Pomeranian J Life Sci 2023;69(1):23-29 doi: 10.21164/pomjlifesci.833

Vascular-derived tumours localized in the upper extremity – a review

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ABSTRACT
Vascular-derived tumours localized in the upper extremity are relatively commonly encountered, particularly in children. They are divided into 2 groups: vascular-derived neoplasms and vascular malformations. These 2 groups differ in several aspects, although their clinical presentation may be similar. Haemangiomas constitute the greatest group of benign vascular neoplasms, which are seen predominantly in children. Vascular malformations are morphogenetic disorders associated with the formation of dysplastic vessels. This article presents the current information on the classification, aetiology, diagnostic, symptomatology, methods, and outcomes of treatment of vascular-derived tumours localized in the upper extremity. It may be useful in diagnosing and managing these conditions.
Keywords: vascular tumours; haemangioma; vascular malformation; upper extremity.

INTRODUCTION

Vascular-derived tumours localized in the upper extremity are relatively commonly encountered, particularly in children. The nomenclature for these lesions is not uniform and has been frequently used inadequately or inconsistently. Vascular-derived tumours are divided into 2 groups: vascular-derived neoplasms and vascular malformations. These 2 groups differ from each in several aspects, although their clinical presentation may be similar. Haemangiomas constitute the greatest group of benign vascular neoplasms, which are seen predominantly in children. Vascular malformations are morphogenetic disorders and are composed of dysplastic vessels. These lesions develop usually in the course of foetal life and are often present at birth, but go unnoticed until later in life. Vascular malformations are caused by errors in vascular tree morphogenesis [1, 2].

The objective of this study was the presentation of updated knowledge on vascular-derived tumours localized in the upper extremity.

HAEMANGIOMAS

Haemangiomas belong to benign vascular-derived tumours. Three distinct forms of these lesions are distinguished: tinfantile, mature and intramuscular haemangiomas. Apart from these basic types, there are also mixed forms such as angiolipoma and angioleiomyoma.

Infantile haemangioma

Infantile haemangiomas are the most common benign tumours observed in children, accounting for approx. 65% of all childhood tumours. Thirty percent of these lesions are present at birth, whereas the rest of the cases are apparent by the end of the first year. Haemangiomas have a characteristic phase of rapid growth followed by a static period and then a slow involution. In the rapid growth phase, cellular proliferation occurs, but not hypertrophic growth. In this stage, the size of the lesion increases disproportionately to the growth of the child and lasts until approx. 1 year of age. The lesion may involve a large area of the extremity (Fig. 1), but usually does not alter the growth of the affected limb and rarely causes functional problems. However, following injury bleeding from haemangioma is usually more intensive than from the normal skin. During the growth phase, the haemangioma is firm, varies in colour, and does not change the size or consistency by maintaining the arm in elevated or dependent positions. After achieving the static phase, the lesion remains unchanged with regard to size and consistency; however, there can be colour changes during this phase. The static phase is actually still a growth phase, but the growth in the tumour now matches the growth of the child, so the size of the lesion does not seem to change. This phase can last for years. The involution of the haemangioma is typically a slow process of softening, shrinkage, and colour change. It begins at various ages: 50% of haemangiomas disappear by the end of the fifth year of life, and 70% by the end of the seventh year. In this phase, colour, consistency, and size of the lesion change, until it completely disappears. The skin on the involuted tumour may not appear as normal and frequently looks more or less "abnormal". Telangiectasias, fibrous mass, and inelastic skin commonly remain. Haemangiomas never appear in the later part of life, in contrast to vascular malformations. After disappearing from the skin, hemangiomas practically do not recur [1, 2, 3].

