autoantibody screen on serum yielded negative results. Intrinsic factor type I (blocking) antibody and parietal cell antibody were not detected in gastric juice. Resting gastric juice pH was 2, but difficulties in collection of gastric juice prevented a satisfactory pentagastrin test. A Schilling test showed intestinal malabsorption of vitamin B₁₂ with 3.56% of free ⁵⁸CoB₁₂ and 3.06% of intrinsic factor bound ⁵⁷CoB₁₂ excreted into urine over 24 hours. Plasma concentrations of ⁵⁷CoB₁₂ and ⁵⁸CoB₁₂ were assayed between 7 and 11 hours after oral administration, and both showed a peak concentration of 30% of the predicted normal. Repeated testing for proteinuria (now 19 months after presentation) has yielded negative results. Stool microscopy did not show parasites (including fish tapeworm) or fat globules. Transcobalamin concentration was normal. Urinary indican was low. Barium study of the stomach and small bowel yielded normal results, apart from showing a hiatus hernia.

She has been treated with five 1 mg doses of hydroxocobalamin followed by 1 mg every other month. She made a rapid haematological response, with a normal haemoglobin and blood film one month after starting treatment. All her symptoms have disappeared and she has gained 2500 g in six months.

Discussion

The diagnosis of specific malabsorption of vitamin B₁₂ was confirmed by the low serum vitamin B₁₂, impaired intestinal absorption of vitamin B₁₂, the presence of normal gastric acid, and the absence of intrinsic factor antibody and parietal cell antibody in serum and gastric juice. The rapid clinical response to treatment with vitamin B₁₂, the lack of

steatorrhoea, the normal small bowel barium study, and the low urinary indican make more general malabsorption unlikely, and further investigation was not thought to be justified.

Specific malabsorption of vitamin B₁₂ was described by Imerslund³ and has an autosomal recessive inheritance. It is associated with proteinuria in 90% of cases,⁴ but proteinuria may not occur for 18 months.⁵ Small bowel electronmicroscopy and histology is normal,⁴ and aetiology is unknown. Diagnosis is made by showing intestinal malabsorption of vitamin B₁₂ in the absence of general malabsorption.

Doctors tend to stereotype Down's syndrome children,⁶ symptoms of lethargy and mental slowness being interpreted as part of the syndrome. It is important to consider other causes and to be as assiduous in tracking down the diagnosis as one would be for otherwise normal children.

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Neonatal malaria and obstructive jaundice

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SUMMARY A case is presented of transplacental malaria in an infant associated with persistent conjugated hyperbilirubinaemia and liver disease.

Malaria presenting in the neonatal period is a rare disease even in endemic areas.¹

Case report

A female term infant was born in Bradford, England, weighing 2800 g to Indian parents of a consanguineous marriage who had two other healthy children weighing 5600 g at term and 1700 g at 32 weeks. The mother had spent four months of the pregnancy in India, and two days after delivery a

thick blood smear had shown malarial parasitaemia. This was later confirmed as *Plasmodium vivax*. There was satisfactory postnatal progress, and the baby was discharged home at 8 days free of jaundice. Consultation was requested at the age of 3 weeks because of feeding difficulties, lethargy, and the occurrence of jaundice.

On admission the infant was small (3000 g; <10th centile) and icteric and had a liver edge palpable 1 cm below the costal margin. The stools were pale coloured and the urine dark. Laboratory findings were as follows: haemoglobin 97 g/l, white blood cell count 21×10^9 /l (37% neutrophils, 54% lymphocytes, 4% eosinophils, 5% others), bilirubin 390 μ mol/l (22.8 mg/100 ml) with a conjugated fraction of 270 μ mol/l (15.8 mg/100 ml), alkaline phosphatase activity 491 IU/L (normal range 73–226 IU/l), aspartate aminotransferase activity 235 IU/l (normal range 67–108 IU/l) alanine aminotransferase activity 521 IU/l (normal range 0–54 IU/l), total protein 53 g/l (5.3 g/100 ml) (normal range 60–80 g/l (6–8 g/100 ml)), albumin concentration 26 g/l (2.6 g/100 ml) (normal range 35–50 g/l), and globulin concentration 27 g/l (2.7 g/100 ml) (normal range 21–36 g/l). Serology for toxoplasma, rubella, cytomegalovirus, herpes virus, and hepatitis B were all normal. α_1 Antitrypsin was 2.8 g/l (280 mg/100 ml) (normal range 2.1–5.0 g/l), caeruloplasmin 490 mg/l (49 mg/100 ml) (normal range 200–600 g/l), serum copper 30 μ mol/l (normal range 13–27 μ mol/l), and glucose-6-phosphate dehydrogenase 7.9 IU/gHb (normal range 8–16 IU/gHb). Sweat test chloride was 16 mmol/l (50 mg sweat) (normal range 8–40 mmol/l).

