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PICTORIAL ESSAY

Imaging of vascular tumors with an emphasis on ISSVA classification

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Abstract The International Society for the Study of Vascular Anomalies (ISSVA) classification is becoming the international standard classification system for vascular tumors and vascular malformations. The ISSVA classification strictly distinguishes vascular tumors (neoplastic lesions) from vascular malformations (non-neoplastic lesions) based on whether there is a proliferation of vascular endothelial cells present, and it is an extremely useful classification system for determining therapeutic measures. For vascular tumors, it is clinically significant in terms of discriminating infantile hemangioma and rapidly involuting congenital hemangioma, which are expected to spontaneously regress, from other vascular tumors requiring treatment. Needless to say, clinical courses are important for diagnosis, and it is also important for radiologists to understand imaging findings on vascular tumors because such tumors have unique findings on diagnostic images. In this paper, vascular tumors are classified based on the ISSVA classification, and clinical and imaging findings are reviewed.

Keywords Vascular tumors · Hemangioma · ISSVA classification

Introduction

Vascular tumors and malformations may occur at any site in the body, and various specialists from different fields treat them depending on the location of occurrence. Traditionally, different names have been applied in describing these lesions, resulting in confusion. In the WHO classification, two sections are related to vascular tumors and malformations: "bone and soft tissue tumors" and "skin tumors" (Tables 1, 2) [1]. The term "hemangioma" in these descriptions includes both vascular neoplasms and malformations in the WHO classification.

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Table 1 WHO classification of vascular tumors of soft tissue and bone

Benign	Hemangiomas
	Synovial hemangioma
	Intramuscular angioma
	Venous hemangioma
	Arteriovenous malformation/hemangioma
	Epithelioid hemangioma
	Angiomatosis
	Lymphangioma
Intermediate	Kaposiform hemangioendothelioma
	Retiform hemangioendothelioma
	Papillary intralymphatic angioendothelioma
	Composite hemangioendothelioma
	Kaposi sarcoma
	Pseudomyogenic hemangioendothelioma
	Other intermediate vascular neoplasms
Malignant	Epithelioid hemangioendothelioma
	Angiosarcoma of soft tissue

Table 2 WHO classification of vascular and lymphatic tumors of skin

Vascular tumors	Hemangioma of infancy
	Cherry hemangioma
	Sinusoidal hemangioma
	Hobnail hemangioma
	Glomeruloid hemangioma
	Microvenular hemangioma
	Angiolymphoid hyperplasia with eosinophilia
	Spindle cell hemangioma
	Tufted angioma
	Bacillary angiomatosis
	Reactive angioendotheliomatosis
	Verrucous hemangioma
	Pyogenic granuloma
	Cavernous hemangioma
	Angiokeratomas
	Arteriovenous hemangioma
	Cutaneous angiosarcoma
Lymphatic tumors	Lymphangioma circumscriptum
	Progressive lymphangioma
	Lymphangiomatosis

In recent years, the ISSVA classification, in which vascular tumors are distinguished from vascular malformations, is gaining traction as the international standard. This classification system distinguishes between vascular tumors and vascular malformations based on whether neoplastic proliferation of vascular endothelial cells is present (i.e. vascular tumors are defined as those having neoplastic proliferation while vascular malformations lack neoplastic proliferation) (Table 3) [2].

Several recent review articles have focused on vascular anomalies, because their diagnosis and treatment has progressed with the advent of new drug therapies such as propranolol and sirolimus. However, these articles include breadth without depth, detailing vascular anomalies overall, including neoplasms and malformations. To the best of our knowledge, no pictorial essay has simply focused on the clinical and imaging features of vascular neoplasms based on the ISSVA classification. This paper outlines the clinical and imaging features of vascular tumors in soft tissues based on the ISSVA classification. We also compare and contrast the ISSVA classification with the classical classification systems, including the latest WHO classification.

ISSVA classification versus classical classification systems

In the WHO classification of tumors of soft tissue and bone (4th edition, 2013), "hemangiomas" include synovial hemangioma, intramuscular angioma, venous hemangioma and arteriovenous hemangioma. They assert that these "hemangiomas" are likely vascular malformations and that the early presentation/congenital nature and pathologic architectural features of "lymphangioma" favor a developmental malformation. On the other hand, the WHO classification of tumors of pathology and genetics of skin tumors (3rd edition, 2006) asserts that the term "cavernous hemangiomas" was erroneously considered neoplastic, when in reality it is a vascular malformation, and "lymphangioma" is either a vascular malformation or a neoplasm. Thus, the term "hemangioma" and "lymphangioma" may refer to either vascular malformations or vascular neoplasms in the latest WHO classifications.

