildly symptomatic and declined surgery. All lesions were completely resected with minimal disruption to affected muscles. Surgery was performed under general anesthesia in most cases, with regional ischemia utilized when feasible. No complications occurred during surgery, and no transfusions were required (Fig. 4).

Histopathological findings

Histopathological analysis uniformly described fibroadipose tissue with multiple dilated vessels, predominantly venous, infiltrating the muscle. Thrombi and phleboliths were present in some samples, and fibrous infiltrating tissue was commonly observed. Nerve involvement was identified in two samples. Genetic testing

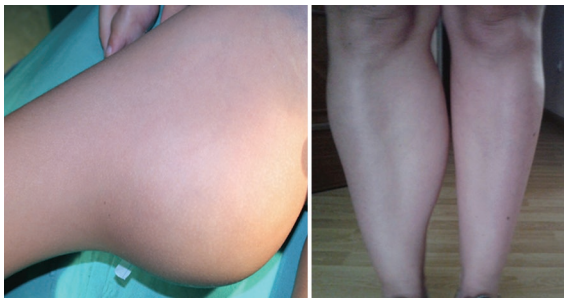

Figure 1. Involvement of the lower limb. Left, enlargement of the thigh with unremarkable skin. Right, enlargement of the right calf.

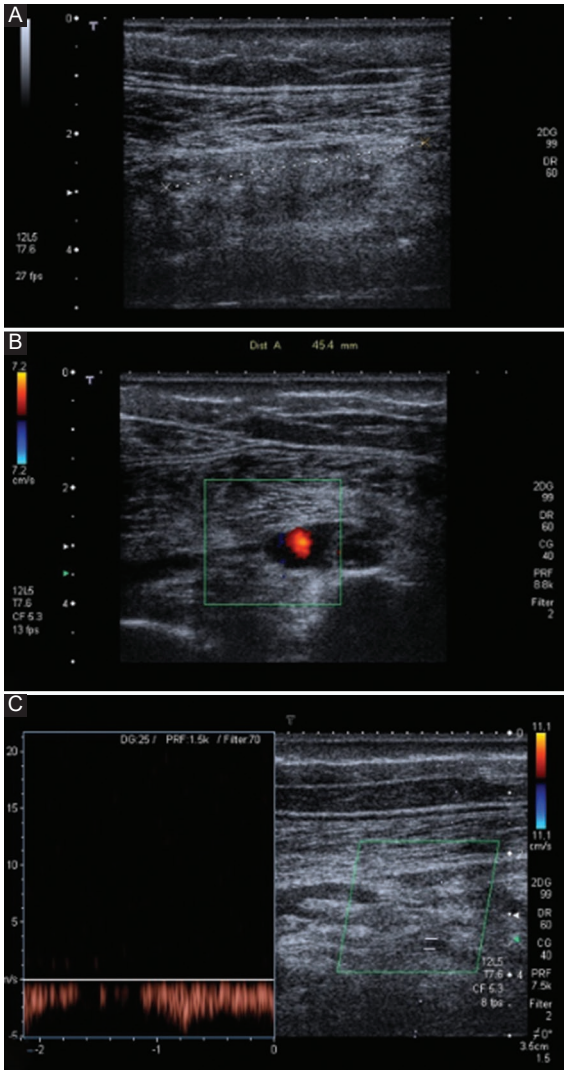

Figure 2. **A:** B-mode shows heterogeneous echogenic changes in the fibrillary pattern of the muscle. **B:** color Doppler revealed low vascular density. **C:** spectral Doppler analysis shows venous flow when we apply distal compression.

for the *PICK3CA* mutations and the relevant genes was positive in two cases.

Medical monitoring

The mean length of hospital stay post-surgery was 2.2 days, with no complications prolonging hospitalization. Most patients were discharged with low-molecular-weight heparin (LMWH) for 4-7 days. Follow-up visits at 1 month and 3-6 months post-surgery revealed improvements in pain, swelling, and functional restriction in all patients. Complications during follow-up included one case of surgical wound infection and dehiscence, managed conservatively, and two cases of deep venous thrombosis, treated with LMWH for 3 months. One patient required reintervention for residual malformation tissue, and no recurrences were reported.

