Treatment of vascular naevi in children

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This article will summarize the treatment options available for the two commonest vascular birthmarks of childhood: port wine stains and capillary haemangiomas. The treatment of port wine stains is primarily cosmetic and performed with lasers. The treatment of capillary haemangiomas is needed for both cosmetic and medical reasons and can include lasers, corticosteroids, interferons and surgery.

The two main types of vascular naevi that require treatment are capillary malformations: port wine stains and capillary haemangiomas, also known as strawberry naevi.

Port wine stains are congenital vascular naevi that affect 0.3–1% of the population. They persist throughout life and the majority occur on the face. Port wine stains can cause significant psychological morbidity (Lanigan and Cotterill, 1989).

Capillary or strawberry haemangiomas are common benign tumours of infancy. Most develop between the first and fourth week of life, and are characterized by an early proliferative phase that usually lasts for 6–9 months. This growth phase slows down and is followed by a gradual spontaneous involution, which is complete in most children by 5–10 years of age. Deeper (cavernous) haemangiomas often do not regress completely.

Most strawberry haemangiomas are of cosmetic concern only. However, some can cause difficulties through interference with organ function. For example, periocular haemangiomas can affect vision, and subglottic and intranasal haemangiomas can interfere with swallowing and respiration. Bleeding and ulceration can also occur — particularly in perineal haemangiomas.

Most complications happen during the proliferative phase of the haemangiomas; once regression is under way, complications associated with the haemangioma usually settle. The regression of many haemangiomas remains incomplete, leaving either a flat telangiectatic patch or an area of redundant discoloured skin. If ulceration has occurred, scarring may follow.

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TREATMENT OF PORT WINE STAINS

The treatment of choice for port wine stains is laser therapy. Cosmetic results with laser treatment are generally far better than with other treatment modalities.

Principles of selective photothermolysis and the treatment of port wine stains

Current successful treatment of port wine stains follows the principles of selective photothermolysis proposed by Anderson and Parrish (1981). The target in port wine stains is haemoglobin in cutaneous blood vessels. By the appropriate selection of wavelength, pulse duration and energy fluence, the chosen chromophore can be selectively thermally damaged. Laser treatment that successfully reduces the number, size and erythocyte content of these vessels results in observable lightening of the port wine stain.

Port wine stains treatment with the flashlamp pulsed-dye laser

The pulsed-dye laser was the first laser specifically designed for the selective photothermolysis of cutaneous blood vessels. It is activated by the discharge of a high-power flashlamp, which produces yellow light at 585 nm. Despite the original title of tunable-dye laser, these lasers are not tunable in clinical situations and the wavelength is fixed. The pulse duration is also fixed at 450 μs, so the main variables are the spot size and the fluence.

Which fluence to use can be determined by doing a test treatment over a range of fluences and reviewing the patient 8 weeks later. The lower range of fluences should be used in the paediatric patient at delicate skin sites. In the UK, a small illustrated book *Puss Puss And The*

Magic Laser (Doreen Trust, 1993) helps inform children of the treatment process.

Pulsed-dye laser treatment causes discomfort or pain to the patient. Topical anaesthetic agents can help reduce this pain. A eutetic mixture of local anaesthetic cream (EMLA cream) has been shown to reduce pulsed-dye laser-induced pain (Lanigan and Cotterill, 1987). The cream must be applied thickly under occlusion to the port wine stain for 90 minutes to 4 hours before treatment. It is not indicated for children under 1 year of age.

An alternative to this cream is Ametop**,** a 4% amethocaine gel that has the advantage of a more rapid onset of action (30–45 minutes). It also should be applied under occlusion and is not recommended in infants under 1 month old. There are concerns about absorption of Ametop from highly vascular surfaces, and large areas should not be treated with this drug.

In children, these anaesthetic techniques are often insufficient, and many will require general anaesthesia as a day-case procedure (Rabinowitz and Esterly, 1992). Some investigators recommend sedation in combination with other anaesthetic techniques, without general anaesthesia. The procedure can cause anxiety in children as well as discomfort, since their eyes are covered and the laser emits noises as well as light during treatment.