In contrast, the ISSVA classification (1996) is simpler, emphasizing the presence or absence of neoplastic cells (i.e., tumor or malformation). Thus, "venous malformation" refers to a venous vascular anomaly without neoplastic cells and corresponds approximately to "cavernous hemangioma", "venous hemangioma" and "intramuscular hemangioma" in the WHO classification; "capillary malformation" corresponds approximately to "port-wine stain", "hemangioma simplex", and "angiokeratoma" in the WHO classification; and "lymphatic malformation" corresponds approximately to "cystic hygroma" and "cavernous lymphangioma" in the WHO classification. Mixed vascular lesions are represented as well, with "arteriovenous malformation" in the ISSVA classification corresponding to "arteriovenous hemangioma" in the WHO classification. "Infantile hemangioma" and "congenital hemangioma" in the ISSVA classification corresponds

Table 3 ISSVA classification of vascular tumors and malformations

Vascular tumors	Vascular malformations	
Infantile hemangiomas	Slow-flow	Capillary malformation (CM)
Congenital hemangiomas (RICH and NICH)		Port-wine stain
Tufted angioma		Telangiectasia
Kaposiform hemangioendothelioma		Angiokeratoma
Spindle cell hemangioendothelioma		Venous malformation (VM)
Other, rare hemangioendotheliomas (epithelioid, composite, retiform, polymorphous, Dabska tumor, lymphangioendotheliomatosis, etc.)		Common sporadic (VM)
Dermatologic acquired vascular tumors (pyogenic granuloma, targetoid hemangioma, glomeruloid hemangioma, microvenular hemangioma, etc.)		Bean syndrome
		Familial cutaneous and mucosal Venous malformation (VMCM)
		Glomuvenous malformation (GVM) (Glomangioma)
		Maffucci syndrome
		Lymphatic malformation (LM)
	Fast-flow	Arterial malformation (AM)
		Arteriovenous fistula (AVF)
		Arteriovenous malformation (AVM)
	Complex-combined	CVM, CLM, LVM,CLVM, AVM-LM, CM-AVM

Table 4 ISSVA classification versus classical classification

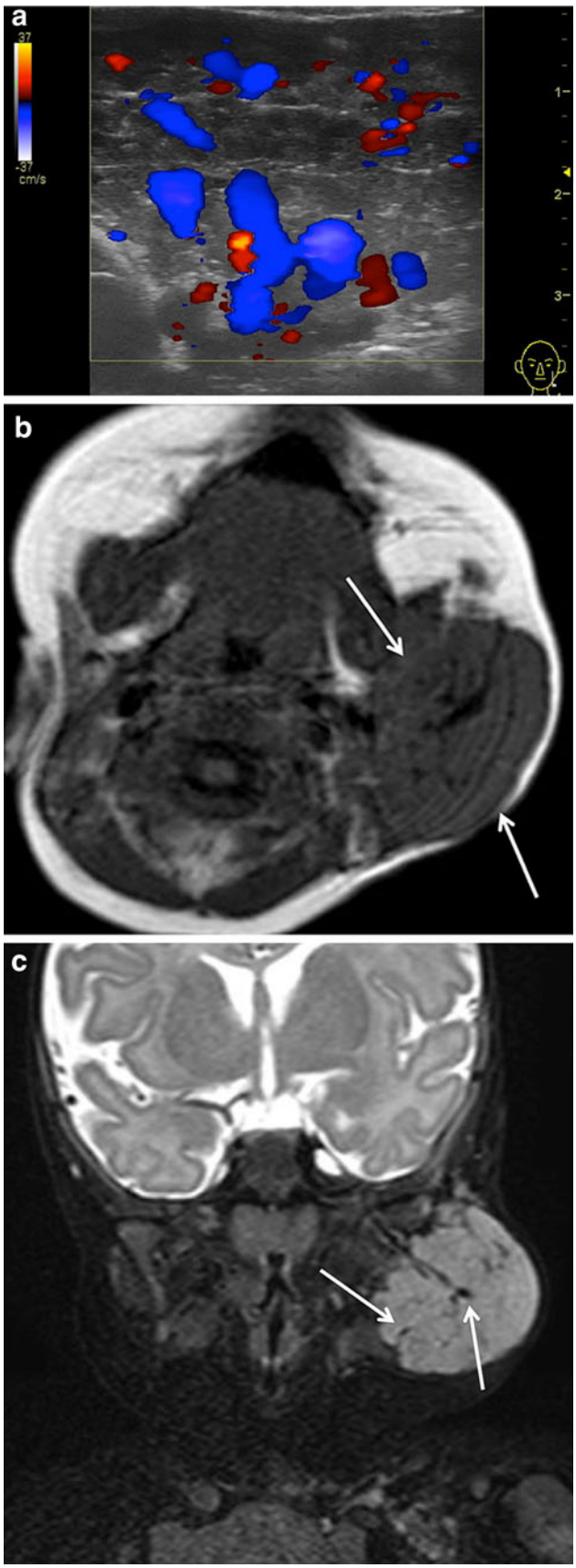
ISSVA classification	Classical classification (including WHO classification)
Vascular tumors	
Infantile hemangioma	Strawberry mark (Cherry hemangioma)
	Hemangioma of infancy
	Capillary hemangioma
Congenital hemangioma	Strawberry mark (Cherry hemangioma)
	Hemangioma of infancy
	Capillary hemangioma
Vascular malformation (High-flow)	
Arteriovenous malformation (AVM)	Arteriovenous hemangioma
Vascular malformation (Slow-flow)	
Venous malformation (VM)	Cavernous hemangioma
	Venous hemangioma
	Intramuscular hemangioma
Capillary malformation (CM)	Port-wine stain
	Hemangioma simplex
	Angiokeratoma
Lymphatic malformation (LM)	Lymphangioma, cystic hygroma, cavernous lymphangioma

approximately to "strawberry mark", "hemangioma of infancy" and "capillary hemangioma" in the WHO classification (Table 4).

