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Role of imagistic techniques in diagnosing soft-tissue vascular anomalies in pediatric population – a 5-year experience

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Abstract

Soft-tissue vascular anomalies have a worldwide estimated prevalence of 4.5% in the pediatric population. From January 1, 2014 until December 31, 2018, imagistic and histological evaluations were performed in 214 patients aged between one day and 18 years old, who were diagnosed with different soft-tissue vascular anomalies in our Center. From the 214 patients included in the study, 36.45% (*n*=78) were males, 63.55% (*n*=136) were females and 37.38% (*n*=80) of the patients were less than one year of age at time of admission. Infantile hemangioma was the most frequent type of soft-tissue vascular anomaly (35.51%) and the face was the most frequent affected region (25.7%). Ultrasound (US) examination is the most used imaging technique due to its wide accessibility and for providing valuable information about the anatomical localization of the lesions, the type of vessels involved, distribution and density of vascularization. Magnetic resonance imaging (MRI) can be used for assessing the extent of deep or large lesions, but it usually requires anesthesia. Computed tomography (CT) is useful when patients present contraindications to anesthesia and it has the advantage of a shorter image acquisition time. Histological studies have an important role in establishing the diagnosis even for the atypical cases of soft-tissue vascular anomalies. Furthermore, the prognosis depends on the histological type. In conclusion, there is a need for collaboration between the clinician, radiologist, pathologist and surgeon in order to establish a precise diagnosis and therapeutic strategy for each patient.

***Keywords*:** vascular anomalies, hemangioma, ultrasound, soft tissue.

Introduction

Vascular anomalies represent a broad spectrum of diseases affecting the vessels that can be classified into vascular tumors (benign, locally aggressive, malignant) and vascular malformations (simple, combined, malformations associated with other anomalies, malformations of major vessels) (Table 1) [1].

Table 1 – *Soft-tissue vascular anomalies*

	Benign	***Borderline (locally aggressive)***	***Malignant***
Vascular tumors	▪ Infantile hemangioma; ▪ Congenital hemangioma; ▪ Tufted angioma; ▪ Spindle-cell hemangioma; ▪ Epithelioid hemangioma; ▪ Pyogenic hemangioma; ▪ Others.	▪ Kaposiform hemangioendothelioma; ▪ Retiform hemangioendothelioma; ▪ Papillary intralymphatic angioendothelioma; ▪ Composite hemangioendothelioma; ▪ Kaposi sarcoma; ▪ Others.	▪ Angiosarcoma; ▪ Epithelioid hemangioendothelioma; ▪ Others.
	Simple	***Combined***	***Associated with other anomalies***
Vascular malformations	▪ Capillary; ▪ Lymphatic; ▪ Venous; ▪ Arteriovenous malformations; ▪ Arteriovenous fistula.	▪ Capillary-venous malformations, capillary-lymphatic malformations; ▪ Lymphatic-venous malformations, capillary-lymphatic-venous malformations; ▪ Capillary-arteriovenous malformations; ▪ Capillary-lymphatic-arteriovenous malformations; ▪ Others.	▪ Klippel–Trenaunay syndrome; ▪ Parkes Weber syndrome; ▪ Servelle–Martorell syndrome; ▪ Sturge–Weber syndrome; ▪ Maffucci syndrome; ▪ CLOVES syndrome; ▪ Proteus syndrome; ▪ Bannayan–Riley–Ruvalcaba syndrome.

CLOVES: Congenital, Lipomatous, Overgrowth, Vascular malformations, Epidermal nevi, Spinal/skeletal anomalies.

Vascular tumors are defined by a clonal proliferation of endothelial cells, while vascular malformations occur secondary to errors in different stages of embryogenesis, but without any endothelial hyperproliferation [2].

The worldwide estimated prevalence of vascular anomalies in pediatric population is 4.5% [3]. Infantile hemangioma is the most frequent type of pediatric vascular anomaly [4]. The worldwide incidence of infantile hemangiomas diagnosed in the first three days of life is 1.1–6% and it rises to 8.7–12.7% in children aged between one month and one year [5].

