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Sir,

Proteus syndrome: a variant with eye involvement

Proteus syndrome (PS) is a rare neurocutaneous syndrome wherein epidermal naevi are associated with disproportionate overgrowth phenomena, tumours, and occasionally vascular malformations and facial dysmorphism.[1]

We present a young girl with PS and outline the clinical features and differential diagnosis. Besides skin lesions, hemihypertrophy and hemimegalencephaly, she demonstrated eye changes, severe psychomotor retardation and resistant seizures. Association with ocular anomalies has not been reported previously.

Case report

A 15-month-old infant girl, born to consanguineous parents, presented with progressive left-sided hemihypertrophy and delayed development since birth. There was no history of similar illness in the family. Prominent features on examination were linear hyperpigmentation (more on the left side of the trunk and face) and somatic hemihypertrophy (left half of the body and face was larger than the right). The skin lesions were flat and soft, and had a distinct linear pattern (Fig. 1). The infant showed global delay in development

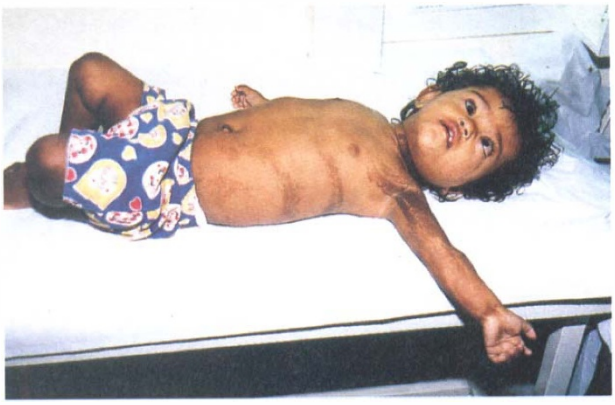

Fig. 1. *Photograph of an infant with Proteus syndrome showing the characteristic skin changes and left-sided hemihypertrophy.*

(development quotient 66%) and was hypotonic, but had no focal neurological deficit. The head circumference was 44 cm (< 3rd centile) and the left half of the skull was larger than the right.

Ocular abnormalities were observed; these were limited to the left side, with the left eyeball being larger than the right, resulting in a severe degree of myopic anisometropia and amblyopia. There was a conjunctival capillary haemangioma in the left eye. The cornea was large but clear and the intraocular pressure was normal. The left optic disc was large with an eccentric coloboma. A trial of spectacles with patching was instituted; this therapy was eventually terminated due to poor patient compliance and lack of any objective benefit.

Computed tomography of the brain revealed left hemimegalencephaly and a spinal radiograph demonstrated thoracic kyphoscoliosis. An ultrasound scan of the abdomen, echocardiography and electroencephalography were normal. Skin biopsy showed papillary hyperplasia of the epidermis, hyperkeratosis and acanthosis with elongation of rete ridges, thus confirming the clinical diagnosis of epidermal naevus.

Comment

Five well-defined syndromes have been described in association with epidermal naevi, namely Schimmelpenning (naevus sebaceous) syndrome, naevus comedonicus syndrome, pigmented hairy epidermal naevus syndrome, Proteus syndrome (PS) and CHILD syndrome.[2] These are distinguished by the type of skin lesions, the spectrum of associated anomalies and inheritance pattern.[3]

PS is characterised by the presence of soft, velvety, flat and non-organoid epidermal naevi, with histological features of hyperorthokeratosis, acanthosis and papillomatosis.[3,4] Connective tissue naevi when present are pathognomonic but are not obligatory for diagnosis.[5] The skin lesions are associated with partial gigantism of limbs, hemihypertrophy, asymmetrical macrocephaly or disproportionate overgrowth of viscera.[6] Hemimegalencephaly is a rare congenital brain anomaly due to a hamartomatous overgrowth and has been

Table 1. *Diagnostic criteria for Proteus syndrome*

General criteria (mandatory)
Mosaic distribution of lesions[a]
Progressive course[a]
Sporadic occurrence[a]
Specific criteria (category signs)
A. Connective tissue naevus
B. 1. Epidermal naevus[a]
2. Disproportionate overgrowth[a]
3. Specific tumours
C. 1. Dysregulated adipose tissue
2. Vascular malformations[a]
3. Facial dysmorphism