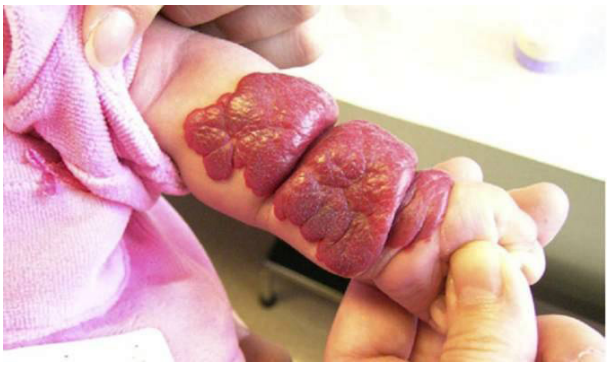


FIGURE 1. A big haemangioma in the infant's hand

There are some rare forms of infantile haemangiomas such as "rapidly involuting" and "non-involuting hemangiomas". They develop during foetal life and appear fully formed at birth. These variants are diagnosed usually based on the natural history which is different from typical lesions; the former disappears more quickly than classical, whereas the latter variant does not involute at all. In these cases, when the haemangioma does not undergo a typical evolution, magnetic resonance imaging (MRI) can be helpful for making a confident diagnosis. Other uncommon variants of the lesions are lymphatic haemangiomas (Fig. 2).

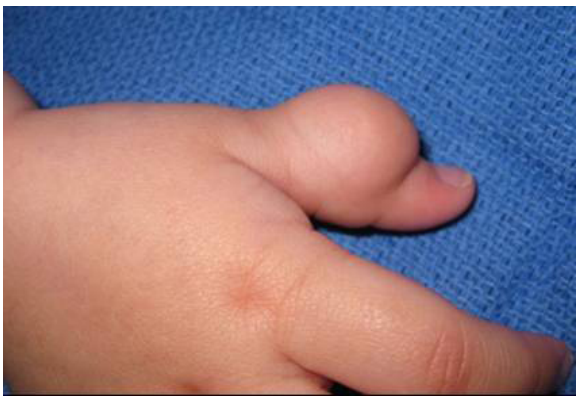


FIGURE 2. Lymphatic haemangioma presenting as a solid mass in the thumb

Mature haemangiomas

Mature (adult) haemangiomas are much less common than infantile ones, accounting for approx. 5–6% of all vascular-derived tumours. These lesions, unlike infantile haemangiomas, do not follow a typical evolution after achieving the static phase and remain stable. Clinically they may present variously – as telangiectasias, soft skin masses and even exophytic lesions resembling dark grapes clusters (called "port-wine stain"). Mature haemangiomas are classified as capillary types (telangiectasias and flat intradermal haemangiomas), venous types (soft, red-purple shining masses) – Figures 3 and 4 – and mixed types [2, 3, 4]. Mixed forms of mature haemangiomas are rare and they may present as angiolipomas and angioleiomyomas (Fig. 5, 6). In many cases, mature haemangiomas are difficult to distinguish from venous type vascular malformations and even histological examination is not fully conclusive in determining the actual character of the tumour. Essentially, the main feature discriminating one lesion from another is their natural evolution: haemangiomas disappear spontaneously over several years, whereas vascular malformations do not involute and remain stable.

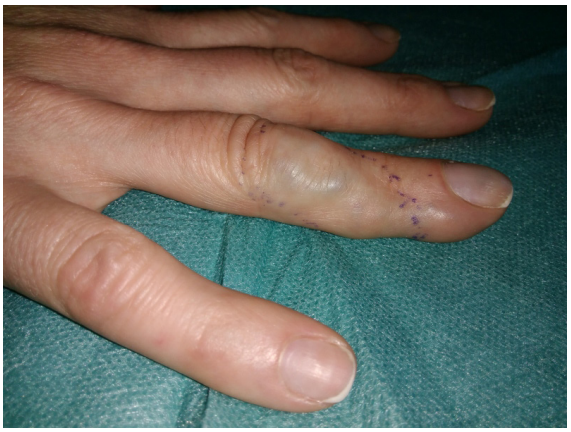


FIGURE 3. Haemangioma in the ring finger. Note a purple discolouration of the lesion under the skin