Aim

The aim of this retrospective study is to present the contribution of different imaging techniques and histological analysis to establishing the diagnosis and the treatment strategy.

Patients, Materials and Methods

This retrospective study was conducted at the "Louis Ţurcanu" Emergency Hospital for Children, Timişoara, Romania, which serves the western region of Romania. The study included 214 patients aged between one day and 18 years old, who had been diagnosed with vascular anomalies in a 5-year period, between January 1, 2014 and December 31, 2018. Patient data was obtained from hospital records, patients' charts, surgical records, imagistic studies and histological exams. The selection criteria for this study were: age at admission between 0 and 18 years old, hospitalization at Department of Pediatric Surgery or at Department of Pediatric Plastic Surgery, during the period of the study, for soft-tissue vascular anomalies.

Every selected patient underwent ultrasound (US) examination and the diagnosis was confirmed in some selected cases by histological testing. Computed tomography (CT) scans were performed in 18 cases and magnetic resonance imaging (MRI) investigations in 57 cases.

The first imaging study that was performed in all patients was the US evaluation. Gray-scale images of the lesions were obtained in longitudinal and transverse planes and three dimensions were measured: length, thickness, width. Color Doppler settings were used to visualize the vessel component and to detect the blood flow. High vessel density (more than 5 vessels/cm^2) and a peak arterial Doppler shift >2 kHz were the diagnosis criteria for hemangioma.

MRI was performed on a 1.5 Tesla scanner. The scanning protocol included axial T2-weighted, axial T2-weighted fat saturation, diffusion-weighted imaging (DWI), axial T1-weighted and coronal contrast-enhanced T1-weighted sequences. CT evaluation was performed on a 64-slice scanner at 0.5 mm slices with three-dimensional (3D) reconstruction (bone and 3D angiography).

This study was evaluated and approved by the Research Ethics Committee of the "Louis Ţurcanu" Emergency Hospital for Children, Timişoara.

Results

From the 214 patients included in the study, 36.45% (*n*=78) were males, 63.55% (*n*=136) were females and 37% (*n*=80) of the total number of patients were less than one year of age at time of admission (Figure 1). The youngest patient was 4 days old (0.13 months), while the oldest was 18 years old (216 months). The average age of the patients included in our study was 61.52±65.34 months, with a median value of 26.5 months and a mode value of five months (Figure 1).

More than two-third of the study population was living in the rural area (72.9%, *n*=156), while 27.1% (*n*=58) of the patients lived in the urban area.

The face was the most frequent affected body region (25.7%, *n*=55) (Figure 2); however, 3.27% (*n*=7) of the patients had a multiple localization of the vascular anomalies (Table 2). Other affected body regions were the oral cavity, thorax, abdomen, upper and lower limbs, genitalia and internal organs.

Table 2 – ***Number and percentage of patients with multiple localization soft-tissue vascular anomalies grouped by year***

Year	No. of cases (percentage)	Affected regions
2018	2 (0.9%)	Scalp + thorax
		Face + oral cavity
2017	1 (0.45%)	Upper limb + genitalia
2016	–	–
2015	2 (0.9%)	Face + thorax
		Face + genitalia
2014	2 (0.9%)	Face + cervical region
		Face + lower limb + genitalia

The distribution of vascular anomalies by histological type was as follows: hemangiomas – 44.39% (*n*=95), pyogenic granulomas – 31.31% (*n*=67), lymphatic anomalies – 5.6% (*n*=12), arteriovenous malformations – 10.74% (*n*=23), others – 8.41% (*n*=18) (Figure 3). From the hemangiomas, 8.87% (*n*=19) of the cases were congenital, while 35.51% (*n*=76) were infantile. Vascular malformations were found in 46.72% (*n*=100) of the patients: Klippel–Trenaunay syndrome, Sturge–Weber syndrome, peripheral arteriovenous malformations, venous malformations, but vascular tumors like Kaposiform hemangioendothelioma, congenital hemangiomas and glomangiomas were also present.

