Normalisation of refractive error after steroid injection for adnexal haemangiomas

Andrew J Morrell, Harry E Willshaw

Abstract

A longitudinal study of 27 patients with infantile haemangiomas is reported. It confirmed the efficacy of local steroid injection as a method of treatment; 81-5% of patients showed a marked improvement, with the lesion reducing to 25% or less of its original size. Involution was most marked in the first two weeks but continued for up to four months after injection. Amblyopia was present in 43% of children and was usually the result of induced refractive error rather than obstruction of the visual axis or strabismus. Anisometropia was found in 68% of children, with a high incidence of asymmetric astigmatism on the side of the haemangioma. Following local steroid injection a marked reduction in astigmatism was noted in 53-8% of children, a lesser reduction in 15-4%, and no reduction in 30-8%. Successful treatment of the haemangioma, therefore, may not remove the risk of amblyopia, and regular refraction and visual assessment remain mandatory.

Infantile haemangiomas affect between 3%1 and 8%2 of the population. They have a predilection for the face and commonly appear within the first two months of life. There is a phase of rapid enlargement over the first four to eight months, followed by a period of stability and subsequent spontaneous involution, with 70% having regressed by seven years of age.3

In addition to the cosmetic blemish 43–60% of children with adnexal haemangiomas will develop strabismic, anisometropic, or deprivation amblyopia. A smaller number will develop other ocular complications including exophthalmos, exposure keratitis, or optic atrophy.4 Previous studies in this unit have shown that the majority of cases of amblyopia result from anisometria rather than strabismus or occlusion of the visual axis.4 Robb5 also found a 46% incidence of asymmetric refractive error in affected children.

Several methods of treatment (including surgical excision, cryotherapy, irradiation, and injection of sclerosing agents) have been used for infantile haemangiomas, but all have a risk of local or systemic complications.6 Similarly, though effective, systemic steroids may adversely affect the child’s growth, and therefore intralesional steroid injections were introduced in the late 1970s. These have been shown to promote rapid resolution of the haemangioma,7,8 but the natural history of the refractive error following treatment has not been explored (though Kushner9 noted reversal of refractive error in one child following early treatment).

Since December 1981 we have treated 27 children with adnexal haemangiomas by means of local steroids. We report the results of treatment in this group with respect to resolution of the lesion, the effect on refractive error, and the long term visual outcome.

Patients and methods

The diagnosis of haemangioma was based on the clinical appearance of either a raised, red, dimpled lesion involving the superficial skin, or a ‘subcutaneous’ swelling or fullness with a dark reddish blue discolouration, together with a history of onset, growth, and tendency of the lesion to increase in size when the patient cried. All children were examined for evidence of haemangiomas in other sites, and a CT scan was performed to define the limits of the adnexal haemangioma where extension into the orbit was suspected. Two patients required biopsy to establish the diagnosis because of clinical suspicion of an underlying rhabdomyosarcoma.

The haemangiomas were measured and photographed immediately before injection and at least once after injection. The size was noted and the position recorded by the same notation as employed in spectacle trial frames. For example, a lesion extending from the 60° axis to the 150° axis was considered to have a 90° extent. Cycloplegic refraction (by streak retinoscopy after the instillation of cyclopentolate 1%) and fundal examination were performed prior to injection in 25 of the children, the remaining two having haemangiomas remote from the eyelids. Refraction and fundal examination were repeated at intervals after injection.

