Peripheral Neuropathy and Ichthyosis in Krabbe’s Leucodystrophy

The association of peripheral neuropathy and ichthyosis is well recognized in Refsum’s syndrome but has not previously been recorded in Krabbe’s leucodystrophy.

Case Report

N.C. was born to West Indian parents at full term weighing 3409 g. She was first referred at the age of 10 months because of generalized ichthyosis which had been present since early infancy.

Her early development was normal and she could sit unaided at 6 months. After the age of 7 months, however, she lost the ability to sit. She became irritable, cried constantly, and refused her feeds. She made no attempt to pull herself to a standing position.

On examination at 12 months, she lay with her arms and legs extended and feet plantar-flexed. She was unable to sit or stand and would not take any weight on her legs. There was increased tone round her elbow and knee joints but marked hypotonia round the wrist joints. Marked head lag with traction on her arms was present. Extensor spasms were frequent and distressed crying resulted from the slightest handling of her limbs. The hands and feet were cold and cyanosed. All the tendon reflexes were absent. The fundi were normal.

The CSF contained 70 mg/100 ml protein with a normal cell count and Lange curve. The EEG showed a preponderance of slow wave activity. The bone age was advanced to a 2-year level at 10 months.

Motor nerve conduction velocities were very slow; that for the right ulnar nerve was 13·0 m/sec; the left ulnar 13·3 m/sec, and the right posterior tibial nerve 10·3 m/sec (normal at one year = 46±1 ± 3·0 m/sec for the ulnar nerve and 38·2 ± 3·3 m/sec for the posterior tibial nerve).

The slow nerve conduction velocities confirmed the presence of a demyelinating peripheral neuropathy. This together with the progressive nature of the central nervous system disturbance suggested the diagnosis of either Krabbe’s leucodystrophy or metachromatic leucodystrophy. The former was thought more likely because of the early onset and rapid progression of the disease.

Urinary examination for intracellular metachromatic material was repeatedly negative. Blood leucocyte arylsulphatase A levels were normal. The combination of ichthyosis and peripheral neuropathy suggested the diagnosis of Refsum’s syndrome. Other features of this syndrome, such as ataxia and retinitis pigmentosa, were absent. There was no increase of phytanic acid in the patient’s serum.

The patient’s condition rapidly deteriorated and she died at 14 months. Histological examination of the nervous system revealed the characteristic globoid cells confirming the diagnosis of Krabbe’s leucodystrophy.

Summary

A retrospective study of bleeding from the gut in 51 children showed no outstanding prevalent condition but rather, a large number of uncommon causes. A high proportion of cases remained undiagnosed. When it has become clear that bleeding is trivial, and not the precursor of more major haemorrhage, the patient need not be extensively investigated since bleeding is unlikely to recur.

I thank Mr. K. W. Wilkinson for his advice with this paper, and Dr. E. M. Belton, for permission to discuss the cases under her care.

REFERENCES


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Teased preparations of the sciatic nerve showed segmental demyelination.

Family History
The mother is 18 years old and unmarried. A 2-year-old sibling from a different father is normal. There is no family history of either ichthyosis or central nervous system disorder.

Discussion
Slow nerve conduction velocities and pathological changes have only recently been described in Krabbe's disease (Sourander and Olsson, 1968; Dunn et al., 1969). A similar demyelinating peripheral neuropathy with slow nerve conduction velocities also occurs in metachromatic leucodystrophy (Fullerton, 1964) and Cockayne's syndrome (Moosa and Dubowitz, 1970). Nerve conduction velocity measurement is therefore useful in separating some of the leucodystrophies from other progressive degenerative diseases of the nervous system, in which demyelinating peripheral neuropathy does not occur.

The association of the ichthyosis with Krabbe's disease in this patient may possibly be fortuitous, but there is some evidence to suggest that the two may be associated. Krabbe's disease is an inborn error of lipid metabolism in which deficiency of the enzyme cerebroside sulphatransferase results in an accumulation of cerebroside (Bachhawat, Austin, and Armstrong, 1967). Esterly (1968) has suggested that ichthyosis may be the result of a disturbance of lipid metabolism in the skin. Ichthyosis and peripheral neuropathy occur in Refsum's syndrome, in which the fatty acid phytic acid accumulates in the body. Ichthyosis also occurs in two other central nervous system disorders, namely Sjögren-Larsson and Rud's syndromes. The ichthyosis and enteropathy in a case of Sjögren-Larsson syndrome was cured by substituting medium chain triglycerides for normal lipids in the diet (Hooft, Kriekemans, and Devos, 1967). A polyneuritis was also present in Rud's original case (Rud, 1927).

Motor nerve conduction studies may therefore be worth doing in patients presenting with ichthyosis and associated nervous system disorders.

Summary
A case of Krabbe's leucodystrophy with ichthyosis and peripheral neuropathy is described. This association has not previously been reported.

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References
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Birthweight in Haemolytic Disease of Newborn
Information about the birthweights of infants with haemolytic disease of the newborn (HDN) is surprisingly scanty. Miller, Johnson, and Durlacher (1944) thought that these infants were heavier than normal, while Lind and Hytten (1969) stated the reverse, though neither author reported figures. Javert (1942) found that birthweights of 22 non-hydropic infants with HDN did not differ from normal, while the mean birthweight of 16 infants with hydrops was 1 kg greater than those of normal infants of equivalent gestation. Naeye (1967) found that the necropsy weights of 23 infants with HDN (12 of whom had hydrops) did not differ from those of normal infants of the same gestational age. Karnicki (1968) found that birthweights of 88 infants with severe HDN were greater than normal. We have analysed birthweights of non-hydropic infants with HDN to determine whether they differed from the normal birthweight distribution of infants born at the Winnipeg General Hospital.

Material
The case records of all Rh negative mothers who had given birth to Rh positive liveborn, singleton infants between January 1966 and December 1968 were reviewed. 687 charts provided the following information about the infant: birthweight, gestational age