We performed US investigations in every selected patient, MRI investigations in 57 (26.63%) cases and CT in 18 (8.41%) cases (Figure 4). Biopsies were performed in 10 (4.67%) cases, in order to establish the histological diagnosis (Figure 5).

Therapeutic surgical interventions were necessary in 78.5% (*n*=168) of the patients. The other patients included in the study (*n*=46) did not require surgical correction: 0.45% (*n*=1) of the patients required chemotherapy, 14.48% (*n*=31) of the patients received medical therapy with Propranolol, watch and wait strategy was chosen for 2.37% (*n*=6) of the patients, while 4.2% (*n*=9) of the patients did not receive any therapy.

Discussions

Our knowledge of the pathological mechanisms underlying the development of the multitude of vascular malformations and associated syndromes has evolved simultaneously with advances in molecular and genetic biology [6].

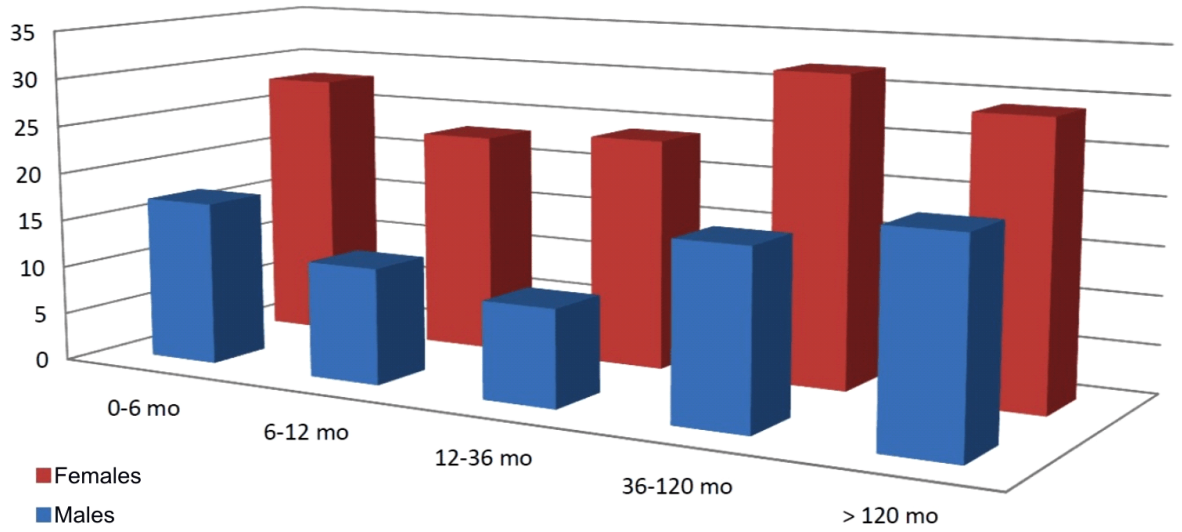

Figure 1 – ***Age distribution for male and female patients at the time of diagnosis (mo: Months).***