Infantile hemangioma (IH)

Infantile hemangioma is the most common benign tumor in neonates and infants. It has a characteristic clinical course in which it rapidly grows after birth (several days to a few weeks after birth) until 12–18 months of age, and then slowly regresses over several years. The former is called "the proliferative phase" and the latter is called "the involuting phase." It is commonly known as a "strawberry mark," the term used in the WHO classification. Histopathologically, it is characterized by positive glucose transporter-1 (GLUT-1) staining. Although superficial lesions are diagnosed easily, diagnostic imaging is required for lesions in deep tissues and intractable alarming hemangioma involving the orbit or the respiratory tract. Interest in this disease has recently increased because it has been reported that beta blockers are highly effective against IH [3].

Imaging findings are different between the proliferative phase and the involuting phase [4]. In the proliferative phase, the pathological findings are the proliferation of vascular endothelial cells and the lobulated mass of tissues, which results in a sharply marginated hypervascular mass radiographically. Low to high echogenicity are observed on ultrasound images and arterial blood flow is seen on color Doppler images (Fig. 1a). On MRI, IHs are well-circumscribed, lobulated masses with isointensity or low intensity on T1-weighted images (Fig. 1b) and relatively uniform



◀ **Fig. 1** Infantile hemangioma in the proliferative phase on the cheek of a 13-month-old boy. **b** Axial T1-weighted MR image shows a well-defined mass, isointense to muscle (*arrows*). **c** Coronal fat-saturated T2-weighted MR image of the neck shows high intensity to muscle with flow voids (*arrows*). **a** Color Doppler US demonstrates arterial flow within a mass

high intensity, with flow voids reflecting arterial blood flow on T2-weighted images and fat suppressed (FS) T2-weighted images (Fig. 1c). On contrast-enhanced MRI, there is vivid staining in the early phase and the staining is maintained until the delayed phase. In the involuting phase, vascular endothelial cells pathologically decrease through apoptosis and are then replaced by fibro-fatty tissues. Reflecting this, decreased arterial blood flow and fat displacement are observed on images (Fig. 2).

Congenital hemangioma (CH)

Congenital hemangioma was first reported by Boon et al. [5] in 1996 as IH-like lesions that presented the peak proliferation or were regressing at birth. It is classified into two types: rapidly involuting CH (RICH), which achieves a complete regression by approximately 12–14 months after birth, and non-involuting CH (NICH), which may partially

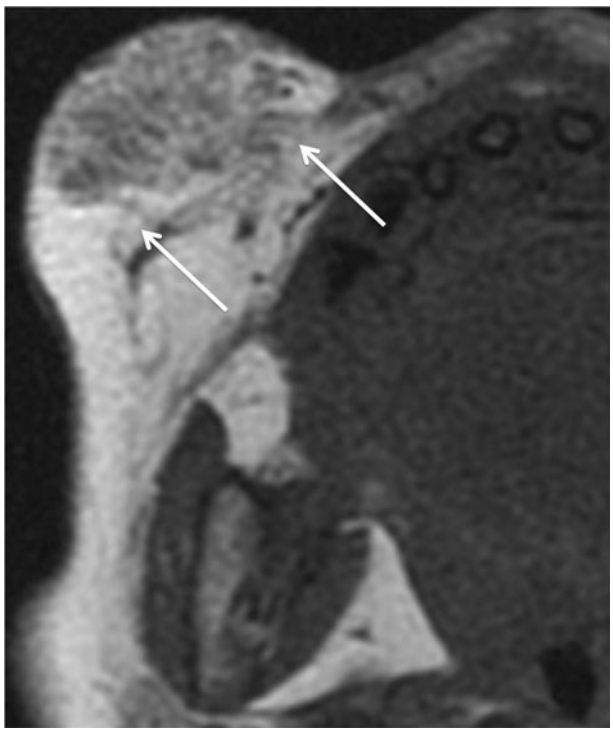


Fig. 2 Infantile hemangioma in the involuting phase on the right mandible of a 2-year-old boy who received laser treatment. Axial T1-weighted MR image shows a mass including loose fibrofatty tissue (*arrows*)

grow but does not regress. Unlike IH, immunostaining with GLUT-1 is negative in vascular endothelial cells. The incidence of CH is unknown but is believed to be low, and the incidence of NICH is believed to be lower than that of RICH. It is difficult to clinically distinguish between RICH and NICH at a given time point, and it is important to monitor the clinical course.

There have been few reports on imaging findings [6, 7]. Imaging findings on CH are basically similar to those on IH, and arterial blood flow is also seen in the mass (Fig. 3a–c). Unlike IH, CH tends to show inhomogeneous parenchyma in the mass with poor margins on ultrasound and MR images and it sometimes shows calcification (Fig. 4a–g). In angiography, aneurysm formation with AV shunt and venous dilatation tend to be obvious.

Kaposiform hemangioendothelioma (KHE)/tufted angioma (TA)

Kaposiform hemangioendothelioma was first reported by Zukerberg et al. [8] in 1993 as a Kaposi's sarcoma-like tumor that occurred in infants. KHE has been reported to occur in infants at birth and aged 10 years and younger in many cases, and reports on adult cases have been increasing recently. It is a locally invasive tumor showing progressive proliferation of vascular endothelial cells with poor margins. It sometimes invades the muscle and bone [9].

