

Norrie's disease in an Asian family

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SUMMARY Norrie's disease, a congenital progressive oculo-acoustico-cerebral degenerative condition, is a sex linked recessive disorder. Previously described as atrophía oculi congeniti, it is associated with bilateral pseudotumour of the retina, lens, and corneal opacities, and phthisis bulbi. Some patients develop progressive deterioration of mental function and hearing. We report a Sri Lankan family with typical features of Norrie's disease.

Norrie,¹ a Danish ophthalmologist, surveyed the causes of blindness in Danish institutes for the blind, and described a congenital type of blindness as atrophía oculi congeniti. It affected only males and occurred in several generations. Warburg² subsequently reviewed the data available and suggested the name Norrie's diseases for congenital bilateral pseudotumour of the retina, of sex linked recessive inheritance, with complete penetrance but varied expressivity. Mental deficiency occurs in about a third of the patients, and 25%–30% develop a progressive neural hearing loss.³ The ocular lesion produces lens and corneal opacities and subsequently phthisis bulbi.²

Most of the reports of Norrie's disease are from Denmark and Sweden.³ But subsequently reports from Australia, the Netherlands,⁴ and the United States^{5,6} have been published. The first report from the United States was in a Negro family.⁵ A similar condition has been described among Greek Cypriots⁷ and Canadian Indians,⁸ which from genetic, clinical, and histopathological studies closely resemble Norrie's disease.⁹ Warburg³ interpreted many other cases reported from England, Germany, Austria, Spain, Switzerland, and Cuba as Norrie's disease. There are no reports of this condition in Sri Lankans, and to our knowledge it has not been reported in Asians.

Case reports

CASE 1

A 3-year-old boy presented with a history of blindness from birth and delayed milestones. He was delivered normally at term, and the postnatal period

was normal. The mother's antenatal period was uneventful. The mother noticed during early infancy that he did not respond to light and appeared blind. His milestones were delayed in comparison with his elder sister's. At the age of 3 years he could roll over and grasp objects when handed over, and he could sit without help. Though his hearing appeared to be normal, he could not speak single words. He was also in the habit of head banging. On examination of the eyes, he had an irregular pupil on the right side, bound by synechiae. A central cataract was seen, the pupil was occluded by a yellowish grey mass, and the fundus could not be visualised. An extensive corneal opacity of the left eye was observed, and the globe was soft and phthisical.

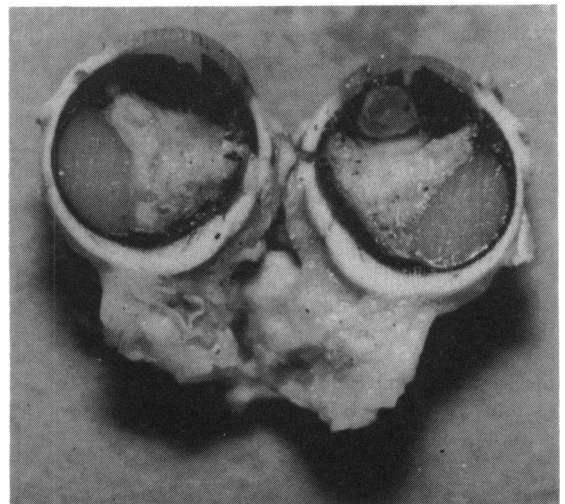


Fig. 1 Post-mortem section of right eye, of case 1 (IV²) showing pseudoglioma.

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At the age of 4 years the child died suddenly after an episode of vomiting and drowsiness. Histological examination of the right eye (Fig. 1) showed fibrovascular granulation tissue behind the lens, in which many areas were hyalinised, with scar formation. Marked hyperplasia of pigment epithelium and areas of ossification behind the lens were seen. Hypoplasia of the inner layer of the retina, and necrosis with infiltration by lymphocytes, plasma cells, and a few multinucleated giant cells, was observed.

CASE II

The younger sib of case I, this 1-year-old boy also presented with a history of blindness from birth. His milestones were normal and he could sit up without help and speak single words. He had bilateral central cataracts. There was a central corneal leucoma in the right eye. The left cornea was hazy, and the pupil was completely occluded by a proliferative yellowish grey mass. The fundi could not be visualised. He was referred to Colombo for a second opinion, where both cataracts had been removed without any improvement in the sight. At the age of 16 months there was evidence of regression of milestones. Although he could sit up without help at the age of 8 months, he was not able to do so on his own at the age of 16 months, and he made rocking movements of his body back and forth.