Discussion

Alomari et al. introduced FAVA in 2014, delineating its clinical, radiological, and histopathological features, which include fibrofatty infiltration of muscle, phlebectasia causing pain, and contracture of the affected extremity. Before its identification, cases resembling FAVA were likely misclassified as intramuscular VMs or "cavernous hemangiomas" in the literature.

The ISSVA approved Mulliken and Glowacki's classification system in 1996[5], where FAVA is recognized as a distinct entity but remains provisionally unclassified.

Differential diagnosis (Table 4) with common VM is imperative due to differing management approaches[6]. Distinctive clinical features, such as constant pain in FAVA versus episodic pain in VMs, aid in differentiation. As described by Alomari et al., the etiology of the pain in FAVA patients is probably multifactorial; diffuse pain may be explained by the solid fibrofatty tissue invading the muscle, and focal pain can be caused by venous thrombosis, subcutaneous focal fibrotic lesions, or neurogenic. Skin uninvolved is typical of FAVA, in contrast to the frequent dermal involvement of VM.

Imaging modalities, such as ultrasonography, reveal echogenic solid components in FAVA and hypoechoic components in common VMs. Furthermore, histological examination distinguishes FAVA by the presence of fibrofatty tissue within the muscle, unlike the disorganized dilated vascular channels found in common VMs[7,8].

Accurate identification of FAVA is paramount to avoid unnecessary treatments. Sclerotherapy has limited success due to the dominant fibrofatty component[9], associated with poor pain improvement, prompting

Table 3. Clinical features of FAVA patients

Case	Age	Muscle involved	Other findings	Signs and symptoms	Treatment	Complication
Male	21	Right gastrocnemius	Phleboliths	Pain. Increased limb girth	Resection	
Male	15	Left gastrocnemius		Increased limb girth	Embolization	
Female	21	Left gastrocnemius		Pain. Increased limb girth	Resection	Deep venous thrombosis
Male	10	Left vastus medialis		Pain with mobility. Increased limb girth	Resection	
Male	20	Left semitendinosus		Severe and continuous pain. Increased limb girth	Resection	
Female	31	Left triceps		Pain. Increased limb girth	Resection	
Female	36	Right soleus		Increased limb girth	Refused surgery	
Male	26	Left latissimus dorsi		Severe and continuous pain. Big mass. Increased limb girth	Resection	
Female	29	Right gastrocnemius		Severe pain. Increased limb girth	Resection	
Female	42	Left brachioradialis		Big mass. Increased limb girth	Previous treatment, refused surgery	
Male	18	Left gastrocnemius		Severe pain. Increased limb girth	Resection	
Female	13	Right gastrocnemius		Severe pain, a big mass, and limited mobility. Increased limb girth	Resection	
Female	32	Left major pectoral		Severe pain and limited mobility. Increased limb girth	Resection	
Female	13	Right gastrocnemius		Severe pain. Big mass and limited mobility. Increased limb girth	Resection	Wound infection and dehiscence
Male	11	Right gastrocnemius		Pain. Increased limb girth	Resection	
Female	6	Left gastrocnemius	Phleboliths	Pain. Increased limb girth	Resection	
Female	33	Left deltoid		Pain. Increased limb girth	Refused surgery	
Female	11	Left brachioradialis	Osseous changes	Pain. Increased limb girth	Resection	
Male	23	Right deltoid		Pain with limited mobility. Big mass. Increased limb girth	Waiting list	
Female	41	Left vastus lateralis		Pain. Increased limb girth	Sclerotherapy	Deep venous thrombosis
Female	38	Left gastrocnemius		Pain. Increased limb girth	Previous treatment, refused surgery	
Female	28	Right biceps femoris		Severe pain. Increased limb girth	Resection	
Male	16	Right rectus femoris		Pain. Increased limb girth	Resection	
Male	27	Left infraspinatus		Pain. Increased limb girth	Resection	
Female	29	Left gastrocnemius		Pain. Increased limb girth	Refused surgery	
Female	18	Right flexor digitorum profundus		Increased limb girth	Refused surgery	
Female	14	Left rectus femoris		Pain. Increased limb girth	Resection	
Female	9	Right adductor magnus		Severe pain and limited mobility. Increased limb girth	Refused surgery	
Female	21	Right gastrocnemius		Pain. Increased limb girth	Refused surgery	

FAVA: fibroadipose vascular anomaly.