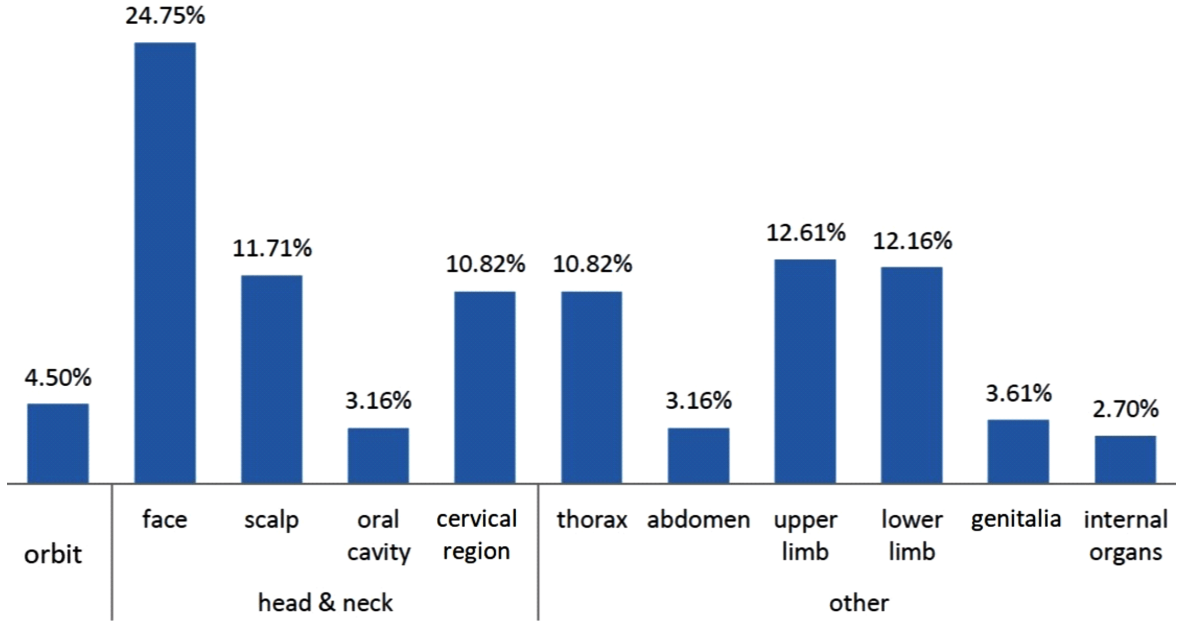

Figure 2 – ***Distribution of vascular anomalies among different body regions: orbit – 10 anomalies; face – 55 anomalies; scalp – 26 anomalies; oral cavity – seven anomalies; cervical region – 24 anomalies; thorax – 24 anomalies; abdomen – seven anomalies; upper limb – 28 anomalies; lower limb – 27 anomalies; genitalia – eight anomalies; internal organs – six anomalies.***