Indications for treatment of adnexal haemangiomas were as Kushner9 advised: occlusion of the visual axis, strabismus, an asymmetric refractive error sufficient to cause amblyopia, or the tumour enlarging and showing the potential for the above problems. Intralesional injections of steroids were undertaken under general anaesthetic, a combination of triamcinolone (20–40 mg) and dexamethasone (4 mg) being given. In one early case methylprednisolone (40 mg) was used in place of dexamethasone. In the first five cases the steroid was injected round the margins of the lesion; thereafter injections were

<table>
<thead>
<tr>
<th>Complication</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymmetric astigmatic error &gt;0-75 D</td>
<td>7</td>
</tr>
<tr>
<td>Asymmetric astigmatic error + strabismus</td>
<td>1</td>
</tr>
<tr>
<td>Asymmetric astigmatic error + lid occlusion</td>
<td>1</td>
</tr>
<tr>
<td>Asymmetric anisometropia – hypermetropia</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 1 Degree of resolution of haemangioma following local steroid injection

<table>
<thead>
<tr>
<th>Grade of response</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
</tr>
</tbody>
</table>

Table 2 Ophthalmic sequelae in children with an adnexal haemangioma and amblyopia

<table>
<thead>
<tr>
<th>Complication</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymmetric astigmatic error &gt;0-75 D</td>
<td>7</td>
</tr>
<tr>
<td>Asymmetric astigmatic error + strabismus</td>
<td>1</td>
</tr>
<tr>
<td>Asymmetric astigmatic error + lid occlusion</td>
<td>1</td>
</tr>
<tr>
<td>Asymmetric anisometropia – hypermetropia</td>
<td>1</td>
</tr>
</tbody>
</table>
given directly into the lesion at multiple sites to minimise the possibility of subcutaneous fat atrophy following treatment. Care was taken to avoid direct injection into the vascular channels. If resolution of the haemangioma was incomplete, a further injection was carried out between six weeks and eight months after the first.

The response to treatment was graded from 0 to 4:

1. 0 representing <25% resolution
2. 1 representing ≥25% <50% resolution
3. 2 representing ≥50% <75% resolution
4. 3 representing ≥75% <100% resolution
5. 4 representing 100% resolution

Where possible monocular visual acuities were obtained before injection and at subsequent post-injection visits. Methods appropriate for age were used, including the acuity card procedure in some infants.

Results

Of the 27 children treated 19 were female and eight male. Fifteen lesions involved the upper lid, eight the lower lid, and two both the upper and lower lids. One haemangioma was located over the left parotid gland and one on the upper lip.

The age at treatment ranged from 3 months to 34 months (mean 10.6 months), with the exception of one patient who was treated at 14 years of age. Twenty patients were under the age of 12 months at the time of first injection. Follow-up ranged from six months to 73 months (mean 24.1 months). One child showed a grade 2 response two weeks after injection, but died of a streptococcal pneumonia three weeks after injection; there was no evidence at the time of any systemic effect of the steroids on this child and in particular no evidence of immune suppression.

Sixteen of the 27 patients received a second injection because of incomplete resolution of the haemangioma, the time interval between injections ranging from six weeks to eight months. Two patients received a third injection before achieving satisfactory resolution, and one patient received four injections but showed a grade 0 response. Involution was most marked in the first two weeks and continued for up to four months after injection.

RESOLUTION OF HAEMANGIOMA

Table 1 summarises the response of the patients to injection. Twenty two patients showed a grade 3 or 4 response, three patients showed a grade 1 or 2 response, and two patients showed a grade 0 response. Of the children showing no response to treatment one was aged 3 months and the other 14 years at the time of first injection.

Table 3 Asymmetric astigmatism related to the site of the haemangioma

<table>
<thead>
<tr>
<th>Site of haemangioma</th>
<th>No. patients with asymmetric astigmatism</th>
<th>No. patients without asymmetric astigmatism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper lid</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>Lower lid</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Combined upper + lower lid</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

Following injection one child developed an area of subcutaneous fat atrophy which resolved over a period of six months. This child was one of the first five to receive treatment, and steroid had been injected round the margins of the lesion. To minimise the possibility of this complication subsequent injections were given directly into the haemangioma at multiple sites, with no evidence of subcutaneous fat atrophy in the following 22 children.

A second girl developed an abscess at the site of injection, though this occurred three weeks after injection and followed a direct blow to the lid. One child showed an unusual response with apparent complete resolution of the haemangioma within four weeks of injection, but with recurrence of the lesion which then remained at one-quarter of its original size despite two further injections.