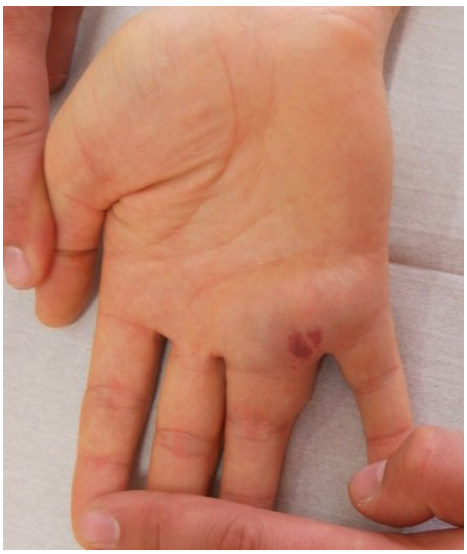


FIGURE 4. Haemangioma localized on the palmar side of the metacarpus

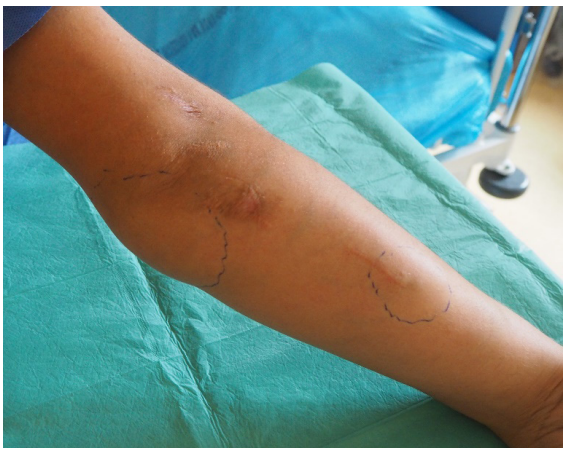


FIGURE 5. Angiolipoma localized around the elbow and forearm

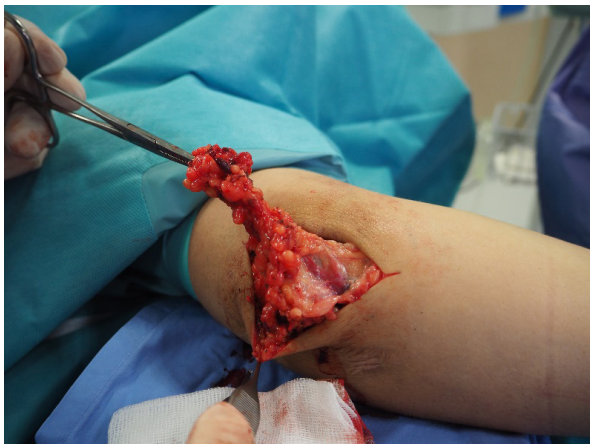
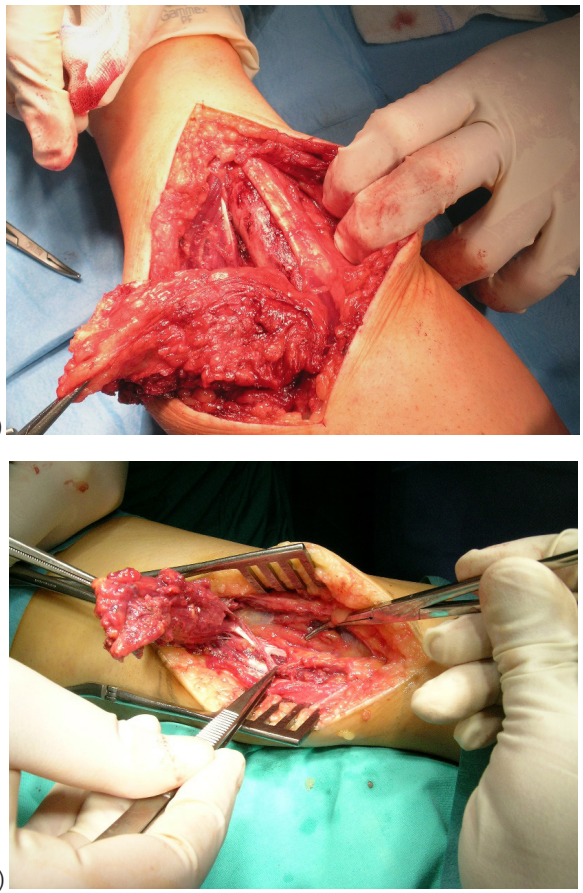