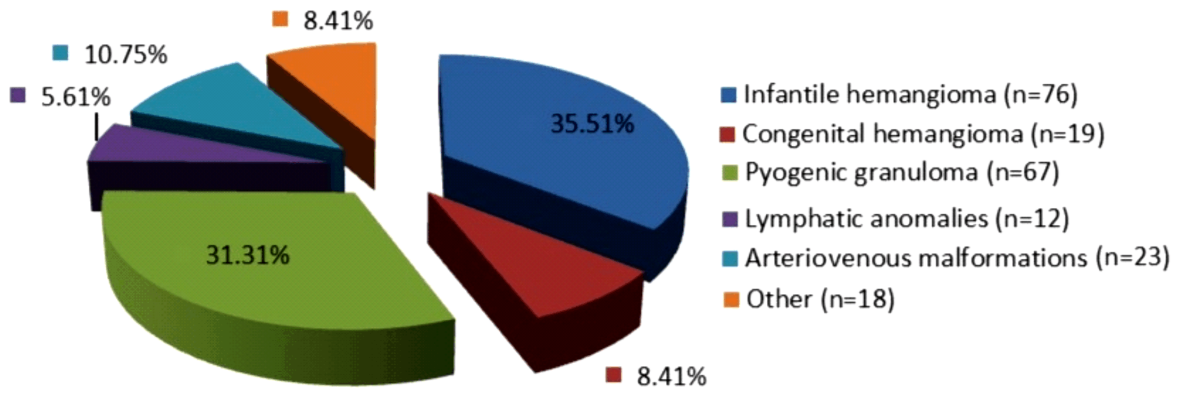

Figure 3 – ***Distribution of vascular anomalies by histological type.***

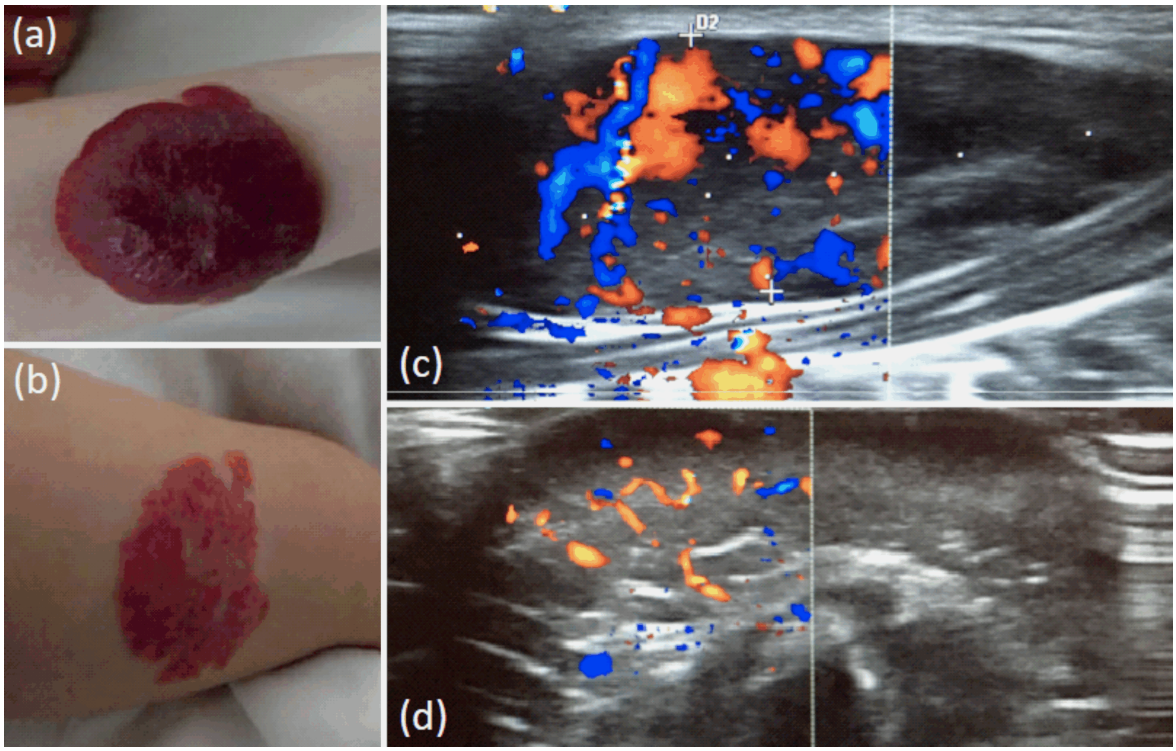

Figure 4 – ***Clinical picture of infantile hemangioma in a 6-week-old girl who presented with a growing strawberry red lesion in the upper limb that was not present at birth (a). The corresponding color Doppler ultrasound examination shows high vascular density characteristic for hemangioma (c). After nine months of treatment with Propranolol, involution of the hemangioma can be observed (b). A decrease in the vascular density can be observed as the result of medical therapy (d).***