A thick blood smear showed heavy parasitaemia due to *P. vivax*, and, therefore, a diagnosis of transplacental malaria was made.

Definitive treatment with chloroquine (75 mg base daily for four days) and an abbreviated course of primaquine was begun. There is no requirement to treat this form of malaria with an 8-aminoquinoline.

A liver scan (p. butyl iminodiacetic acid labelled with ^{99m}Tc ; International CIS Ltd) showed slow hepatic uptake with no significant change in the pattern of radioactivity over six hours, suggesting minimal biliary patency. A Rose Bengal I^{131} test confirmed this impression, with 5.3% of the administered dose being collected in uncontaminated faeces in 48 hours (<6% collected suggests extra hepatic biliary atresia).

At six weeks an operative cholangiogram showed a normal extra hepatic biliary tree, therefore excluding surgically correctable biliary atresia. A liver biopsy examination at this time had equivocal features comprising feathery degeneration of

hepatocytes, early ductular proliferation and islands of extramedullary haemopoiesis and a polymorphonuclear cell infiltrate. The jaundice was declining (bilirubin 130 μ mol/l (7.6 mg/100 ml), all of which was conjugated), and the infant was discharged home.

The jaundice persisted and the infant failed to thrive. At the age of 4 months the infant was readmitted. The bilirubin concentration was 105 μ mol/l (6.1 mg/100 ml) (all conjugated) and the alkaline phosphatase activity 1400 IU/l. The infant had moderate hepatosplenomegaly and weighed 5800 g (<10th centile). The liver scan was repeated and a further percutaneous liver biopsy specimen obtained. This showed progression of the histological features and was more typical of 'neonatal hepatitis' with giant cell transformation, canalicular cholestasis, and persisting portal tract infiltrate of lymphocytes and polymorphonuclear leukocytes.

At last follow up (age 10 months) the infant was still icteric with massive hepatosplenomegaly and below the appropriate weight for age. Bilirubin concentration was 70 μ mol/l (4.1 mg/100 ml), alkaline phosphatase activity 3610 IU/l, albumin concentration 47 g/l, and cholesterol concentration 3.78 mmol/l (146 mg/100 ml) (normal range 3.5–7.5 mmol/l (135–290 mg/100 ml)). Repeated investigations have not shown persisting malarial infection.

Discussion

An association between obstructive jaundice and neonatal malaria was noted by Patwari.² In this Indian study of 10 infants with neonatal malaria an increase in bilirubin concentration was noted in eight (mean 167 μ mol/l (9.8 mg/100 ml)) and in two of these was mainly conjugated. Only six, however, had good evidence of transplacental transmission, and their type of jaundice is not commented upon.

Hepatomegaly is rather less commonly noted than splenomegaly.³ All four cases of an American study of imported congenital malaria from South East Asia showed hepatosplenomegaly and jaundice (mean bilirubin concentration 104 μ mol/l (6.1 mg/100 ml)).⁴ In another report, albeit with a different age range, of 80 children (<3 years) with *P. vivax* malaria 63% had hepatomegaly and 83% splenomegaly.⁵ It would seem that the younger the age of malarial onset the greater the severity of hepatic damage (and therefore jaundice). In this particular case the presumed lack of passive maternal immunity may be contributory.

The differential diagnosis between 'neonatal hepatitis' and biliary atresia is an important one because surgical relief, if it is to be successful, must be performed early.^{6,7} The current diagnostic pro-

cedures did not clarify the nature of the hepatic disease, and even liver biopsy specimens were equivocal, although it should be noted that interpretation of biopsy material can be extremely difficult.⁸

In this case the prognosis is uncertain, and it is still not clear whether the persisting jaundice and liver disease is due to the malarious infection or idiopathic 'neonatal hepatitis'. A chance association between these two rare diseases would seem to be unusual.

I thank Mr J M Beck for allowing me to report on this patient while under his care and for his helpful comments used in its preparation.

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