

Ocular lesions in the blue rubber bleb naevus syndrome*

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SUMMARY Investigations of a neonate presenting with multiple pleomorphic vascular skin lesions enabled a clinical and histological diagnosis of blue rubber bleb naevus syndrome to be made. This child had lesions in the conjunctiva, iris, and retina, associated with local haemorrhages at the time of birth. All the lesions regressed spontaneously, and a conservative approach to management of the ocular lesions in this syndrome is therefore suggested.

In 1860 Gascoyen¹ reported an association between cutaneous 'naevi', intestinal lesions, and gastrointestinal bleeding. Almost a century later Bean² separated the blue rubber bleb naevus syndrome (BRBNS) from the other cutaneous vascular conditions and gave the syndrome its name. Hence the BRBNS is known eponymously as the bean syndrome. Subsequently there have been many case reports in the literature,¹⁻¹⁸ but none mention ocular lesions in detail.

Case report

A 48-hour-old male infant was admitted to the Hospital for Sick Children, London, for investigations of multiple pleomorphic skin lesions. Both parents had been investigated for infertility for several years but no drugs had been used. There was no consanguinity and no relevant family history. There were no siblings. The pregnancy was uneventful except for the use of diazepam early in the first trimester. Lower segment caesarian section was done after failed medical induction of labour. The baby was in good condition at birth, but multiple nodular lesions on the skin were noted, and he was therefore admitted for investigation (Figs. 1 and 2).

The only significant findings on general examination were the skin lesions, which were of 3 types: (1) superficial telangiectatic-like lesions 1-2 cm in diameter that blanched on pressure; (2) deep

bluish, poorly circumscribed nodules up to 1.5 cm in diameter; and (3) Similar but more superficial purplish nodules that did not blanch. These lesions were scattered over the face, trunk, and limbs.

Initial ophthalmological examination showed the right eye to have normal anterior and posterior segments. Pupillary reactions and external ocular movements were normal, and there was no latent or manifest strabismus. The left eye had a bulbar conjunctival haemangioma upper temporally and a subconjunctival haemorrhage near the temporal limbus. In addition there was a small haemangioma in the upper temporal quadrant of the iris which had bled into the anterior iris stroma. Temporal to the left macula was a raised haemorrhagic lesion suggestive of a small arteriovenous malformation. Regular review was suggested in case recurrent hyphaema with secondary glaucoma should develop from the iris lesion or a serous retinal detachment from the posterior polar lesion.

Laser photocoagulation of the vascular lesions or sector iridectomy were considered as possible future options should treatment be necessary.

INVESTIGATIONS

Haematological investigations suggested the presence of haemolysis, but the Coombs test was negative. The bone marrow was normal. Liver function studies and ultrasound of the liver were normal. Chest, skull, and spine x-rays were normal. Viral titres were normal and blood cultures negative. A barium meal demonstrated normal oesophagus, stomach, duodenum, and jejunum, but the ileum showed a 12 cm long segment of uniform narrowing and a markedly abnormal mucosal pattern compatible with the presence of multiple mucosal

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lesions (Fig. 3). A skin biopsy report (St John's Hospital) showed dilated vascular channels present in a well circumscribed area of mid and superficial dermis (Fig. 4). The walls were lined by a single layer of endothelial cells (Fig. 5). The appearances

were those of a haemangioma, compatible with the BRBNS. This ruled out the alternative diagnoses of multiple glomus tumours and Fabry's disease.

PROGRESS

Severe gastrointestinal bleeding requiring blood transfusion occurred when the baby was 2 months old.