Modified from Biesecker *et al.*[1]
[a]Features present in our patient.
Diagnosis can be made in the presence of the mandatory criteria together with certain category signs: either one from A, two from B, or three from C.

reported rarely in PS.[6] The abnormal cerebral hemisphere is often dysplastic. In addition to hemimegalencephaly, our patient also demonstrated severe mental retardation and resistant seizures, possibly related to the brain anomaly; these are unusual in PS.[7,8] Other systemic manifestations of PS include pulmonary cystic malformations (12%) that could lead to persistent atelectasia, pneumonia and chronic lung disease,[9] hyperostosis of the external auditory canal,[5] intra-abdominal lipomas,[2] lymphangiomas and haemangiomas.[2] Associated systemic anomalies and risk of malignancy limit the life span of patients with the syndrome and necessitate extensive investigations, a multidisciplinary approach to management and regular follow-up. Management is restricted to symptomatic and supportive measures.

Due to the variability in manifestations, diagnostic criteria have been established for evaluation of suspected cases of PS (Table 1).[1] Our patient meets these criteria by displaying a mosaic distribution of skin lesions, a progressive course and sporadic occurrence (general, mandatory criteria), and epidermal naevi with disproportionate limb overgrowth (specific criteria or category signs). The main differential diagnoses are outlined in Table 2.

Ocular changes are well known in Schimmelpenning (naevus sebaceous) syndrome and naevus comedonicus syndrome. These include coloboma, lipodermoid of the conjunctiva and cataract. However, eye changes have not previously been reported in PS. Left macrophthalmia seen in our patient, paralleling the left somatic hemihypertrophy, resulted in severe anisomyopia. Deep amblyopia and esotropia were already manifest at the time of presentation. Our patient failed to demonstrate improvement with correction of refractive error and was unable to tolerate patching therapy. Underlying optic nerve malformation (coloboma) also contributed to the visual impairment. Additionally, our patient manifested a conjunctival haemangioma.

Table 2. *Differential diagnosis of Proteus syndrome*

Klippel-Trenaunay syndrome
Hemihyperplasia/lipomatosis syndrome
Parks Weber syndrome
Maffucci syndrome
Neurofibromatosis type I
Bannayan-Riley-Ruvalcaba syndrome
Solomon syndrome
Encephalocraniocutaneous lipomatosis
Familial lipomatosis
Symmetrical lipomatosis

PS is considered to be sporadic and caused by somatic mosacism. However, several members of a family have been discovered with the syndrome recently and the concept of paradominance (which allows the allele to be transmitted unperceived for generations in phenotypically normal individuals) has been invoked to explain inheritance.[10] Autosomal recessive-lethal inheritance may also explain such a transmission.[11]

In summary, we have presented an infant with PS who has unusual features such as hemihypertrophy, hemimegalencephaly, severe psychomotor retardation, seizures and eye changes; the last have not been reported previously in this condition.

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Sir,

Bilateral sixth nerve palsy treated with augmented vertical muscle transposition

Traditional extraocular muscle transposition surgery for strabismus may fail to correct the more challenging cases of paretic strabismus,[1–4] and sometimes fails to produce significant motility in the direction of the palsied muscle.[5–7] Scott Foster[8] has recently described an augmented form of transposition for such severely affected cases. We describe the use of this procedure in an unusual case of bilateral sixth nerve palsy. The case illustrates the occasional need to extend medical history several decades into the past.

Case report

A 37-year-old patient was referred to the eye clinic with a 2 year history of the eyes turning inwards, and discomfort and redness of the left eye. He had been blind in his right eye since early childhood following a 10 m fall off a roof. He had developed a marked tendency to turn his head to the left in order to see. This extreme head posture had become progressively worse over 2 years and was creating great difficulty with everyday activity: he had become unemployed, his weekly alcohol consumption was over 40 pints of Guinness (Guinness, Dublin) per week and he was encountering social and domestic problems.

