Vascular anomalies

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Abstract

Vascular anomalies are vascular lesions, present from childhood. They are classified into tumours or malformations based on clinical and histological features. Benign infantile haemangiomas are the most common vascular tumour and have a predictable self-limiting course. Management is conservative, with active treatment reserved for the presence of functional or cosmetic complications (ulceration, obstruction and distortion of vital structures). Oral propranolol is useful for troublesome lesions. Rarer tumours may cause platelet consumption. Vascular malformations are structural anomalies of vascular morphogenesis, present at birth, without cellular proliferation that, in general, grow with the patient. They are subclassified by vessel type as low flow (capillary, lymphatic and venous) and high flow (arteriovenous), or lesions with combinations of vessel types. They may become problematic at puberty or during pregnancy. Extensive venous and arteriovenous lesions are the most troublesome. Their effects may be cosmetic, or those of a space-occupying lesion: infection, bleeding, pain or coagulopathy. Venous lesions cause consumptive coagulopathy, sometimes with life threatening risks. Treatment options include medication and symptomatic control with antibiotics, analgesia, control of menses, compression garments, laser intervention, interventional radiology (sclerotherapy and embolization) and surgery. Patients with complex lesions, are best managed by a multidisciplinary team.

Keywords Arteriovenous malformations; capillary malformations; haemangiomas; lymphatic malformations; multidisciplinary team; vascular anomalies; vascular malformations; venous malformations

Introduction

Vascular anomalies are vascular lesions of childhood that result from abnormal cell proliferation (tumours) or abnormal cell architecture (malformations) of vascular endothelia. They may affect any organ, and may traverse tissue planes.

Assessment is based on clinical features and special investigations such as Doppler ultrasound, gadolinium-enhanced magnetic resonance imaging (MRI) and histology. Angiography is only needed during embolization, rather than for diagnosis. Complex lesions should be managed by a multidisciplinary team including surgeons (of relevant disciplines), interventional radiologists, dermatologists, paediatricians and histopathologists. Specialist nurses and parent support groups provide vital reassurance. Lesions vary in size from small and isolated, to complex, with secondary effects that cause significant morbidity and even mortality. Difficulty in treatment means that much management is supportive with emphasis on disease control rather than cure.

Vascular anomalies were classified by Mulliken and Glowacki in 1982 into infantile haemangiomas and vascular malformations, based on clinical and histological characteristics.[1] The International Society for the Study of Vascular Anomalies (ISSVA) modified the terms to tumours and malformations in 1996, and this simple structure is applicable to in excess of 90% of lesions (Figure 1).

The latest version of the ISSVA classification (2014) includes rare tumours including malignant lesions, but the greatest change is in the sub-type of malformations with combination of vessel types and also in recognition of syndromes and identification of specific gene defects (Table 1).[2] Currently, there is interest in genetic abnormalities of the MTOR molecular pathway, important in vasculogenesis (development of vessels) and angiogenesis (differentiation of vessels). Trials are underway testing sirolimus, an MTOR antagonist, on patients with vascular malformations.

Vascular tumours

The majority of vascular tumours are benign and 95% are infantile haemangiomas.

Infantile haemangiomas

These are benign, self-limiting vascular tumours that have been called 'strawberry naevae'. They are more common in Caucasians and are the most frequent tumours of infancy, affecting 10% of full-term babies, with up to 20% incidence in prematurity.[3] There is a female predominance of 2:1. There is a predilection for the head and neck, but this may be due to referral bias, as these are more visible. Haemangiomas are usually not present at birth, although a subtle premonitory red mark (herald patch) may be present. They are first noticed at about 2 weeks of life and undergo a three-stage cycle with characteristic histological features (Figures 2 and 3):[4]

- **Stage 1.** A rapid **proliferating phase** during the first 5–8 months of life is characterized by rapid, distressing and potentially disfiguring growth of the haemangioma. These are soft and warm, with a prominent Doppler signal. When situated on the skin surface they appear bright red (hence the term '*strawberry naevus*'); however, if subcutaneous they may have a blue tinge or no colour. There may be ulceration with bleeding, or obstruction of vital structures. Studies show increased cellular turnover and the presence of plump endothelial cells with multilaminated basement membranes. Active, aberrant angiogenesis is present with up-regulation of angiogenic factors, vascular endothelial growth factor and basic fibroblast growth factor.