Today, tufted angioma is believed to be a subtype of KHE, and is a tumor showing intradermal proliferation of vascular endothelial cells in clusters called "cannon balls." It often develops on the skin and rarely requires diagnostic

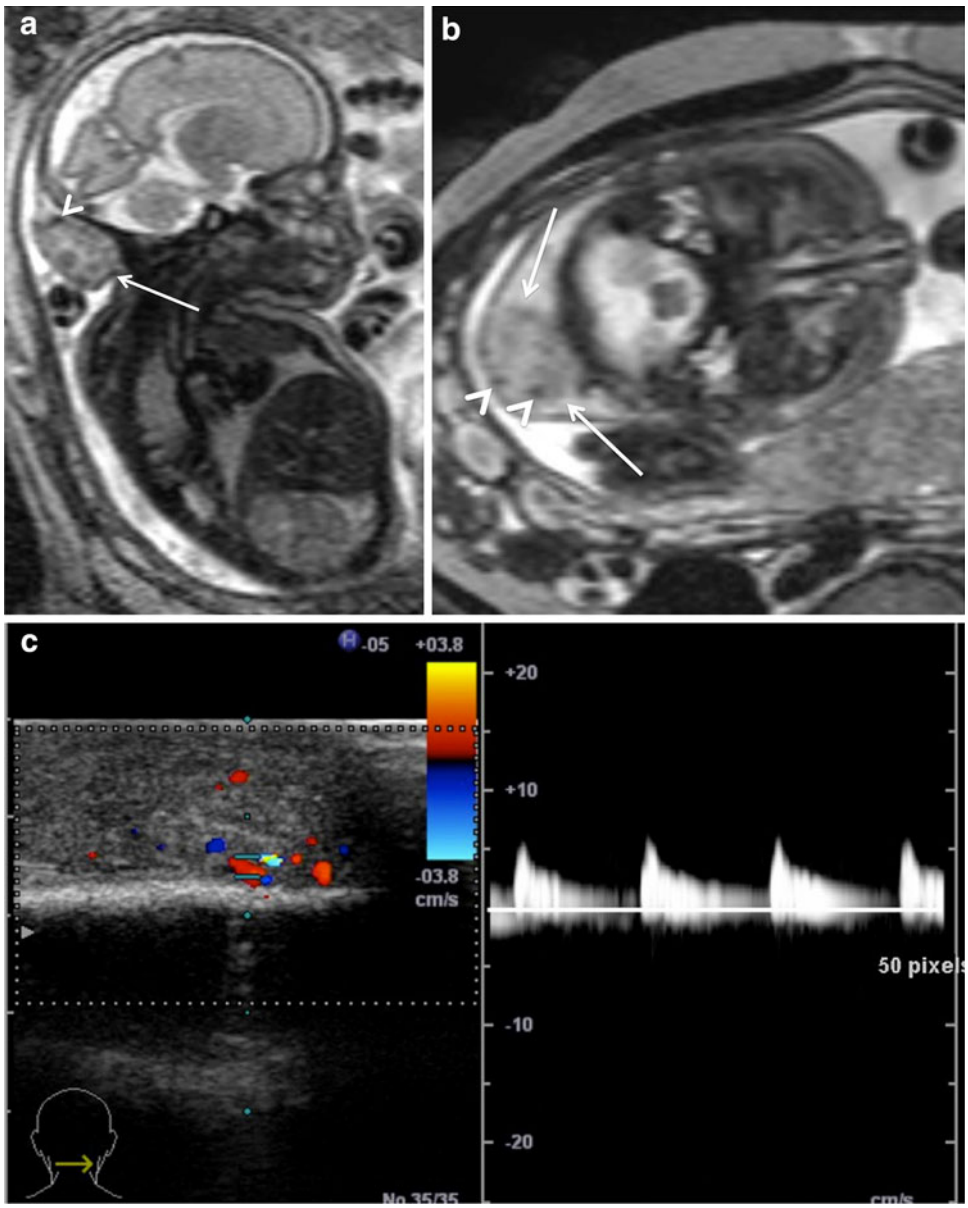


Fig. 3 Rapidly involuting congenital hemangioma (RICH) involving the posterior cervical region. **a**, **b** Sagittal and axial fetal MR images on single-shot FSE sequence show well-defined subcutaneous mass (*arrows*) with flow voids (*arrowheads*) at 29 weeks gestation. **c** Color Doppler US shows arterial flow in the mass. The lesion demonstrated significant involution in 6 months