VISUAL OUTCOME

Two of the 27 patients were treated for non-sight threatening lesions and two were lost to follow-up before accurate monocular acuities were obtained. Of the remaining 23 patients (43%) developed amblyopia, all on the side of the haemangioma, with amblyopia defined as two or more lines of Snellen acuity less than the preferred eye. With the exception of one child who presented at the age of 14 years these children are still receiving amblyopia therapy.

By Jampolsky's criteria for significant anisometropia all 10 children had significant asymmetric refractive error (Table 2). Seven had astigmatism alone, one astigmatism and strabismus, one astigmatism combined with lid closure, and one anisohypermetropia.

Of the 25 patients with lid involvement refractive data were not available for one child.
with an upper lid lesion and two children with a lower lid lesion. Of the remainder 15 (68%) had significant astigmatism (Fig 1) with only two children with upper lid involvement and five children with lower lid involvement showing no astigmatic error on the side of the haemangioma (Table 3).

In all 15 patients with astigmatism the axis of the plus cylinder was found to be perpendicular to the main axis of the haemangioma (Table 4). Table 4 also indicates the change in astigmatism between the preinjection and postinjection refractions for the 13 children with complete refractive data. In seven of the 13 children (53.8%) astigmatism was either eliminated or greatly reduced (by 1-50 dioptres or more). In two children (15.4%) astigmatism was reduced by 0-50 dioptre, but in four children (30-8%) astigmatism remained unchanged despite the fact that three showed a good response to treatment in the first 18 months of life. Three children showed a reduction in astigmatism in the uninvolved eye of 1-50 (two) or 2-00 dioptres (Fig 1).

The spherical equivalents of refractive error for 22 patients prior to treatment are presented in Figure 2. Three patients were found to be myopic on the side of the haemangioma and two on the uninvolved side. Only one patient with myopia was noted to have amblyopia and he was also found to have an asymmetric astigmatic error of +2-50 dioptres cylinder on the side of the haemangioma. This patient had a reduction of myopia following treatment from −0-75 dioptre to +0-25 dioptre. One further patient, who was not amblyopic, had a reduction of myopia from −1-25 dioptres to −0-50 dioptre following steroid injection. The third patient was unchanged at −0-75 dioptre.

**Discussion**

This study confirms that local injections of steroids are a simple method of achieving a high rate of resolution of adnexal haemangiomas. 81-5% of patients (22 of 27) showed a marked response, the lesion reducing to 25% or less of its original size. Only two patients showed no response, and this included one girl who was 14 years old at the time of first injection.

The mechanism of action of local steroid is uncertain, though a vasoconstrictor effect is thought to be most likely. Zweifach et al have shown that the terminal vascular bed is rendered sensitive to the vasoactive drugs by steroids, suggesting that the vessels in the haemangioma may be sensitised to naturally occurring vasoactive amines by local steroid injections. This would imply that steroids are simply accelerating the natural involutional process.

Only two of the lesions in this series were examined by biopsy and it is therefore difficult to comment on the relative response of either the capillary or the cavernous portion of the haemangioma (the classification being based...
on the calibre of the predominant vascular channels present in the harmatoma\(^3\)). In previous reports only the haemangiendothelioma has been thought to be less responsive to treatment,\(^1\) and this may explain why the two children in this series failed to respond.

This study lends support to the view that loss of visual function in these children is usually the result of induced refractive change, rather than obstruction of the visual axis or strabismus.

Anisometropia was present in 68% of children (15 of 22) with adnexal haemangiomas. We did not find myopia to be a common refractive error, but did note a high incidence of asymmetric astigmatic errors. Upper lid lesions carried a high risk of astigmatism, with only two out of 14 patients showing no such error. Lower lid lesions were less likely to lead to astigmatism, though this was not invariable with one haemangioma leading to 2-00 dioptres of astigmatism. In every case the axis of astigmatism (plus convention) was found to point towards the haemangioma.