FIGURE 6. Intraoperative view of the lesion from Figure 5



a)

b)

FIGURE 7. Intramuscular haemangioma resected from the: a) forearm; b) calf

Intramuscular haemangiomas

Intramuscular haemangiomas are rare and specific forms of vascular tumours characterized by intramuscular growth. They represent a group of benign yet locally aggressive tumours composed of ectatic blood channels. Intramuscular haemangiomas can occur in a patient of any age but are commonly diagnosed in young adults. The lesions are encountered in the upper limb (forearm and arm), more frequently among the flexor muscles, and in the lower limb in the thigh and calf (Fig. 7). They can be seen anywhere in the body, including the head and neck region, the chest and even in the heart. Two histological types of the tumour are differentiated; the capillary type is nonvascular and spongy in appearance, whereas the cavernous type is composed of large, thin-walled, dilated vessels lined by flattened endothelial cells [1]. As the growth of these tumours is asymptomatic for a long time, they may reach quite a large size prior to being diagnosed. Although intramuscular haemangioma is a benign tumour, it may be locally aggressive with a tendency to invade adjacent structures and tissues. The most commonly reported symptoms and signs of the tumour include:

— deep, dull pain at rest in the involved part of the extremity, i.e. in the forearm, arm or leg;

— pain is increased during some activities, i.e. grasping and handling objects, at walking (in the lower limb);

— weaker grip of the hand, gait disturbances;

— increase in volume (girth) of the involved part of the extremity.

As intramuscular haemangioma is deeply located and is not visible through the skin, its clinical suspicion requires imaging studies such as ultrasonography (USG) or MRI to make a diagnosis.

Aetiology

The aetiology of haemangiomas is unknown. Because some of them are present fully formed at birth, their association with genetic and developmental disorders seems obvious. Results of genetic investigations have indicated that genes responsible for the normal development of the vascular system might malfunction to cause hemangiomas. An association has been found between the development of hemangiomas and the expression of the Notch gene in tumour cells. "Notch" signalling plays a role in the stabilization and angiogenesis of arterial endothelial cells. Overexpression of the Notch gene is observed in the rapid growth phase of haemangiomas, followed by underexpression in the involution phase. Another mechanism leading to the development of haemangioma is abnormal production of vascular endothelial growth factor, caused by the overexpression of the corresponding gene. Similar to the Notch gene case, the production of vascular endothelial growth factor in tumour cells is increased in the rapid growth phase and reduced in the involution phase. Hormonal influence is also considered; there is a female predominance of hemangiomas and increased oestrogen concentration has been demonstrated in children with hemangiomas. A connection with oestrogen is further evident because oestrogen levels decrease after effective therapy. Another mechanism is suspected in the aetiology of these tumours, namely angiopoietin/Tie composition which plays the role in the development of vascular system of the foetus. An increased number of Tie 2 receptors, increased cellular response to angiopoietin and dysregulation of angiopoietin 2 have been discovered in haemangioma cells. Unlike vascular malformations and other vascular tumours, hemangiomas do not express the erythrocyte-type glucose transporter 1 (*GLUT-1*) gene, encoding the production of the specific protein. The expression of this gene may be helpful in distinguishing true hemangiomas from other vascular tumours and may provide therapeutic targets for treating hemangiomas [1].

Histological structure

There are 3 distinct types of haemangiomas, differing in histological structure: capillary, cavernous, and mixed types. The capillary lesions are nonvascular, and they resemble a sponge in appearance and consistency. The cavernous haemangiomas have large vessels, with thin walls lined by flat endothelium. The mixed type is composed of capillary and vascular tissues present in various proportions. As was mentioned earlier, there is also a specific subtype – intramuscular haemangioma. Apart from vessels, other structures such as fat tissue and phlebolites may be present in vascular-derived tumours. The histological structure of these tumours undergoes changes parallel to the subsequent phases of their evolution. During the proliferating phase, the histological appearance demonstrates rapid turnover of the endothelium with enlarging vessel diameter. There are large endothelial cells lining the capillary lumens. In the static growth phase, there is flattening of the endothelial cells. During the involution phase, there is considerable mast cell infiltration and progressive fibrosis of the mass. It is considered that mast cells might be required for the involution of the hemangioma [1, 2, 3].