At the age of 3 months an electroencephalogram, electroretinogram, and visually evoked cortical responses were normal. Some of the cutaneous lesions had already regressed, but 5 new lesions were seen in the mouth, with 3 haemangiomas on the palate and 2 on the tongue. At examination

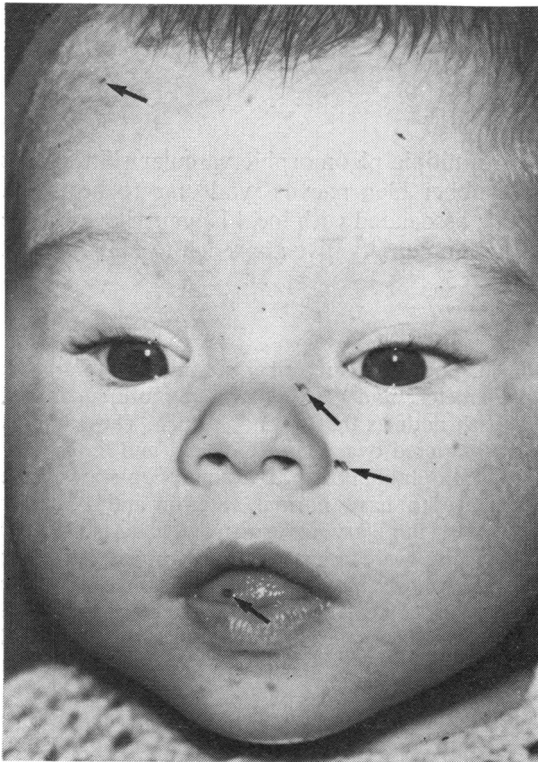


Fig. 1 Age 4 months. Haemangiomas on forehead, side of nose, and tongue (arrows).

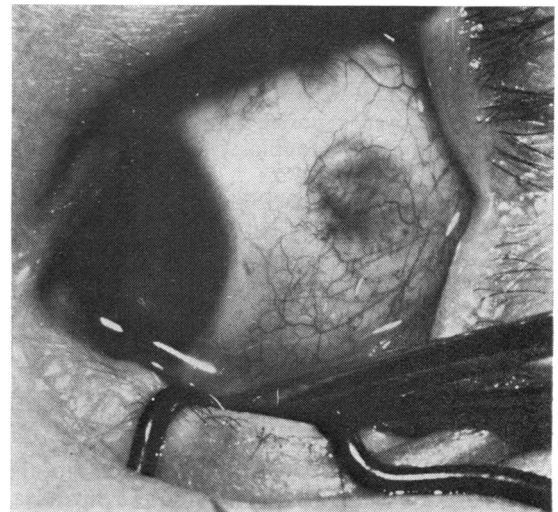


Fig. 2 Age 4 months. Subconjunctival haemangioma of left eye with overlying fibrosis.



Fig. 3 Neonate. Barium meal showing uniformly narrow segment of ileum with markedly abnormal mucosal pattern.

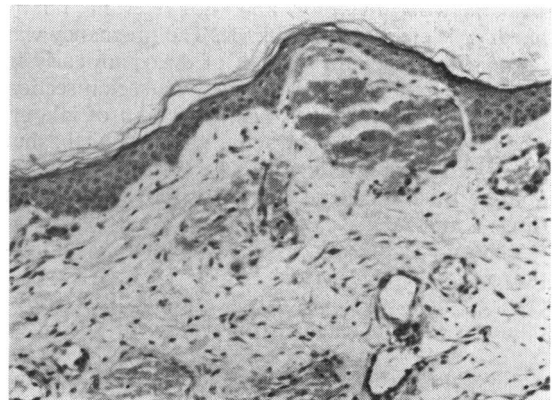


Fig. 4 Neonate. Skin biopsy (low magnification) showing multiple dilated vascular channels in the mid and superficial dermis.

under general anaesthesia several areas of 'white without pressure' were seen in the temporal peripheral retina of the right eye. The haemangioma temporal to the left macula was raised and larger, but the haemorrhage had absorbed. There were 2 inferior peripheral areas of depigmented retinal pigment epithelium. Anterior and posterior segment fluorescein angiomas confirmed the haemangioma-tous nature of the lesions (Figs. 6 and 7).

