Vascular anomalies

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Abstract

Vascular anomalies are vascular lesions that are present from childhood. They are classified into tumours and malformations based on clinical and histological features. Infantile haemangiomas, the most common vascular tumour, are benign and have a predictable self-limiting course. Management is conservative, with active treatment reserved for presence of functional or cosmetic complications (ulceration, obstruction and distortion of vital structures). Oral propranolol is useful for troublesome lesions. Rarer tumours exist and some 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 sub-classified by vessel type as low-flow (capillary, lymphatic and venous) and high-flow (arteriovenous) or lesions with a combination of vessel type. They become problematic under certain circumstances, usually puberty and also pregnancy. The most troublesome are extensive lesions, especially venous and arteriovenous. 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 laser (capillary), percutaneous sclerotherapy and surgery (venous and lymphatic), and embolization and surgery (arteriovenous). Such 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 all organs, and 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, (craniofacial, otolaryngological, ophthalmic, orthopaedic, paediatric, plastic and vascular), interventional radiologists, dermatologists, paediatricians, and histopathologists. Specialist nurses are invaluable in supporting parents, and parent support groups are important. Lesions vary in size from isolated small lesions to complex lesions, with secondary effects that cause significant morbidity and even mortality. Difficulty in treatment means that much management is supportive, aimed at disease control rather than cure.

Understanding of vascular anomalies has been poor owing to lack of a common nomenclature and use of a plethora of terms such as strawberry naevus, cavernous or capillary haemangioma, cystic hygroma and salmon patch.

The classification of vascular anomalies was first proposed in seminal work by Mulliken and Glowacki, in 1982, into infantile haemangiomas and vascular malformations based on their clinical and histological characteristics.[1] The International Society for the Study of Vascular Anomalies (ISSVA) is now a large body of clinicians and scientists at which the latest research and treatments are presented. ISSVA modified the terms to tumours and malformations in 1996 and this simple structure is suitable for over 90% of lesions (Figure 1).

The latest version of the ISSVA classification (2013) includes the rare tumours including malignant lesions, but the greatest change is in the sub-type of malformations with a combination of vessel type and also the recognition of syndromes and identification of specific gene defects (Table 1).[2] Current interest is 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. There is hope that help may be available for some patients with chronic debilitating symptoms (see below).

Vascular tumours

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

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 and have up to a 20% incidence in prematurity.[3] There is a female predominance of 2:1 but higher rates have been reported. 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 (Figure 2):[4]

- A rapid **proliferating phase** during the first 5–8 months of life is characterized by rapid, distressing and potentially disfiguring growth of the haemangioma. They are soft and warm with a high Doppler signal. On the surface they are a bright strawberry red; however, subcutaneously 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 multi laminated basement membranes. Active, aberrant angiogenesis is present with

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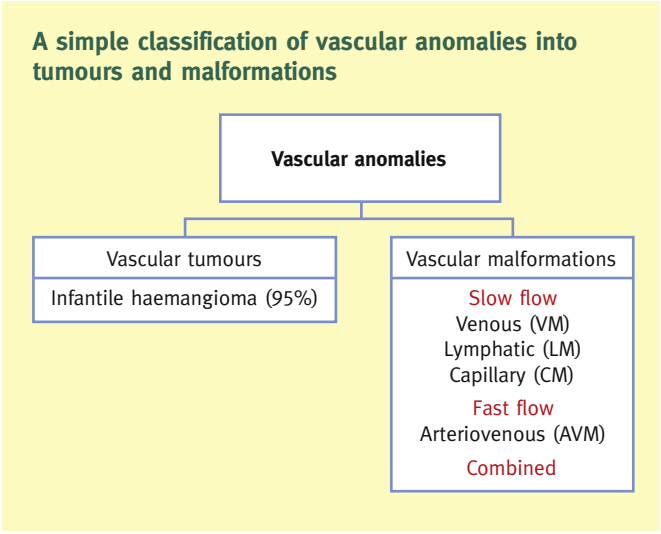

Figure 1

up-regulation of angiogenic factors, vascular endothelial growth factor and basic fibroblast growth factor.

- 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 fibrofatty tissue. Angiogenesis suppression factor, tissue inhibitor metalloproteinase is characteristic in this phase.
- 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 fibrofatty 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 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 with a request for GLUT-1 immunostaining.[7] Similarly, a full blood count is done to exclude thrombocytopenia (see below). MRI or ultrasound is indicated to look for internal lesions if there are eight or more skin lesions in order to predict the likelihood of cardiac failure.

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

- large size or causing disfigurement
- multiple lesions causing high-output cardiac failure
- obstruction of vital structures (vision, airway)
- persistent ulceration (Figure 2).

Several active treatments are used.

Propranolol is now the first line of systemic therapy and treatment is best led by a paediatrician.[8,9] Theoretical reasons why propranolol works include vasoconstriction and possibly decreased expression of pro-angiogenic factors of the haemangioma growth phase, causing apoptosis of capillary endothelial cells (Figure 3).

In the absence of contraindications (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 intralesional injection for localized lesions may be used (triamcinolone 2 mg/kg) every 4–6 weeks depending on response. A third of patients have a good response, another third a moderate response and a further third are not responsive to steroids.

With systemic therapy (propranolol or steroids) rebound growth is a problem so the dose has to be tailed off 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 airway lesions. This may be combined with endoscopic excision of the lesion. During infancy, if there is a threat to vision as indicated by decreasing visual evoked response, excision of peri-orbital lesions may be indicated (less so with the use of propranolol). 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 the fibrofatty residue, or the loose skin of the involuted may usually be planned after the age of four 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 main form of wound care.

The other vascular tumours are much less common.

Kaposiform haemangioendotheliomas

Kaposiform haemangioendotheliomas (KHEs) are locally aggressive vascular tumours characterized by rapid growth and