Imaging

The vast majority of infantile haemangiomas do not require any imaging to make a confident diagnosis unless a surgical treatment is considered. When surgery is planned, a USG is useful to delineate the extent of the depth of the invasion of the lesion within the tissue. Doppler USG allows the assessment of vascularity of the tumour as well as the identification of large vascular channels in its structure. It is particularly important in diagnostics of arteriovenous vascular malformations as well as in intramuscular haemangiomas. Another useful imaging technique is angiography (Fig. 8). Magnetic resonance imaging and magnetic resonance (MR) angiography allow the most precise assessment of the structure of the lesion and its relation to adjacent structures such as tendons, vessels and nerves. Haemangiomas show low signal in the T1-weighted sequence (on display present as low-intense or isointense to surrounding muscles). The T1 sequence can be high-intense when there is fat tissue or blood infiltrating the tumour. In contrast, the T2-weighted signal is high (high intense – dark on display), with some heterogeneity. The heterogeneity corresponds to the feeding and draining vessels that are higher flow areas. In MRI performed with gadolinium contrast, the signal of the lesion is enhanced [1].

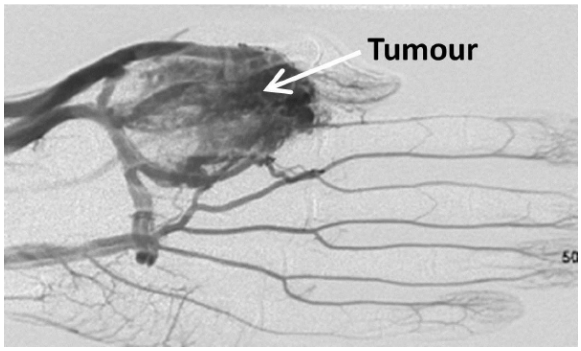


FIGURE 8. Angiography of vascular malformation in the thenar eminence

Treatment

The vast majority of haemangiomas, and almost all infantile lesions, do not require any treatment, because they involute spontaneously. Only persistent tumours and those causing troublesome symptoms, functional problems or complications (ulceration, bleeding) may require additional intervention. The range of treatment options is wide, although precise guidelines concerning their use are not determined. Treatment options include intralesional or systemic steroids, pulsed dye lasers, particularly in ulcerated hemangiomas, endovascular measures (embolization or sclerotherapy), intralesional bleomycin injections and resection of the tumour. Surgical excision is a first-line treatment for intramuscular haemangiomas [1, 2, 3, 4, 5].

VASCULAR MALFORMATIONS

Vascular malformations are vascular-derived proliferative lesions caused by errors in vascular tree morphogenesis. Thus, in contrast to haemangiomas, they are not neoplasms. Their appearance and clinical presentation resemble haemangiomas, but their natural history is different: they do not undergo 3-phase evolution and do not involute spontaneously. As was already mentioned, it is a fundamental attribute distinguishing these 2 types of vascular-derived tumours. Vascular malformations may present in various tissues and organs (i.e. in the liver or the brain), but they are most commonly encountered in the limbs. When untreated, they match the growth of the child's body, although their growth may accelerate in periods of natural hormonal changes, i.e. during puberty or pregnancy. Male and female patients have equal incidence. Unlike haemangiomas, these lesions frequently impair the status of the affected limb, causing anatomical (bone atrophy, finger hypertrophy) and functional problems, particularly when involving a substantial part of the extremity. In the upper limb, vascular malformation presents as an elastic, irregular red-purple shining mass, frequently with palpable pulsation. These lesions are usually symptomatic and the spectrum of symptoms they give is wide, including pain, parasthesiae, and feeling of heat. The skin over the tumour may be thin and sensitive to trauma with subsequent ulceration, bleeding, or even necrosis. In cases of arteriovenous malformations, if the diameter of vessels is large enough, an arteriovenous shunt may cause cardiopulmonary complications and circulatory insufficiency [1, 5, 6].