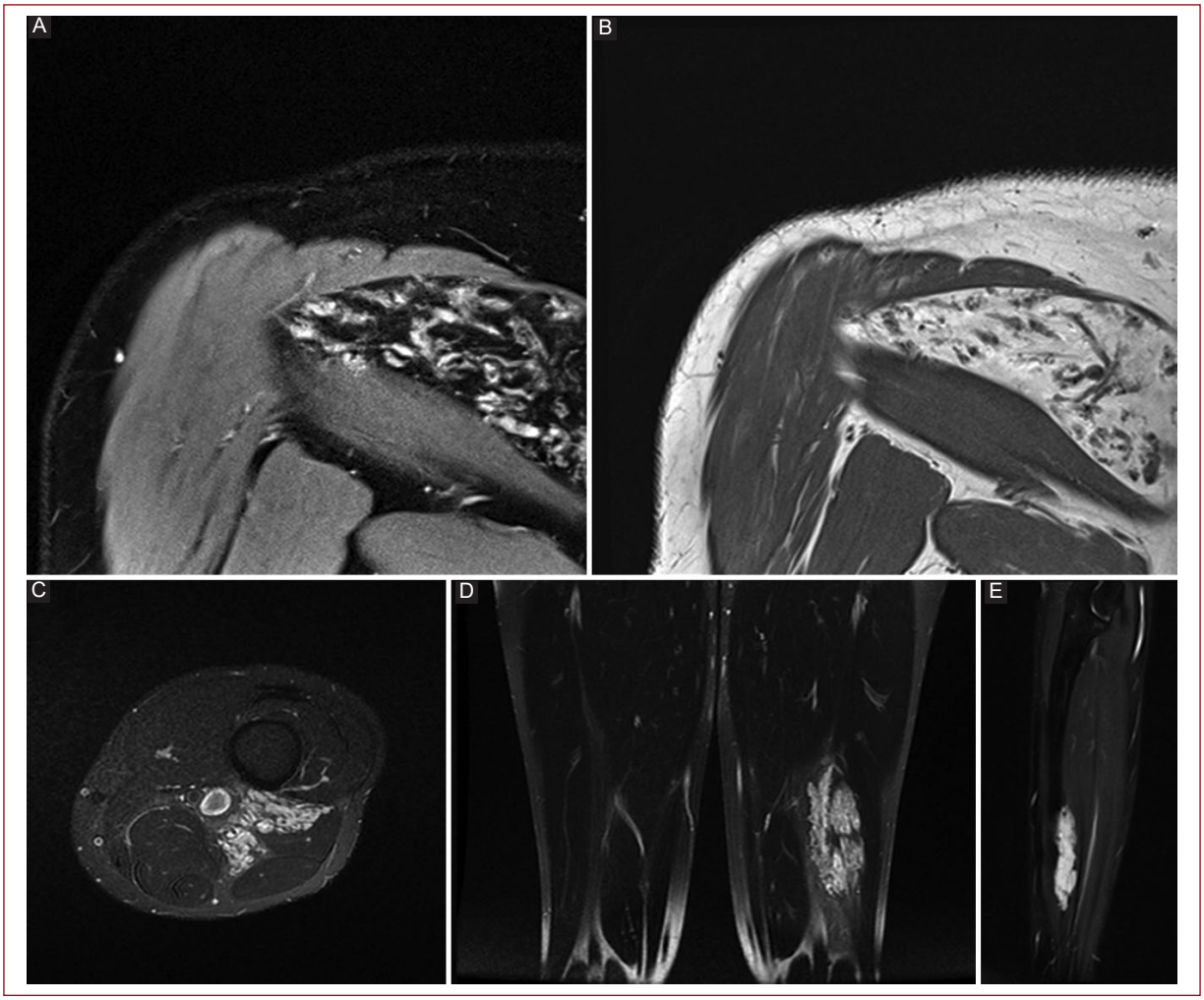

Figure 3. **A** and **B**: fibroadipose vascular anomalies involving the deltoid, **C:** the vastus lateralis, **D:** the gastrocnemius, **E:** the right flexor digitorum profundus.