By the age of 7 months many of the lesions were fading, but new ones had appeared on the buttocks. No lesions were apparent in the iris. Funduscopy showed that the retinal lesions had disappeared, leaving a fairly large retinal pigment epithelial defect (Fig. 8). When the patient was last reviewed



Fig. 5 Neonate. Skin biopsy (high magnification) showing dilated vascular channels lined by a single layer of endothelial cells.

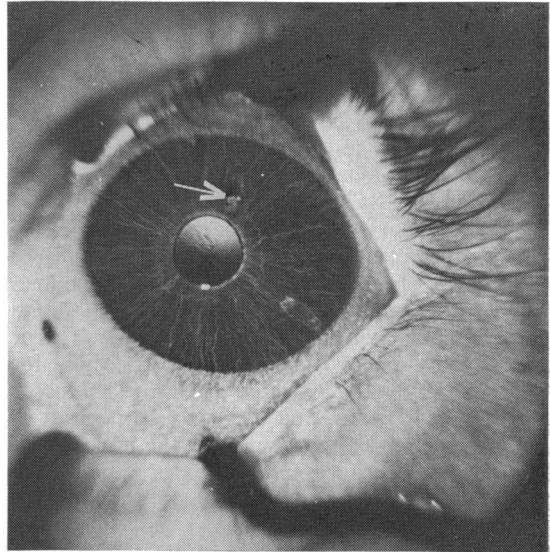


Fig. 6 Age 4 months. Fluorescein angiogram of left anterior segment showing a haemangioma (arrow) in the iris near the pupil.



Fig. 7 Age 4 months. Fluorescein angiogram of the left fundus showing the lobulated character of the retinal cavernous haemangioma.

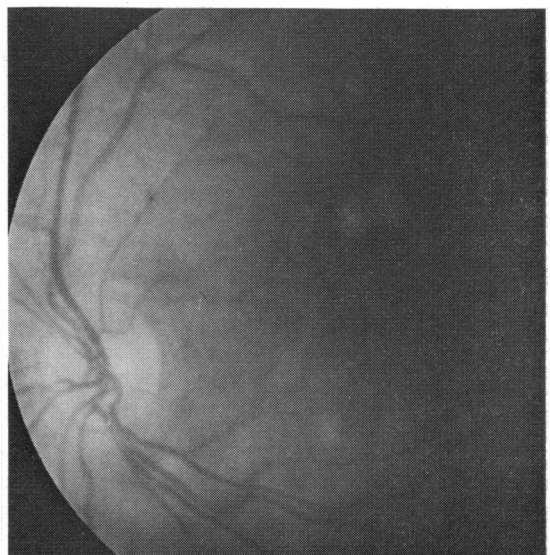


Fig. 8 Age 2 years 2 months. Fundus photograph of the left eye showing a pigment epithelial defect at the site of the previous vascular malformation.

at 18 months of age, there had been no further ocular problems.

Discussion

Bean described 3 forms of vascular lesions: firstly, large disfiguring cavernous angiomas which can replace vital structures or obstruct an airway or alimentary canal; secondly, a compressible blood sac like a blue rubber nipple covered by milk-white skin; and, thirdly, irregular blue marked or black punctate spots whose borders merge into the skin. The second type is the typical form.

The cutaneous lesions are usually present from birth. The commonest variety are bluish red with a wrinkly surface varying in size from 0.1 to 5 cm. Blood can be expressed from the lesions (blebs) leaving an empty sac and a depression in the surface of the skin.³ Feeding blood vessels are sometimes obvious in the skin. Any number can be found from a single lesion to many hundreds. They occur anywhere on the body but with a predilection for the trunk and arms. Profuse sweating can occur over the skin lesions, and they may be painful⁴ or they may be tender to palpation.⁵ The histology of the lesions is variable and includes venous and cavernous haemangiomas, capillary telangiectasia, arteriovenous malformations, and venous aneurysms.