Classification

Vascular malformations are divided into 2 categories, depending on the volume (velocity) of the blood flow: high-flow and low-flow. Low-flow malformations are much more common than high-flow (rate 7:1). These lesions present clinically as soft, elastic masses. Depending on the predominant type of vessel comprising the mass they are divided into 4 types: capillary, venous, lymphatic, and combined (Fig. 9, 10). High-flow lesions are typically arterial-venous malformations [1].

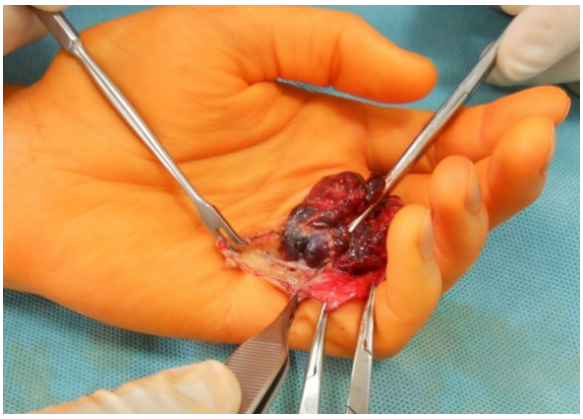


FIGURE 9. Intraoperative view of venous malformation resected from the palmar side of the hand

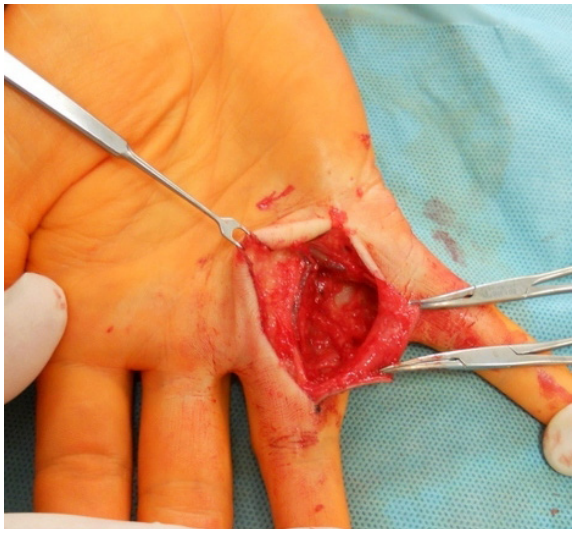


FIGURE 10. The cave after resected tumour from Figure 9

Imaging

Although the diagnosis of the vascular malformation localized in the limb is usually clear, most of them need additional imaging because of further treatment requirements. Magnetic resonance imaging and MR-angiography are the first-line techniques that allow the most precise assessment of the structure of the lesion and its relation to adjacent structures such as tendons, vessels, and nerves. It is particularly important when endovascular therapies (embolization or sclerotherapy) are considered. Angio-CT allows precise identification of the main vessel supplying the tumour. Conventional arteriography has similar diagnostic value (Fig. 8). Ultrasonography allows an adequate assessment of the structure of the tumour, its penetration into the tissues, reveals phlebolites and cysts, and the use of Doppler allows assessment of blood-flow intensity in the tumour [1, 5, 6].

Treatment

Treatment of vascular malformations depends on symptoms and dysfunction that they cause. In large lesions localized in hands and digits, treatment may be challenging due to the high risk of ischaemia and subsequent necrosis, as well as functional impairment after surgery or endovascular therapy. The spectrum of treatments includes conservative measures and endovascular and operative methods. To date, there have been no uniform rules of management of these lesions. Endovascular interventions (embolization, sclerotherapy, and thermal ablation) are increasingly popular, both as an independent therapeutic modality as well as an adjunctive therapy to surgery. The most popular agents used to obliterate tumour vessels include ethanol, bleomycin, cyanoacrylate, and tetradecyl sulfate. Among these agents, ethanol is the most powerful agent, and, therefore, it carries a higher risk of local or systemic complications, such as necrosis of the skin over the tumour, requiring further coverage usually with a skin graft or local flap. Another complication is damage to the sensory nerve passing nearby the lesion. The potential systemic complications are pulmonary arterial hypertension, acute alcohol intoxication, and red blood cell haemolysis [1, 5, 6]. Operative treatment of vascular malformations within the upper extremity can be difficult, owing to the abnormal anatomy and the potential for severe bleeding. The range of operations varies and is related to the size of the tumour, its location (deep or superficial), and the presence of nerves in the vicinity. Small lesions are resected *in toto*, whereas large tumours occupying the whole digit or a part of the hand, may require staged operations, as resection of such a mass in 1 session can result in ischaemia and subsequent necrosis. Surgery for vascular malformations requires excellent knowledge of anatomy, microsurgical skills, and is burdened with the high risk of complications and recurrences. Nevertheless, most literature on this topic concerns just surgery.