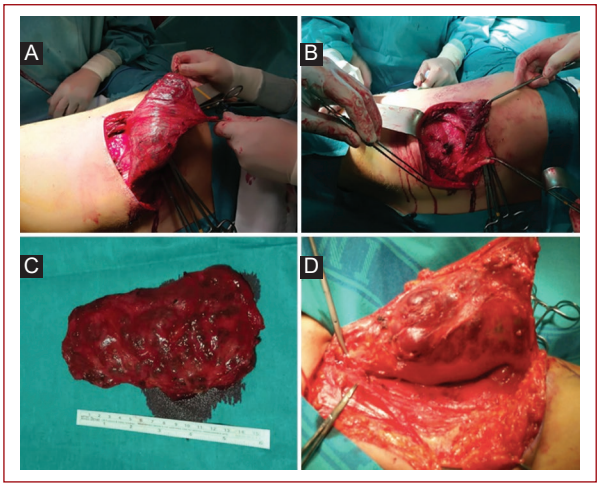

Figure 4. **A-C:** fibroadipose vascular anomaly in a patient affecting the latissimus dorsi muscle. **D:** fibroadipose vascular anomaly placed in the trunk.
Left infraspinatus muscle affected.

surgical resection as the preferred option for long-term symptom control.

Percutaneous cryoablation, a newly described technique, shows promise in providing pain relief and reducing morbidity[9].

In our experience and literature, surgical resection proved efficacious with low morbidity, likely due to predominantly focal or focal infiltrative lesion patterns. However, limitations include the retrospective nature of our study and incomplete data collection due to patients coming from across the country.

Notably, our findings diverge from some literature, with less pronounced female predominance and lower rates of limb dysfunction. We also noticed that our patients were older than those described by Alomari et al.; this could be explained because we collected the age at diagnosis in our center and not the age at which they presented their first symptoms.

Table 4. Differential features of FAVA versus common VM

Features	FAVA	Common VM
Pain	Constant Disproportionately severe	Episodic
Contracture	Common	Typically, absent
Skin	Frequently uninvolved	Frequent
Ultrasonography	Echogenic solid component with slow flow on Doppler exploration	Hypoechoic component with slow vascular flow on Doppler exploration
MRI	Solid Adipose tissue component in the muscle Occasional phleboliths	Fluid High vascular component Common phleboliths
Histopathology	Fibrosis Fat The lymphatic component is occasionally present Echogenic solid component with slow flow on Doppler exploration	Vessels The lymphatic component is typically absent Echogenic solid component with slow flow on Doppler exploration

FAVA: fibroadipose vascular anomaly; MRI: magnetic resonance imaging; VM: venous malformation.

Genetic analysis in our study was positive for *PIK3CA* in two patients, whereas literature suggests somatic mosaic *PIK3CA* mutations[10,11] or PTEN involvement in most FAVA patients[12], highlighting the need for further investigation into genetic underpinnings and refining diagnostic and treatment strategies for FAVA.

Conclusion

To our knowledge, this study represents the first documentation of a series of FAVA cases in Europe, and one of the largest series worldwide since its initial publication by Alomari et al. in 2014.

Managing vascular malformations remains a complex challenge. The diagnosis of FAVA is straightforward when clinical, radiologic, and histopathologic features are considered. Increased clinical awareness of this disease can help reduce misdiagnoses. Surgical management generally has low morbidity, can alleviate pain, and may be curative in some cases. The identification of new vascular entities with well-defined clinical, radiological, and histopathological characteristics is essential for refining our approach to these conditions.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed the confidentiality protocols of their institution, obtained informed consent from the patients, and have approval from the Ethics Committee. The recommendations of the SAGER guidelines have been followed, according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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