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Multiple nerve palsies in β thalassaemia major

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SUMMARY A patient with β thalassaemia major is described who developed a lower motor neurone facial nerve palsy on the left side, together with a phrenic nerve palsy on the same side, during the course of the illness. This complication has not been reported before in haemoglobinopathies.

β thalassaemia major is the commonest haemoglobinopathy found in Sri Lanka. Neurological complications have been described in thalassaemia but these are mostly confined to spinal cord compression due to extramedullary haematopoiesis¹⁻³ and auditory nerve involvement.⁴

Case report

An 11 year old Sinhalese girl, who developed pallor together with progressive abdominal distension during the latter half of infancy, was diagnosed as a case of β thalassaemia major after relevant haematological investigations. She was the youngest in a family of five children and the other siblings were in good health. There was no history of consanguinity and the father had died of ischaemic heart disease at 50 years of age. From late infancy onwards she received numerous blood transfusions at infrequent intervals due to poor compliance. The aim was to maintain the haemoglobin concentration above 80 g/l. Only a few doses of desferrioxamine were given to her because it was not readily available.

At the age of 7 years she developed a classical left lower motor neurone facial palsy that did not resolve with time. There was impairment of taste in the anterior part of tongue but no hyperacusis. There was no evidence of middle ear infection or

mastoiditis. Audiometry was normal. She developed corneal scarring due to exposure keratitis and a tarsorrhaphy was performed to minimise further damage to the cornea. At 7½ years of age she was admitted with severe pallor and congestive cardiac failure. A chest radiograph showed an elevated left dome of the diaphragm. Fluoroscopic screening confirmed paralysis of the left dome. The rest of the neurological examination, including funduscopy, was normal. At 9 years of age, as her splenic size had increased to 15 cm below the left costal margin and the transfusion requirements had increased, a splenectomy was performed. Since then she has been on monthly prophylactic benzathine penicillin treatment.

At present both her height and weight are below the 3rd centiles, she is normotensive, and has the typical thalassaemic facies. Her liver span extends 13 cm below the right costal margin. The most recent investigations were as follows: haemoglobin concentration 85 g/l; white cell count $10.5 \times 10^9/l$ with polymorphs 55%, lymphocytes 35%, monocytes 3%, eosinophils 6%, and basophils 1%; reticulocyte count $0.4 \times 10^{-3}/l$. The peripheral blood picture showed hypochromic and microcytic red cells, pronounced anisocytosis, normoblasts, hypersegmented neutrophils, and few macrocytes; platelet count $290 \times 10^9/l$; alkaline denaturation test positive; haemoglobin electrophoresis showed adult haemoglobin 15% and fetal haemoglobin 85%. Radiographs of the hand showed rectangular metacarpals with reticulation and a radiograph of the skull showed widening of diploe with 'hair-on-end' appearance. Radiographs and serial tomograms of the cervical and thoracic spine did not show any paravertebral soft tissue shadows. Consent for a myelogram was refused.

Discussion

Neurological complications in thalassaemia are rare. Extramedullary haematopoiesis is well recognised in thalassaemia at sites such as the liver and the spleen. Rarely such haematopoietic tissue may be found within the spinal canal, extradurally, causing compression of the spinal cord.¹⁻³ Infrequently, infiltration of the middle ear by haematopoietic tissue may lead to hearing loss.⁴ These complications are more common on a low transfusion regime because it leads to bone marrow hyperplasia with widening of bones and extramedullary haematopoiesis.³ This patient was on a low transfusion regime due to poor compliance and had radiological evidence of widening of bones.

The commonest cause of an isolated unilateral lower motor neurone facial nerve palsy at this age is Bell's palsy; however, in about 85% of cases, resolution occurs with time. Absence of evidence of middle ear infection, or a vesicular eruption around the external auditory meatus at the time of the facial palsy, excludes otitis media and herpes zoster as likely causes. Poliomyelitis or another enteroviral infection as a potential cause is unlikely in this patient as she had received appropriate doses of oral polio vaccine in the past and also because the two nerve lesions were spaced out in time. Therefore, the probable cause for the facial nerve palsy is

pinching of the nerve at one of the narrow points along its course, such as within the facial canal, due to widening of diploic bone. The radiological evidence of widening of skull diploe supports this hypothesis, although an unresolved Bell's palsy cannot be conclusively ruled out.

The reason for the phrenic nerve palsy is more difficult to explain. It may have been due to pressure from a small paravertebral mass of haematopoietic tissue. Although irradiation has been used successfully to treat paravertebral masses,² it could not be used in this patient because exact localisation was not possible.

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Betaine for treatment of homocystinuria caused by methylenetetrahydrofolate reductase deficiency

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SUMMARY A 24 day old girl with homocystinuria and hypomethioninaemia caused by methylenetetrahydrofolate reductase deficiency presented with rapidly progressing encephalopathy and myopathy. An almost complete recovery was achieved by treatment with betaine.

5,10-Methylenetetrahydrofolate reductase (MTHFR) deficiency¹ leads to deficient remethylation of homocysteine and is one of the causes of homocystinuria (figure). The other causes of homocystinuria are defects in cobalamin metabolism or deficient cystathionine β -synthase activity.

Methionine accumulates with homocystine in cystathionine β -synthase deficiency,¹ whereas in patients with disorders in cobalamin metabolism or with MTHFR deficiency methionine synthase is functionally deficient and the increased concentration of homocystine occurs with normal or decreased methionine concentrations. In the latter conditions neurological impairment is the most important clinical finding. When symptoms occur in early infancy there is often rapid deterioration with respiratory failure.

Methylmalonic aciduria or macrocytic or megaloblastic changes of the bone marrow, or both, usually occur with homocystinuria in patients with disorders of cobalamin metabolism. These condi-