Similar findings have been reported with haemangiomas by Robb\(^2\) and for varied adnexal masses by Bogan et al\(^6\) Robb concluded on the basis of keratometry readings that the astigmatic component of the refractive error originated in the cornea. It is known that the maximum rate of change in the corneal radius of curvature following birth occurs in the first year of life.\(^8\) A difference of less than 0-1 mm between the principal radii of curvature of the cornea will cause an astigmatism of 0-50 dioptre. It would therefore seem possible that the refractive error associated with haemangiomas, which appear within the first two months of life, is induced by pressure of the lesion leading to a mechanical distortion of the cornea.

Studies of children with normal eyes by techniques of near retinoscopy,\(^9\) cycloplegic retinoscopy,\(^3\) and photorefraction\(^10\) have demonstrated a higher incidence of astigmatism in infants than adults. The predominant axis of the positive cylinder remains controversial,\(^11\) though there is agreement that the astigmatism decreases and has largely disappeared by school age (4 to 5/6 years of age). The possibility that the astigmatic errors we have recorded reflect the normal astigmatism of infancy is small, because in each case the axis of astigmatism was related to the location of the haemangioma.

In contrast to the studies on normal infant eyes in which astigmatism was shown to decrease over the first five years of life Robb\(^1\) found that astigmatism associated with haemangiomas persisted despite resolution of the lesion. Only two out of 16 patients lost astigmatism during observation - one at 1 year of age and one at 8 years of age. Astigmatism persisted in 11 beyond 6 years and in six beyond 12 years. He concluded that a permanent corneal change had resulted from the presence of the haemangioma. A review of 14 children seen in this unit before the introduction of steroid injection has also shown this failure of the astigmatism to disappear spontaneously in children with haemangiomas (unpublished data).

In those of our children who had an astigmatic error and responded to treatment with local steroids, we noted a marked reduction of astigmatism in 53-8% (seven of 13), a lesser reduction in 15-4% (two of 13), and no reduction in 30-8% (four of 13). These results may in fact simply reflect a return to the rate of spontaneous reduction in astigmatism that might be expected in unaffected children, though greatly exceeding the rate of reduction seen with untreated haemangiomas. It cannot, however, be argued that successful treatment of the haemangioma removes the risk of amblyopia and therefore regular refraction and visual assessment remain necessary.

No serious complications were seen in this study. Reported complications, however, include eyelid necrosis,\(^2\) permanent subcutaneous fat atrophy,\(^3\) and central retinal artery occlusion\(^4\) – presumed to be due to retrograde arterial flow leading to embolism of steroid suspension in the central retinal artery. We believe these risks can be minimised by accurate injection technique at multiple sites in the lesion, taking care to avoid direct injection into the vascular channels by drawing back on the syringe before injection. In addition the potential for adrenal suppression and the risks of a general anaesthetic exist. Although the dosages used are high, we believe the acute and sustained suppression of cortisol levels,\(^7\) the half life of the steroid regimen used is less than 30 hours and we observed no major systemic effects. We found only one case of subcutaneous fat atrophy which resolved over a period of six months.

**Conclusion**

Intralesional injection of steroids is an effective way of managing haemangiomas in children. Most respond to one or two injections within a period of two to four months and achieve a satisfactory resolution of the lesion. In view of the high incidence of visual disability associated with vascular hamartomas and the possibility that treatment may have a role in reducing the high rate of induced astigmatism found, we would suggest treatment is carried out at an early stage for any lesion thought likely to lead to anisometropia, strabismus, or lid closure. Particular attention should be paid to children with a haemangioma of the upper lid, and follow-up refraction and visual assessment are essential.

Normalisation of refractive error after steroid injection for adnexal haemangiomas

Normalisation of refractive error after steroid injection for adnexal haemangiomas.

A. J. Morrell and H. E. Willshaw

Br J Ophthalmol 1991 75: 301-305
doi: 10.1136/bjo.75.5.301

Updated information and services can be found at:
http://bjo.bmj.com/content/75/5/301

Email alerting service

These include:
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/