Visceral lesions are common, as is noted in 15 of 20 cases mentioned in one paper.⁶ This type of lesion can cause overt or occult gastrointestinal bleeding, but the lesions may occur in any viscera (gut, liver, adrenals, kidneys, heart, thyroid, spleen, lung, etc.), tending to spare the oral, nasal, and genitourinary mucosa.

The central nervous system is rarely involved. Waybright *et al.*⁷ described a patient with BRBNS, focal seizures, and lateralised neurological signs. Neuropathological examination revealed a clot within a vein of Galen malformation and numerous telangiectasia and haemangiomas over the surface of the posterior half of one hemisphere. Jaffe¹⁴ described a patient with cutaneous, visceral, and cervical anterior nerve root haemangiomas plus asymptomatic similar leptomeningeal lesions. Wood *et al.*¹⁵ found haemangiomas in the brain of a patient with cutaneous and visceral stigmata of what is now recognisable as the BRBNS.

We have been unable to find any reports of ocular vascular lesions in diagnosed cases of the BRBNS. However, Burke *et al.*¹⁶ described 2 such possible cases. Their first case was an infant with multiple purplish nodular haemangiomas in the skin who developed severe internal hydrocephalus requiring a ventriculo-atrial shunt. The child was

blind, however, by the age of 18 months. There was a lesion (presumably vascular) in the iris of the right eye. At necropsy bilateral infarction of the occipital lobes was noted, and a pontine haemangioma was found to be obstructing the aqueduct. No mention was made of histopathological study of the eye. Their second case was a child with multiple skin lesions that seem typical of the BRBNS. Ocular examination at 5 months of age revealed 'punctate spots' twice the diameter of the retinal vessels temporal to each optic disc, and it was considered that these were possibly dilated choroidal vessels. By 1 year of age these fundal lesions were regressing, and by 28 months no fundal lesions were seen. By this time there was some involution of the skin lesions as well. Although no mention is made of fluorescein angiography, we consider that these fundal lesions could well have been retinal angiomas.

Gass¹⁷ described 3 cases of cavernous retinal haemangiomas. His first patient had a single cutaneous vascular lesion in addition, while her identical twin sister had a skin lesion only. His second patient had several vascular tumours on her face and legs and suffered from grand-mal seizures. Her father had seizures and multiple cavernous haemangiomas of the brain, but neither ocular nor cutaneous lesions were recorded. Gass's review of 9 other cases of cavernous retinal haemangioma culled from the literature includes that of Weskamp and Cotlier¹⁸—a 12-year-old girl with capillary vascular malformations of the skin plus a cavernous haemangioma of the brain causing seizures. The patient's father was epileptic and died from unknown causes.

Recently 2 further cases of cavernous retinal haemangiomas were reported, one of whom had skin and CNS angiomas, the other congenital cardiovascular defects and multiple neurological defects but no skin lesions.¹⁹ The latter's cavernous haemangioma underwent spontaneous partial sclerosis during a 5-year interval.

The BRBNS is transmitted in autosomal dominant fashion.⁸ Families with the syndrome appearing in 5, 5, and 3 successive generations were recorded by Berlyne and Berlyne⁹ and Walshe *et al.*,³ supporting this mode of transmission. Many cases are sporadic, perhaps representing new mutations.

There have been a few reports of the seemingly chance association of the BRBNS with other clinical conditions: medulloblastoma,¹⁰ Maffucci's syndrome,⁵ Klippel-Trenaunay-Weber syndrome,^{11,12} chronic lymphocytic leukaemia, and hypernephroma.¹³

It is evident that vascular malformations can

occur in the skin, eye, viscera, and central nervous system or in any combination of these sites, not only in the skin and gastrointestinal tract.

The BRBNS probably qualifies for inclusion in the neuro-oculo-cutaneous group of syndromes. Our case report emphasises that the ocular aspects of this rare condition may be subtle. A conservative approach to management is recommended, as the ocular lesions may regress with the passage of time.

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