FAMILY HISTORY

The pedigree of the family (Fig. 2) was studied extensively. Two of the mother's (III¹⁴) brothers (III¹²

and III¹⁷) were affected; the elder brother (III¹²) had been blind from birth and had died of an unknown cause, associated with helminthiasis. The other (III¹⁷, aged 27 years) had also been blind from birth. His milestones were normal, and had been an inmate of the Rathmalana Blind School. In recent years he gradually became withdrawn and psychotic in his behaviour. His hearing is apparently normal. The maternal grandmother (II¹¹) had four brothers (II³, II⁶, II⁹, II¹⁰) who were blind from birth. One (II⁶) had died during childhood of an unknown cause; the others had been to the Blind School, and the relatives did not know where they are now. The grandmother's (II¹¹) eldest sister's (II²) one son (III⁴) was also affected. He had initially been diagnosed as having bilateral malignant tumours, probably retinoblastoma, and both eyes had been enucleated during childhood. After surgery the parents had been informed that it was not a malignant condition. He is now partially deaf, but not retarded. The grandmother's (II¹¹) younger sister (II¹³) too has had two male children who were blind. Both of them died during childhood, one (III²²) being drowned in a well and the other (III²⁸) dying of an illness associated with helminthiasis.

Discussion

The study of the pedigree in four generations strongly suggests a sex linked recessive disorder, which makes acquired conditions very unlikely.

The evidence of sex linked inheritance, blindness

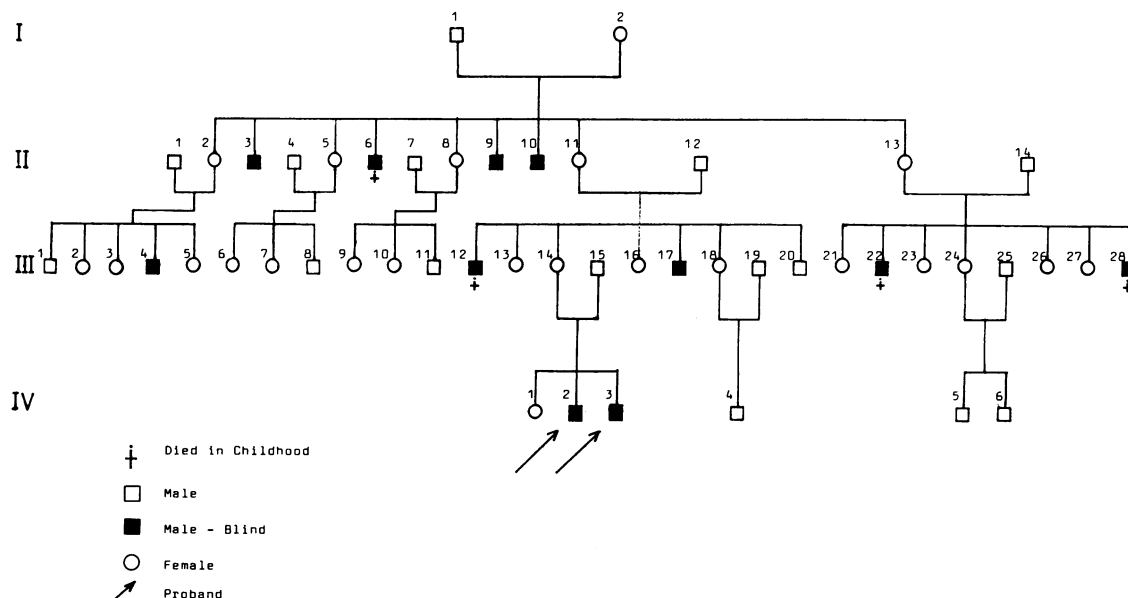


Fig. 2 Family pedigree.

from birth, mental retardation, and the characteristic ocular changes of bilateral pseudotumour, cataracts, corneal degenerative changes, phthisis bulbi, and associated deafness in one family member, justify the diagnosis of Norrie's disease in this family. The histological appearance of the eye in case I is also consistent with those described in Norrie's disease.³

It is of interest to note that one of the family members (III⁴) had his eye enucleated for suspected malignancy. Warburg's first case³ also underwent enucleation for suspected retinoblastoma. Of the 16 families traced in the literature enucleation has been performed in three patients.³

Warburg³ suggests that the disease causes degenerative changes in the retina, sometimes in the cerebrum and in the acoustic nerves. This could account for the progressive withdrawal and psychotic behaviour in one member of this family (III¹⁷), and mental retardation and early regression in our two patients. Strikingly similar regressive mental changes have been observed by Hansen⁵ and Holmes.⁶ Hansen⁵ describes rocking movements back and forth made by his patient. Warburg³ also mentions similar movements in one patient (family BJ—IV¹⁰). One of our patients (IV³) behaved in a similar manner. Self mutilation was observed by Warburg³ in some of the patients studied; one of our patients (IV²) was in the habit of banging his head.

Blindness, especially if associated with mental retardation, increases the risk of fatal accidents in early childhood. An example of this was seen in patient III, who had drowned in a well. A child belonging to a family in Warburg's series³ had also drowned in a well.

A striking feature in the pedigree is that many of the females in the third generation are not married.

On questioning the mother (III¹⁴) it was apparent that the female relatives of the mother are well aware of the nature of the disease and its inheritance. They are therefore reluctant to get married. It is of interest to note that both these children were referred to the first author (DGH de S) by an obstetrician, when the mother (III¹⁴) had insisted on permanent sterilisation in spite of having only one normal girl. In contrast, Warburg³ stressed the need for urgent eugenic counselling in the families studied by her, because very few were aware of the risk factors.

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