There was no light perception in the right eye and 6/4 visual acuity in the left. A marked right esotropia (100Δ) was associated with an extreme left face turn. Dilated episcleral blood vessels were present in the left eye (Fig. 1a) but there was no bruit. Extraocular motility examination revealed absence of voluntary abduction (−5) of the left eye (Fig. 1a). Some limitation of abduction (−3) of the right eye was present (Fig. 1a). Vertical eye movements were intact. The right optic nerve was atrophic. The patient was diagnosed as having bilateral sixth cranial nerve palsy. Tests for a medical cause were negative.

CT scan showed a large partially calcified lesion within the right cavernous sinus (Fig. 2a). The right superior ophthalmic vein was dilated (Fig. 2a), but the left superior ophthalmic vein was of normal calibre. CT was not able to differentiate between traumatic carotico-cavernous sinus fistula and true or false aneurysm of the internal carotid artery.

On MRI, the intracavernous portion of the left internal carotid artery appeared normal. Reconstruction of time-of-flight MR angiography images showed a saccular aneurysm of the intracavernous portion of the right internal carotid artery. The upper right internal carotid artery had been displaced by the aneurysm (Fig. 2b). Selective angiography also demonstrated the unopacified aneurysmal sac on the right. The aneurysmal sac did not

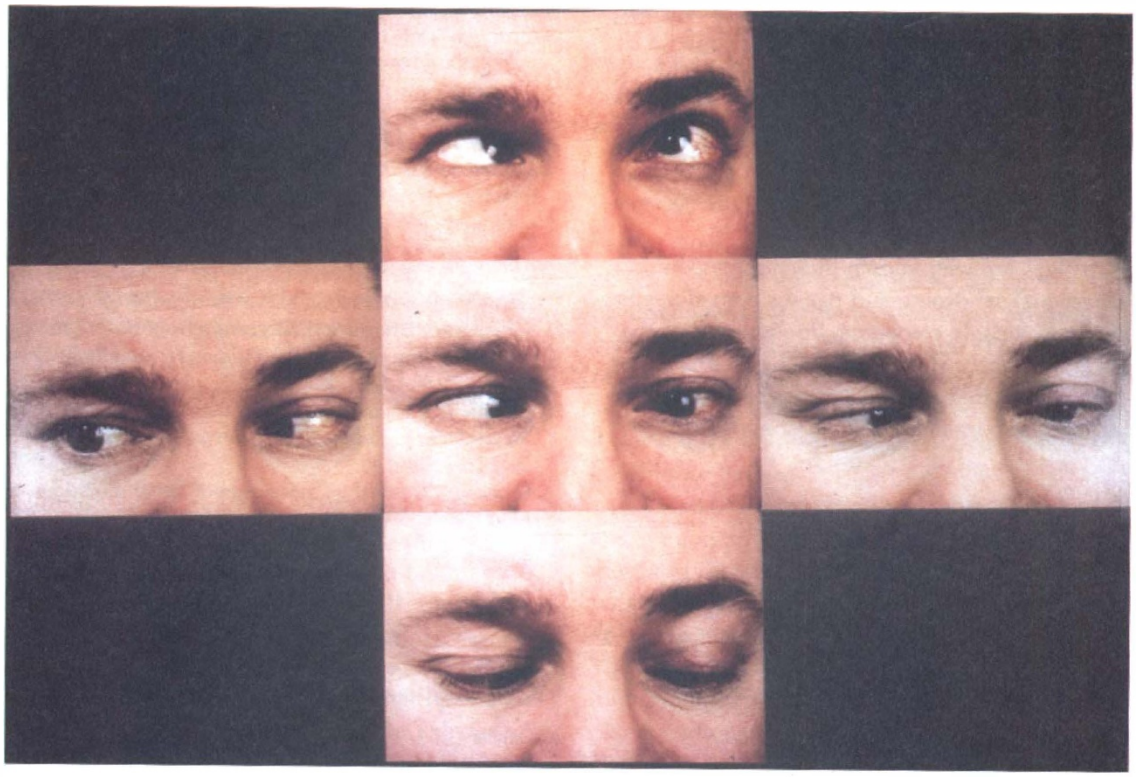

Fig. 1*(a) (Legend opposite.)*