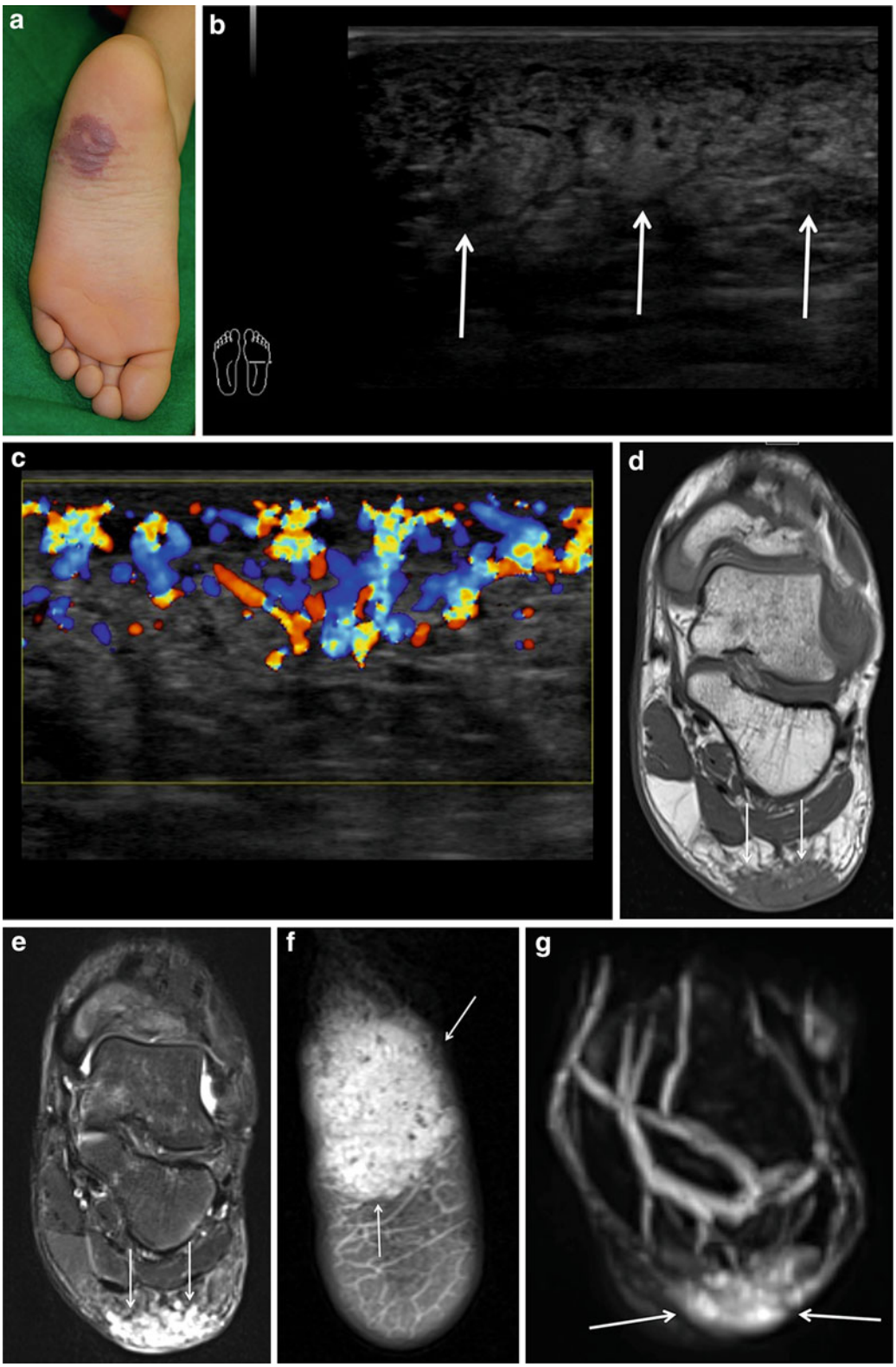


Fig. 4 Non-involuting congenital hemangioma (NICH) in the left sole. **a** A soft-tissue mass with reddish discoloration present since birth in a 12-year-old boy. **b** US shows ill-defined heterogeneous plantar solid mass (*arrows*). **c** Color Doppler US shows hypervascular mass with arterial flow. **d** Coronal T1-weighted MR image shows an ill-defined mass isointense to muscle (*arrows*). **e** Coronal fat-saturated T2-weighted MR image shows high intensity to muscle (*arrows*). **f** Axial fat-saturated contrast-enhanced T1-weighted MR image shows vivid enhancement of the lesion (*arrows*). **g** Time-resolved MR angiogram shows prominent enhancement in the arterial phase (*arrows*)

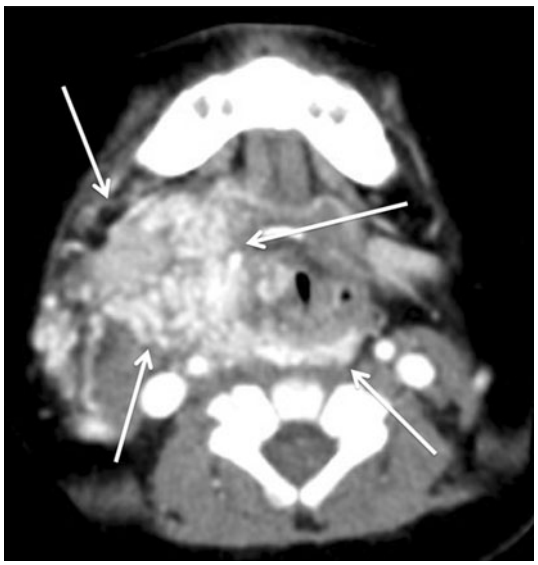


Fig. 5 Kaposiform hemangioendothelioma in a 2-month-old boy with Kasabach–Meritt syndrome. Axial contrast-enhanced CT image shows an ill-defined mass with prominent enhancement in the arterial phase (*arrows*)