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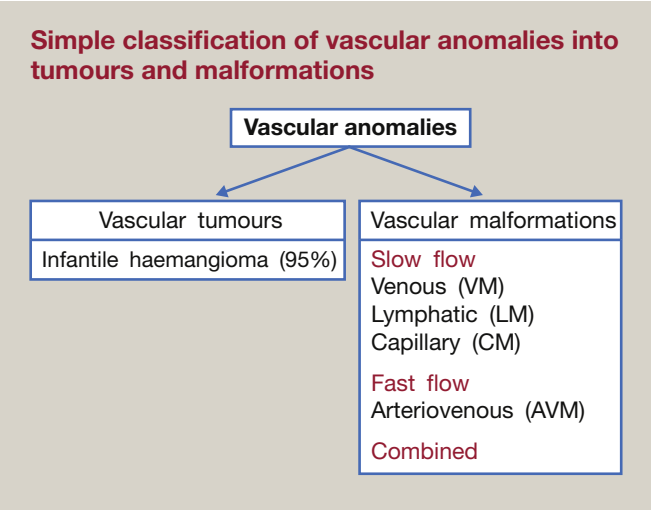

Figure 1

- **Stage 2.** A prolonged **involuting phase** lasts until the age of 7–9 years. During this phase the lesions initially become darker with a grey hue, slowly lose their colour and have fine capillary telangiectasia. There is an increased inflow of mast cells and fibroblasts with apoptosis of, and gradual substitution of, endothelial cells by fibro-fatty tissue. Angiogenesis suppression factor, tissue inhibitor metalloproteinase is characteristic in this phase.
- **Stage 3.** A final **involuted phase** is characterized by the presence of a soft lump that is visible in the case of superficial lesions and less so in deeper lesions. The lesion regresses by the age of 7 years in 70% of cases, and by 9 years in 90%. Histologically, the cellular parenchyma has been substituted almost completely with a fibro-fatty residue.

Features: infantile haemangiomas may be localized or diffuse. Histopathologically they share features with placental tissue and both have positive expression for very specific tissue markers such as the glucose transporter protein GLUT-1[5] and others.[6]

They may be associated with other abnormalities in PHACE syndrome (posterior fossa malformations, haemangiomas, arterial anomalies, coarctation of the aorta and cardiac defects, and eye abnormalities).

Management: treatment is mostly expectant, with an explanation to the parents of the natural history and provision of availability to deal with complications. After the anxious proliferative phase, patients are seen yearly or every few years; if the child and family accept the final appearance of the lesion, they are discharged.

In rare circumstances, if the diagnosis is uncertain or a differential diagnosis with malignant lesions is required, a biopsy is indicated, requesting GLUT-1 immunostaining.[7] Similarly, a full blood count is undertaken to exclude thrombocytopenia.

MRI or ultrasound is indicated for seeking internal lesions if eight or more skin lesions are present, in order to predict likelihood of cardiac failure.

Active intervention is necessary in the presence of complications such as:

- large size or disfigurement
- multiple lesions causing high-output cardiac failure
- obstruction of vital structures (vision, airway)
- persistent ulceration.

Several active treatments are used. Propranolol is now the first-line of systemic therapy, to which most patients respond, and treatment is best led by a paediatrician.[8,9] Propranolol may work by vasoconstriction and possibly decreased expression of pro-angiogenic factors of the haemangioma growth phase, causing apoptosis of capillary endothelial cells[10] (Figure 4).

In the absence of contra-indications (sensitivity to beta-blockers, bronchospasm, hypotension or bradycardia) and following routine haematological and biochemical investigations, a dose of 1 mg/kg per day in three divided doses, titrated up to 2 mg/kg/day, if tolerated, may be initiated. Monitoring and adequate follow-up are mandatory to exclude and manage the complications of this treatment.[9] The long-term effect of propranolol is still unknown. For superficial or peri-ocular lesions, topical timolol has been used.

Steroids – propranolol has replaced the use of systemic steroids, but intra-lesional injection for localized lesions may be used (triamcinolone 2 mg/kg) every 4–6 weeks depending on response. One third of patients have a good response; another third a moderate response; the remaining third are not responsive to steroids.

With systemic therapy (propranolol or steroids) rebound growth is a problem, necessitating tailing-off of the dose under close supervision.

Patching – of the non-involved eye may be required for lesions obstructing vision and threatening amblyopia. These patients must be referred early to an ophthalmic surgeon.

Embolization – is useful in high-output cardiac failure and for treating troublesome, bleeding lesions.

Surgery – early surgery such as a tracheostomy is sometimes needed in the neonatal period for obstructing airway lesions. During infancy, if vision is threatened, excision of periorbital lesions may be indicated. There may be parental pressure to excise facial lesions during infancy, but there are few indications. Between the ages of 2 and 4 years there are occasions when surgery is appropriate to minimize deformity from attenuation of vital structures such as the eyelids, nasal margin and lips. Late excision of fibro-fatty residue, or the loose skin of the involuted lesion may be planned, usually after the age of 4, but some lesions are still 'involuting' and it is best to wait (Figure 2).

Pulsed-dye laser – there is no evidence that laser treatment alters the natural history of haemangioma. It is useful for surface residual telangiectasia (after the age of 10 years). It was used to help coagulate the surface of ulcerated lesions, but dressings are the principal form of wound care.

The other vascular tumours described below are much less common.

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