After the test treatment, each subsequent procedure involves placement of laser impacts over the whole port wine stain with the lowest fluence needed to achieve lightening. The fluence may need to be reduced over the eyelids, upper lip and neck. Each impact of the laser produces a visible purpuric discoloration that appears either immediately or within minutes.

After treatment, the port wine stain will show a bruised discolouration for up to 28 days. Small areas may crust, but large areas of blistering suggest that the fluence should be reduced at the next treatment. After each treatment, the port wine stain should be lighter in appearance. Treatments are repeated at intervals of about 8 weeks. Gradually, through a course of treatment, the lightening after each treatment gets smaller until no further progress can be seen. Most patients will experience satisfactory lightening of their port wine stain in the first four to ten treatments.

Several studies report the efficacy of pulsed-dye lasers in the treatment of port wine stains. Results are generally reported in terms of lightening rather than clearance, which occurs only in a minority. Roughly 40% of patients with port wine stains achieve 75% lightening or more after laser treatment, and more than 80% of port wine stains lighten by at least 50%. Several prognostic criteria have been advanced to assist in predicting the outcome of treatment. Some researchers report best results in pink lesions (Fitzpatrick et al, 1994). Others report better results in red lesions (Taieb et al, 1994). In a study of 261 patients treated over a 5-year period (Katugampola and Lanigan, 1997), colour of port wine stain was not found to be a prognostic value. Younger children usually require fewer treatments than adults. van der Horst et al (1998) found no evidence that treatment of port wine stains in early childhood was more effective than treatment at a later stage.

Two features that may affect the outcome are the site of the port wine stains and the size of the naevus. Port wine stains on the face and neck respond better than those on the leg and hand (Lanigan, 1996). On the face, port wine stains on the forehead and lateral face respond better than those over the middle of the face (Renfro and Geronemus, 1993). port wine stains of an area less than 20 cm^2 at initial examination cleared more than those of an area greater than 20 cm^2, irrespective of the patient's age (Morelli et al, 1995).

Side-effects of pulsed-dye laser therapy

In the treatment of port wine stains, the pulsed-dye laser has a low incidence of side-effects. Post-inflammatory hyperpigmentation is the commonest side-effect and occurs in 10–27% of patients (Seukeran et al, 1997). Hyperpigmentation is more common on the leg and is reversible. Hypopigmentation occurs in less than 1% of patients and occupies only a small area of the treated lesion. Atrophic scarring occurs in 1–5% of patients and hypertrophic scarring in less than 1%. Atrophic textural changes often improve spontaneously over 6–12 months.

The pulsed-dye laser is substantially safer and more efficacious than the argon laser when appropriate fluences are selected. Paediatric patients can begin pulsed-dye laser treatment in the first year of life and often complete their treatment before starting school.

TREATMENT OF STRAWBERRY HAEMANGIOMAS

There are now several treatments available. The natural history of slow spontaneous regression in most infants must be borne in mind when considering treatments with potential side-effects. The three treatments developed over recent years are

laser therapy, systemic corticosteroids and interferon alpha. Each will be discussed in this review. It is not clear which treatment is best, and each has advantages, limitations and side-effects. Surgical correction of persisting defects, particularly around the lip, may also be beneficial (Zide et al, 1997).

Laser treatment of strawberry haemangiomas

Laser treatment is used either to slow or to arrest proliferation in early haemangiomas, to correct or minimize complications, or to improve cosmetically residual telangiectatic lesions. Apfelberg (1981) first reported the use of the argon laser for the treatment of capillary haemangiomas. Treatment with this laser has been limited by textural and pigmentary alterations. The continuous wave neodymium:yttrium aluminium garnet (Nd:YAG) laser has also been used; is has a deep penetration with thermal coagulation of large volumes of tissue. It is useful for debulking large haemangioma, but hypertrophic scarring frequently occurs. Nd:YAG and KTP lasers can also be used intralesionally in the treatment of bulky haemangiomas. A bare fibre is inserted into the tumour and irradiation carried out as it is withdrawn.