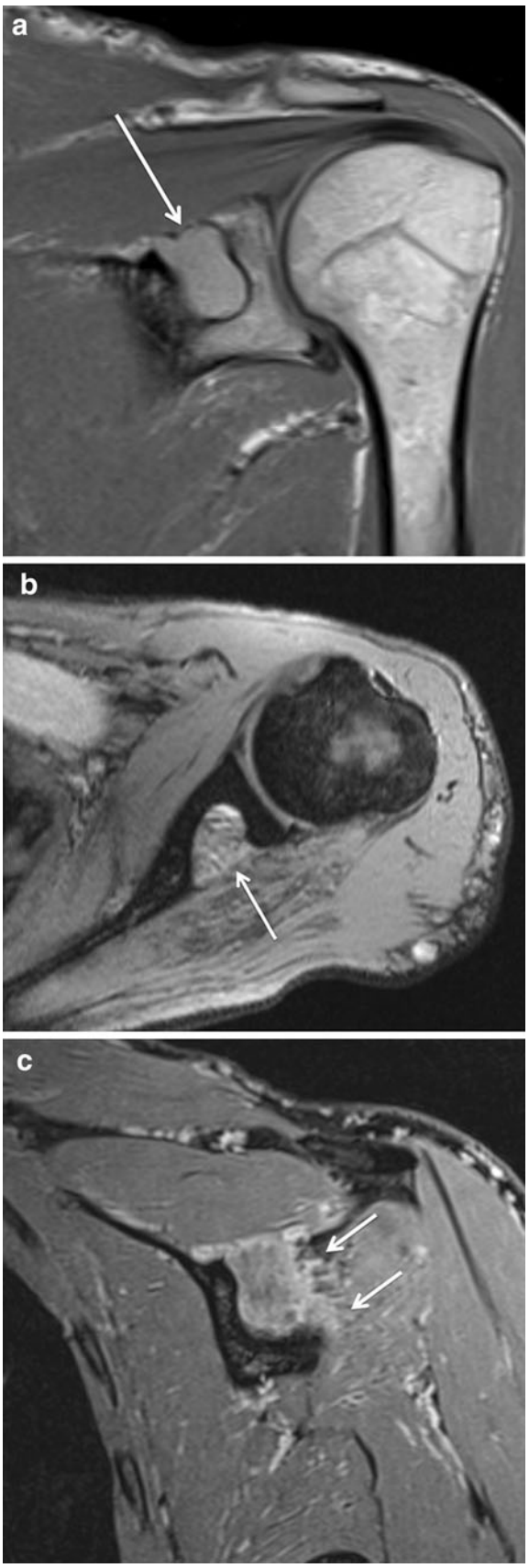


Fig. 6 Retiform hemangioendothelioma in a 42-year-old woman who presented with left shoulder pain. She had undergone several surgical operations for local recurrence from childhood. **a** Coronal T1-weighted MR image shows a slight, ill-defined mass near the suprascapular notch, hyperintense to muscle (*arrow*). **b** Axial fat-saturated T2-weighted MR image shows intermediate intensity to muscle (*arrow*). **c** Coronal contrast-enhanced T1-weighted MR image shows a heterogeneous, ill-defined mass with proliferation of vascular channels of peripheral area (*arrows*)

imaging, and is considered to be the same lesion as angioblastoma (Nakagawa) [10] in Japan. It is now believed that KHE and TA cause Kasabach–Merritt syndrome [11].

On diagnostic imaging, it is characteristically seen as hypervascular invasive tumors with poor margins [12] (Fig. 5). On MRI, KHE/TA typically appears as ill-circumscribed masses with low or isointensity areas on T1-weighted images and high intensity on T2-weighted images. On contrast-enhanced MRI, it often shows inhomogeneous staining. Similar tendencies are observed on ultrasound images, which show poorly-marginated hypervascular lesions with low to high echogenicity.

Other, rare hemangioendotheliomas

Hemangioendothelioma is a vascular tumor of borderline malignancy that develops from vascular endothelial cells, and is positioned between hemangioma (benign) and angiosarcoma (malignant). The subtypes include epithelioid, retiform, composite, pseudomyogenic and papillary intralymphatic angioendothelioma. The assignment of the