LITERATURE REVIEW

There are several articles in the literature reporting the treatment of vascular malformations within the limbs. Some of them are reviewed in this paragraph.

Park et al. reported the treatment of 64 patients, 35 women (55%) and 29 men (45%), aged 31 years on average (from 4 months to 75 years of age) with arteriovenous malformations involving hands. The study group was collected over 15 years. All of the lesions were extratruncal and classified as "infiltrating", when the tumour involved 2 or more tissue layers or as "limited" – when involvement was confined to a single tissue layer. There were 37 cases (58%) of the infiltrating type and 27 (32%) of the limited type. Lesions were clinically evident at birth in 19 cases (28%), and the other lesions were detected later; the vast majority – 59 cases (92%) were diagnosed before the age of 30. Ten cases (16%) became clinically evident or they were aggravated after trauma and 3 cases (5%) became evident after pregnancy. The most commonly reported signs and symptoms were thrill and pulsation of the lesion – in 34 cases (53%), pain – 29 cases (45%), heating sensation – 27 cases (42%), skin ulceration – 13 cases (20%), and port-wine stain in 6 cases (20%). For almost all patients the lesions were only an esthetic concern. Sixteen patients (25%) were treated conservatively

by compression therapy, 41 (64%) received embolization or sclerotherapy with ethanol and 7 patients (11%) received primary finger/fingers amputation, due to previous complications such as ulcer, bleeding, or functional limitations. The embolization or sclerotherapy was interrupted in 20 of the 41 patients, because of complications, mostly skin necrosis which occurred in 17 cases (41%); in 3 of these patients amputation of the finger was necessary. The authors found that "infiltrating" arteriovenous malformations (involving the subcutaneous layer) had a greater risk of skin necrosis than the "limited" lesions ($p < 0.02$). Additionally, 7 neuropathic complications developed but all of them were transient. The median follow-up duration was 27 months (range: from 3 months to 12 years). Functional improvement was noted in 16 patients (25%) after sclerotherapy. The conservatively treated patients who had relatively mild symptoms and no functional impairment also reported slight, although insignificant, improvement. Seven patients after finger amputation reported a variety of clinical outcomes; most of them were satisfied, although they typically complained of functional deficit [6].

The authors conclude that arteriovenous malformations treatment, and especially embolization or sclerotherapy is a long-term prospect, and it carries a potential risk for serious complications [6].

Balakrishnan reported outcomes of treatment of 104 patients, 62 females (60%) and 42 males (40%), with vascular anomalies of the upper limb, collected over a period of 20 years. Haemangiomas were seen in 33 patients (32%), more commonly in female children aged less than 1 year. The most common complaint in this group was a florid lesion or ulceration. Venous malformations were diagnosed in 52 patients (50%) in the age group of 15–20 years. The most common site of the lesion was the palm of the hand. The predominant presentation was tumour and pain restricting the activity. Twelve patients (11%) in the age group of 30–40 years had arteriovenous malformations. They invariably presented with trophic changes in the fingers. Seven patients (7%) were diagnosed with lymphangiomas affecting the fingers. Treatment of all these patients included conservative measures, sclerotherapy, and surgery. Primary excision with closure was performed in 20 of the 33 patients (61%) with haemangiomas, in 38 of the 52 (73%) with venous malformations, in 4 of the 12 (33%) with arteriovenous malformations and in all 7 patients with lymphangiomas. Embolization was performed in 8 of the 12 patients with arteriovenous malformations; 1 of these patients required shortening and closure of his left thumb following gangrene. The author concludes that the treatment of vascular anomalies in the hand may be a serious problem. His preferred treatment option is surgery and ascribes limited value to non-surgical management such as radiation and sclerotherapy [3].