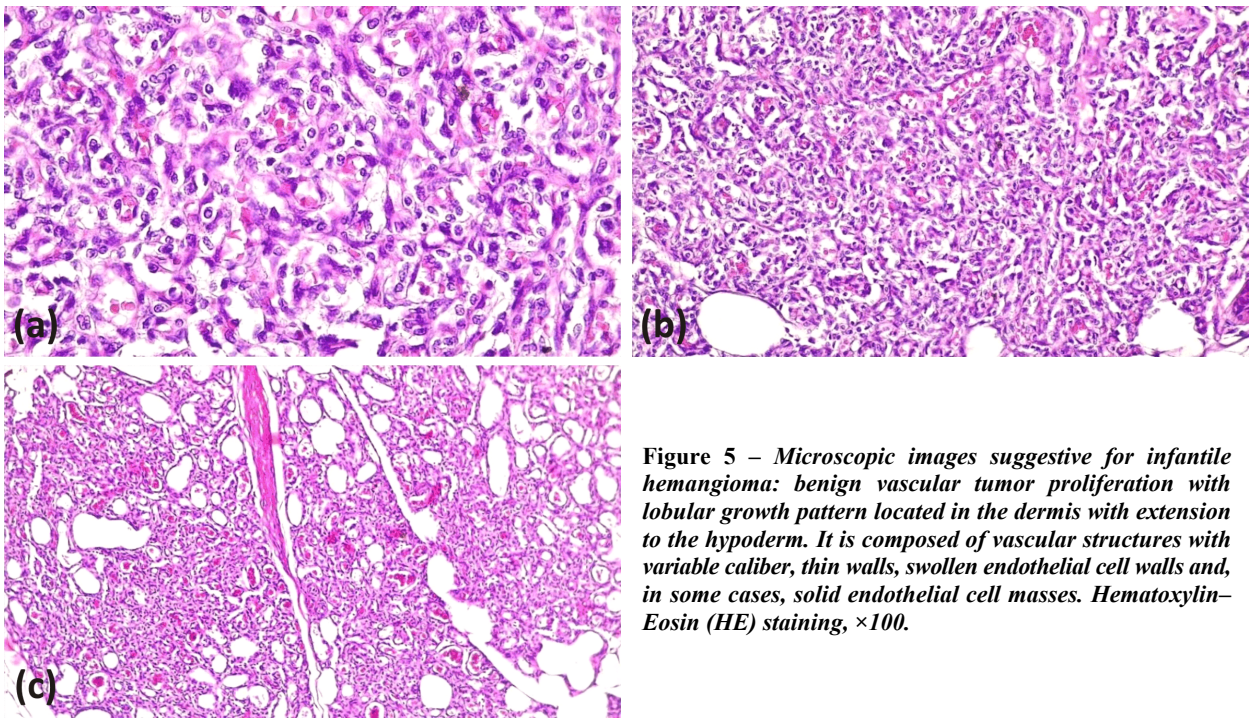

Figure 5 – ***Microscopic images suggestive for infantile hemangioma: benign vascular tumor proliferation with lobular growth pattern located in the dermis with extension to the hypoderm. It is composed of vascular structures with variable caliber, thin walls, swollen endothelial cell walls and, in some cases, solid endothelial cell masses. Hematoxylin–Eosin (HE) staining, ×100.***

Numerous syndromes that associate vascular malformations or vascular tumors develop during childhood and require long-term therapeutic management. They are associated with different signs and symptoms that should not be ignored in the clinical practice [7, 8].

Hemangioma is the most common type of vascular tumor in the pediatric population [9]. Infantile hemangioma represents the most frequent type of hemangioma, it usually appears a few days after birth and it is characterized by an accelerated growth in the first year [10].

The results in our study are consisted with the literature: 44.39% (n=95) of the patients had hemangiomas, out of which 52% of the tumors were located at the level of the head and neck (60% of the infantile hemangiomas occur in the cervical or face region) [11].

A clinical picture characteristic for all vascular

anomalies does not exist. There are some clinical features that can provide clues about the type of vascular anomaly that is affecting the patient: the time of occurrence (were the lesions present before or after birth), the rate of progression, the family history of similar lesions and if the lesion is painful or not [12]. For example, the diagnosis of infantile hemangioma will be highly probable if the vascular anomaly appears after birth, if it has a strawberry red color and if it grows in the first year with slow involution afterwards [9, 13].

With the development of technology, the importance of imaging examinations has increased. The diversity of the exploration methods and the information provided to the clinician became an important part in establishing the diagnosis and in the subsequent therapeutic decisions. At the same time, the monitoring of the treatment should be performed both clinically and by imaging methods. Differentiation of vascular abnormalities in tumors and malformations is important for the subsequent management of cases [14].

We did not find any differences in the imaging diagnostic protocol between the infantile and the congenital hemangiomas.

The two most effective methods of exploration are US and MRI and they can provide information about blood flow and morphological characteristics. In addition, different studies in the literature support the importance of US and MRI in differentiating between vascular malformations and neoplasms [15, 16].