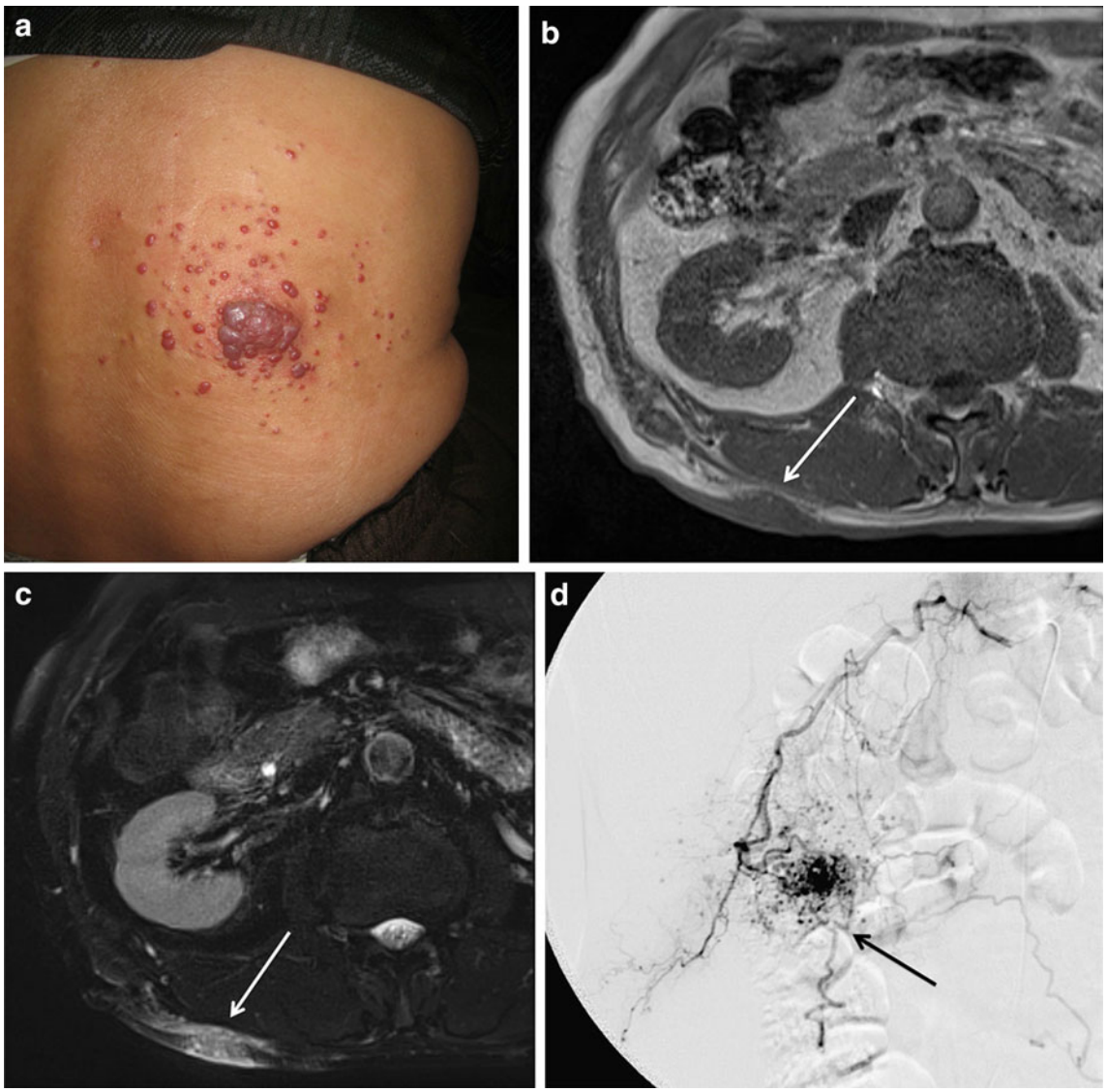


Fig. 7 Pyogenic granuloma of the back in a 66-year-old man. **a** Clinical image shows multiple reddish papules. **b** Axial T1-weighted MR image shows a homogeneous mass isointense to muscle (*arrow*). **c** Axial fat-saturated T2-weighted MR image shows high intensity to muscle (*arrow*). **d** Angiography shows ill-defined prominent enhancement area (*arrow*)

term used for hemangioendothelioma was problematic because it was used for different types, including benign, borderline malignant and malignant tumors, resulting in confusion in the past. Now it is generally used to mean a tumor of borderline malignancy, except for epithelioid hemangioendothelioma.

Hemangioendothelioma includes superficial tumors that occur on or under the skin and tumors that occur in deep tissues such as muscles. Each type has different imaging findings in general [13].

Superficial lesions involve thickening of the skin and subcutaneous tissues, and often form localized masses. Characteristics in lesions are non-specific. Hemangioendothelioma shows moderate echogenicity on ultrasound images. On MRI, the mass shows isointensity on T1-weighted images and iso or high intensity on T2-weighted images. The proliferation and dilation of the vascular channels are not obvious in many cases.

In contrast, deep lesions show obvious proliferation of vascular components compared to other soft tissue masses, and AV shunts are identifiable. On ultrasound images, although the echogenicity of masses are various (low to high echogenicity), bleeding is seen as a cystic change and AV shunts are identified on color Doppler images. On MRI, although they show non-specific findings of isointensity areas on T1-weighted images and high intensity areas on T2-weighted images, an obvious enhancement is seen in the early phase on MRI with gadolinium (Gd), reflecting the proliferation of vascular channels (Fig. 6a–c).