In Polish literature, Jabłecki et al. reported results of the treatment of 11 patients, 8 women and 3 men, aged 24–29 years. The lesions were localized in the digits in 4 patients, within the digits and metacarpus in 2, in the metacarpus in 2 and in the forearm or arm in 4. All lesions were resected and histological examination showed haemangiomas in 6 patients, whereas vascular malformations in 5. Recurrence was noted in 4 patients, but the authors do not provide how long after surgery they occurred. All cases of relapse were following excision of vascular malformations localised in the digits [5].

Tang et al. reported the results of the treatment of 89 patients with vascular-derived tumours, including haemangiomas. The study was based on clinical material collected over a period of 25 years at a single institution. The patients were treated conservatively, endovascularly, and surgically. In the group of 57 patients who underwent operative treatment, the authors noticed that the recurrence rate was statistically significantly lower when the lesion was resected with an adequate margin of healthy tissue. In cases resected without margin or non-radically, the rate of recurrence was 19%. Functional results were excellent in 83% of patients [2].

Palmieri reported the treatment of 160 patients, 99 women (62%) and 61 men (28%) aged 32 years on average, with subcutaneous haemangiomas. Most of the lesions were localized on the palmar side of the hands and presented as soft, red-purple masses of subdermal localization, changing in size or consistency depending on the position of the arm. The most common complaint reported by the patients was unpleasant sensations of pulsation and heat within the tumour. All tumours were resected and functional results were good in most patients. Nine cases (6%) of recurrence were noted in the 4 year follow-up [4].

Reports on the results of the treatment of intramuscular haemangiomas have also been found.

Dammak et al. reported a case of intramuscular haemangioma in a 16-year-old man, localized in the distal part of the triceps muscle. The patient's only complaint was swelling in the distal part of the arm. An MRI showed a hyper-vascularized tumour (75 x 70 x 16 mm), developing at the expense of the brachial triceps muscle and with no involvement of nerves and vessels. The initial open biopsy revealed a cavernous haemangioma. The patient was operated on and the entire tumour was resected. The postoperative course was uneventful and at the 1-year follow-up the patient had no symptoms [7].

Lu et al. reported a case of congenital intramuscular haemangioma in a 16-year-old man. The tumour was huge (14 x 12 cm) and involved the whole right hand and distal forearm. The patient was born with this tumour and over 16 years he underwent several partial resections of the lesion, with recurrence after each surgery. Due to the enormous size of the tumour and the complete disability of the patient's hand, the decision was made to amputate the hand at the distal forearm level. The postoperative course was uneventful, the patient gained a functional recovery and no recurrence was observed until 2 years post-surgery. Histological examination confirmed the diagnosis of intramuscular haemangioma [8].

Four patients with intramuscular haemangiomas in the extremities, 3 women and 1 man (aged 28 on average), were treated at the institution of this author. The lesion was present in the forearm in 3 cases and in the calf in 1 case. The duration of the disease until surgery was 10 months on average. All patients were operated on and the tumours were resected

with about 1 cm of margin of the normal muscle. The results were assessed at a mean of 1.5 years. At the follow-up assessment, all patients declared a significant reduction in pain in the involved extremity. In 1 patient with the tumour localized in the forearm, a significant improvement in hand function was noted, whereas in the other one, with the big lesion in the forearm, the post-operative hand function was roughly the same as at baseline. The patient who underwent the resection of a tumour from the calf was free of pain and walked normally. No case of recurrence was noted [9].

The results of this review of the literature show that vascular-derived tumours constitute a moderately common problem in the clinical practice of hand surgeons. Some discrepancies concerning nomenclature and distinction between haemangiomas and vascular malformations were emphasised. Management of these lesions varies and depends mostly on their character and localization in the extremity. For infantile haemangiomas, the primary treatment is observation, as most of them will spontaneously involute. Various treatments are used in vascular malformations, of which surgery and endovascular interventions are the most popular.

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