The most used imaging technique for diagnosing vascular anomalies in children is the US, due to its accessibility and lack of need for sedation or general anesthesia [17]. The US examination can provide information about the anatomical localization of the lesions (describing the involved layers), the type of vessels involved (venous or arterial), distribution and density of vascularization and whether it is single or it consists of multifocal elements [18]. However, it is difficult to appreciate the deep lesions, the very extensive anomalies or the ones found in areas near bones or air-filled structures [2, 19]. In the present study, ultrasonography was useful for detecting lesions with more than 5 vessels/cm^2 and for monitoring the hemagiomas reduction in size and vascularity after medical therapy.

The MRI is useful for assessing deep and large lesions that cannot be fully visualized by US, especially before pharmacological therapy, surgical excision or interventional radiological treatment [20]. MRI is able to appreciate the tumor extent, invasion of adjacent bones or joints and the involvement of neurovascular bundles [21]. DWI represents a fast and non-invasive method for characterization and differential diagnosis of vascular anomalies [22]. Calculation of apparent diffusion coefficient value can help distinguishing between benign and malignant lesions (values are significantly higher in benign tumors) [23, 24].

MRI characteristics of infantile hemangioma depend on the biological phase. In the proliferation phase, the infantile hemangioma appears as a hyperintense mass in the T2-weighted, while T2-weighted-fat-saturation is used to appreciate the extension of the lesion (if it is well defined, lobulated). During the involutional phase, the infantile hemangioma appears more heterogeneous and it shows a progressive fat content involution and a reduction in the contrast enhancement [25].

Hemangiomas present multiple arteriovenous shunts and they do not exhibit perilesional edema. Therefore, when perilesional edema is identified, other neoplastic lesions should be excluded [25].

Thus, the number of MRI investigations performed in the present study is small compared to the total number of patients enrolled in the study: 57 out of 214 patients performed MRI for diagnostic purposes. More than 50% (n=32) of patients who underwent MRI examination had vascular tumors located in the cranio-cervical and orbit region.

Other imagistic investigations that can be used for establishing the extent of vascular anomalies are conventional radiography (*e.g.*, it can show skeletal alteration) and CT (it has the advantage of requiring a shorter image acquisition time, it can be used in patients with contraindications to anesthesia and it can characterize soft tissue content and precisely locate the lesion) [26, 27].

Histological analysis remains an important step when diagnosing atypical soft-tissue vascular anomalies, despite the current progress of imaging techniques [28].

The *International Society for the Study of Vascular Anomalies* (ISSVA) has an effective system for establishing appropriate therapeutic measures in patients with vascular anomalies. Applying this system in clinical practice helps selecting the proper therapeutic methods. [1]. Imaging techniques play a role in diagnosing different syndromes and they can be used as therapeutic procedures (*e.g.*, sclerotherapy) [29].

Differentiation is important for establishing the proper therapeutic strategy: observation, medical therapy or interventional techniques. For instance, 90% of infantile hemangiomas will involute by themselves, so only observation is needed [30]. Medical therapy with Propranolol or oral Prednisolone will be required only if ulceration or other scarring phenomena occur [31]. Surgical therapy is usually reserved for cases when there is an increased risk for scarring or it is located near the orbit [32]. On the other hand, the first-line therapeutic strategy in capillary malformations is pulsed dye laser, followed by vacuum-assisted laser therapy and epidermal cooling, intense pulse light and photodynamic therapy [10].

Conclusions

Increased awareness of soft-tissue vascular anomalies is required due to their relatively high prevalence in pediatric population and their complex classification. Patient history, clinical picture and US aspects of the lesions should be correlated with histological findings. However, when the lesion extent cannot be fully appreciated only by using clinical and US findings, MRI and CT can provide useful information. The prognosis of soft-tissue vascular anomalies depends on the histological type. The majority of infantile hemangiomas show a spontaneous regression without permanent sequels, while arteriovenous malformations slowly progress and they require treatment in majority of cases. Therefore, there is a need for collaboration between the clinician, radiologist, pathologist and surgeon in order to establish the adequate therapeutic strategy.

Conflict of interests

None to declare.

Authors' contribution

Simona Cerbu, Teodora Smaranda Arghirescu and Maria Corina Stănciulescu equally contributed to the manuscript.

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