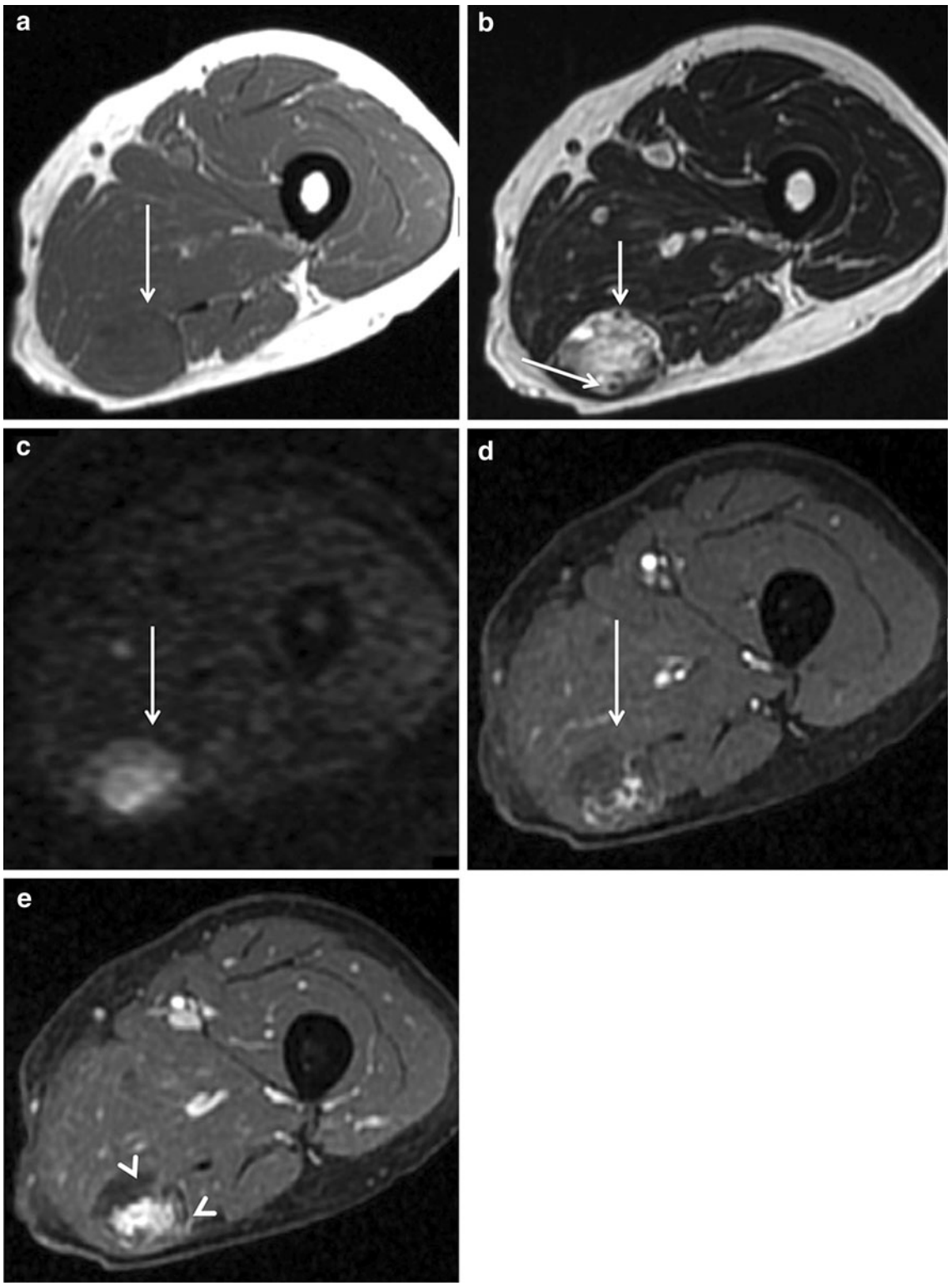


Fig. 8 Angiosarcoma of soft tissue in a 50-year-old female in the thigh. **a** Axial T1-weighted MR image shows a well-defined mass in the hamstring, isointense to muscle (*arrow*). **b** Axial T2-weighted MR image shows a heterogeneous signal with flow voids (*arrows*). **c** Diffusion-weighted MR image demonstrates diffusion restriction (*arrow*). **d**, **e** Axial contrast-enhanced T1-weighted MR image shows gradual enhancement from arterial phase (*arrow*) to venous phase (*arrowheads*)

Dermatologic acquired vascular tumors

These are vascular tumors that are skin lesions and are rarely examined through diagnostic imaging. In this paper, a description is provided only on pyogenic granuloma, which is sometimes found as a subcutaneous mass.

Pyogenic granuloma

Pyogenic granuloma was first reported by Poncet and Dor [14] in 1897. Despite its name, it is not a granuloma but a vascular tumor. It is a protruded lesion with hemorrhagic tendencies that occurs on the skin or mucosa. It often causes ulcers to have a granulation tissue-like appearance and it appears to be pyogenic because of secondary infections and exudative change; and for these reasons it is named "pyogenic granuloma" [15]. The etiology is not clear, and the involvement of local factors such as trauma, infection, and chronic stimulation is suspected. Favorite sites include the areas for cervicofacial and oral surgery and for dermatology, but it sometimes occurs in the gastrointestinal tract or other sites.

There are no detailed reports on imaging findings. Pyogenic granuloma is a sharply marginated mass with slightly high echogenicity on ultrasound images, and shows high flow on color Doppler images. On MRI, when compared to the muscle, the mass shows isointensity on T1-weighted images and high intensity on T2-weighted images and FS-T2-weighted images (Fig. 7a–d). Some case reports (including intravenous variants) state that many pyogenic granulomas are generally highly enhanced in contrast enhanced CT and MRI because they are vascular tumors [16, 17].

Angiosarcoma of soft tissue

Angiosarcoma is a vascular tumor of high malignancy involving vascular and lymphatic cellular elements and often occurs on and under the cervicofacial skin in the elderly [18]. Lesions in the skin account for 33 %, those in the soft tissues account for 23 %, and those in the bones account for 6 % of the total. Local recurrences and metastases are often observed and the most common site of metastasis is the lung. The well-known "Stewart–Treves syndrome" refers to an angiosarcoma, a rare complication that forms as a result of chronic, long-standing lymphedema in patients with breast cancer, who have had mastectomy and/or radiotherapy.

On MRI, it shows non-specific imaging findings of isointensity on T1-weighted images and high intensity on T2-weighted images and FS-T2-weighted images. The mass shows prominent enhancement with Gd, and is characterized by obvious vascular proliferation; in particular, vascular proliferation is often seen along the periphery of such masses. Because of high tumor cellularity, diffusion-weighted images generally show diffusion restriction [19] (Fig. 8a–e).

Conclusion

Although vascular tumors are generally handled as suggested by their traditional term, "hemangioma", it is useful to distinguish tumors requiring treatment from those that are expected to spontaneously regress and only have to be followed up, based on the ISSVA classification. It is essential for radiologists to become familiar with clinical and imaging findings on vascular tumors based on the ISSVA classification.

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Conflict of interest The authors declare that they have no conflict of interest.

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