Most patients who are treated currently undergo pulsed-dye laser treatment. The first report of a patient treated by this method was from Glassberg et al (1989). The baby was 6 days old and the haemangioma was still macular. This report and subsequent research emphasize the importance of early treatment of proliferative haemangiomas to obtain most benefit from treatment (Ashinoff and Geronemus, 1991). The pulsed-dye laser has a penetration depth of just over 1 mm and it is unrealistic to expect significant alterations in a large mature capillary haemangioma. Fluences of 5.5–6 J/cm^2 with a 5 mm spot are generally used, with treatment intervals reduced to every few weeks to achieve clearance of the lesion. Multiple treatments may be required. In small infants, anaesthesia with amethocaine gel may be adequate, although general anaesthesia is sometimes necessary.

The deeper component of the haemangioma may still develop, despite successful treatment of the superficial component. For life-threatening proliferative haemangiomas, a combination of laser treatment, systemic steroids and interferon may be required under supervision in a specialist paediatric unit.

The complications of bleeding and ulceration respond very well to pulsed-dye laser treatment. Usually only one or two treatments are required and there is a prompt response. The pain from an ulcerated haemangioma regresses rapidly after treatment (Barlow et al, 1996). In some patients, the haemangioma will also undergo regression, but this is not always the case. The whole haemangioma, not just the ulcerated or bleeding area, should be treated.

In the incompletely regressed capillary haemangioma in the older child, superficial ectatic blood vessels can easily be treated with the pulsed-dye laser, but scarring or redundant tissue may require surgical repair. It is important to ascertain the patient's expectations before embarking on a course of laser therapy, as surgical excision may be preferred.

Corticosteroid treatment of haemangiomas

Systemic corticosteroids are well-established as a treatment for large, potentially harmful haemangiomas. Most clinicians use doses of prednisolone of 2–3 mg/kg/day for weeks to months, before tapering the dose off by 1 year. Response rates vary from 30 to 90%; most benefit is seen if treatment is started during the proliferative-growth phase of the haemangioma. The mechanism of action of corticosteroids on proliferating haemangiomas is not clearly defined, but there is likely to be some control of endothelial proliferation.

Side-effects are common. In one study (Boon et al, 1999) of 80 children who had received steroid therapy, 71% were cushingoid, 29% had personality changes, and 35% had growth impairment. Of the growth-impaired children, 91% returned to normal at long-term follow-up. Intralesional corticosteroids can also be of value in experienced hands.

Interferon alpha treatment of haemangiomas

There are several studies on the efficacy of alpha interferon (IFα) in the treatment of life-threatening haemangiomas. Interferons have several biological actions and are thought to inhibit endothelial-cell growth. Either IFα–2a or 2b is given subcutaneously at a dose of $3x10^6$ IU/m^2/day. Greinwald et al (1999) considered interferon to be better than corticosteroids with response rates of 58% in infants treated with IFα-2a. Smaller numbers of patients have also been treated with IFα-2b, with similar response rates.

Side-effects of constitutional malaise with fever and fatigue are common. Other side-effects include elevation of liver enzymes, nausea, renal failure and bone-marrow supression. Of concern are the severe neurological side-effects, including spastic diplegia in up to 10%

of infants treated with IFα-2a. It may be wise, therefore, to reserve interferon treatment to alarming haemangiomas in which systemic corticosteroid therapy has either failed or is not tolerated.

CONCLUSIONS

The treatment of haemangiomas in infancy are likely to depend on the clinician's experience of the therapies available, and increasing knowledge of the most appropriate clinical situations to maximise the potential benefits to the patient. Further research into mechanisms of angiogenesis and pharmacological antagonists may offer a wider range of therapeutic options for the paediatric patient with a problematic haemangioma. HM

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KEY POINTS

- The pulsed-dye laser is the treatment of choice for port wine stains.
- Multiple treatments are needed and complete clearance of the port wine stain occurs only in a minority.
- Pulsed-dye laser therapy has a low incidence of side-effects.
- Treatment of strawberry haemangiomas is to arrest progression, prevent complications, or eradicate persisting lesions.
- Treatment of strawberry haemangiomas includes laser therapy, systemic corticosteroids, interferons and surgery.