described by Borrie¹ did have a raised ASO titre and another had exacerbations after tonsillitis. Our patient had shown a raised ASO titre on many occasions. However, she had had neither a sore throat before admission nor a history of sore throat, and repeated throat swabs were negative. She did complain of a sore throat 9 days after admission (20 June 1976) when slight throat inflammation was present and again in mid-November 1976, although at that time nothing abnormal was visible on examination.

Relapse may occur at some time in the future but if it does, there should be spontaneous resolution. It is of course possible but unlikely that she could develop the systemic disease later.

I thank Dr C S Smith and Dr Elizabeth Poskitt who were in charge of this case.

This child was presented (slides and discussion only)

at the Section of Dermatology Meeting at the Royal Society of Medicine, London, in December 1976.

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Correspondence to Dr Julian Verbov, Royal Liverpool Children's Hospital, Liverpool L7 7DG.

Successful pregnancy in transfusion-dependent thalassaemia

R M THOMAS AND A E SKALICKA

Department of Paediatrics, Whittington Hospital, London

SUMMARY Successful pregnancy in a transfusion-dependent thalassaemic patient receiving subcutaneous desferrioxamine is reported. This is the first such case to be described.

Endocrine impairment is well recorded in transfusion-dependent β -thalassaemia major, and puberty is nearly always delayed.¹ This is thought to be due to gonadal or pituitary failure caused by iron deposition, although defective hypothalamic maturation has also been suggested.² Endocrinopathy in nontransfusion-dependent β -thalassaemia intermedia is also well described, although it is less common than in thalassaemia major, and the presumed mechanism is increased gastrointestinal iron absorption or hypoxaemia, or both of these.

The beneficial effect of a high-transfusion regimen and chelation on the marrow hyperplasia, endocrine function, and growth velocity, and perhaps on the onset of puberty in this patient, has been described.³ Due to her irregular menses, pregnancy was not diagnosed until 14 weeks' gestation and she continued to administer her daily 12-hourly infusion of

subcutaneous desferrioxamine during the first 16 weeks of pregnancy.

Case reports

The mother. She was the second child of Greek Cypriot parents, and was born in October 1960. A diagnosis of β -thalassaemia intermedia was made at age 13 months when haemoglobin (Hb) was found to be 6.9 g/dl after a traumatic fracture of her arm. HbF level was 32%. With folic acid supplementation, Hb remained stable until age 3½ years when, with Hb 5 g/dl, she sustained a fracture of the left arm and right leg. At that time, splenectomy was performed because of hypersplenism (9 cm below costal margin).

Until age 12 years, her Hb level remained between 7 and 8 g/dl without transfusion, but her growth velocity was poor (height 6 cm, <3rd centile at age 12½ years) and she developed pronounced 'thalassaemic facies'. Because of conductive deafness and 'chronic serous otitis media', myringotomy was performed and showed the presence of bone marrow in the middle ear. She showed no sign of puberty

and investigations confirmed that she had developed endocrine complications due to her chronic anaemia, ineffective erythropoiesis, and iron overload (as a result of increased gastrointestinal iron absorption).³ Significant impairment of both adrenal and pancreatic function was demonstrated and regular 6-weekly blood transfusions were instituted in order to maintain mean Hb at 11 g/dl. Intramuscular desferrioxamine 1 g daily was also begun and vitamin C supplementation followed 18 months later. In early 1978, at age 18 years, intramuscular injections of desferrioxamine stopped, and the drug was given subcutaneously in an increased dosage of 2 g over 12 hours each day by means of a battery-operated infusion pump. Her serum ferritin level before regular transfusion was 330 µg/l (normal 35 µg/l for adult women), and her total iron load as transfused blood before pregnancy was 21.4 g.

Her health improved greatly and she entered puberty (stage 2) 6 months later. Menarche occurred 20 months after beginning this intensive transfusion and chelation regimen. Transfusions were of ordinary ACD-stored blood until mid-1977 (age 17 years). Since then she has been receiving 'washed' blood (erythrocytes suspended in saline) because of frequent febrile transfusion reactions while having ordinary ACD-stored blood. Irregular menses have taken place about every 2–3 months since puberty at age 13½ years, until her last menses in September 1978 (age 18 years). An intrauterine contraceptive device was inserted in November 1978; however a pregnancy test 4 weeks later was positive. Desferrioxamine and vitamin C were stopped 2 weeks later when gestation was assessed at 16 weeks by uterine size. The father of the infant is British and does not have β-thalassaemia trait. Transfusions during pregnancy were increased to 2 units (420 ml washed blood per unit) every 4 weeks and mean Hb was maintained at 10.5 g/dl. Serum ferritin immediately before pregnancy was 1130 µg/l (normal range 14–148). 4 g iron was transfused in 20 units (420 ml per unit) of washed blood during pregnancy.

Pregnancy was uneventful until 30 weeks' gestation when an antepartum haemorrhage occurred. After a second haemorrhage and spontaneous rupture of the membranes at 33 weeks, an emergency caesarean section was performed. After delivery her serum ferritin level was 1440 µg/l.

The infant. A normal preterm boy was delivered; birthweight was 1780 g (50th centile for 33 weeks), length 35 cm, head circumference 27 cm. Placental weight 420 g. Apgar scores were four at 1, six at 5, and eight at 10 minutes. Endotracheal intubation was required from 2 to 8 minutes. Dubowitz assessment of maturity was 33–34 weeks. Hb was 14.8

g/dl at birth, blood group O Rh-negative (mother was O Rh-negative). Direct Coombs's test negative. Serum ferritin level at age 6 weeks was 180 µg/l (normal for males 39–340).

Despite hourly feeds of breast milk via a nasogastric tube, blood sugar at age 15 hours was 0.9 mmol/l (16 mg/100 ml) and concomitant insulin level 2 mU/l. After a bolus of intravenous 50% Dextrose 1 ml/kg, an intravenous infusion of 10% Dextrose during the next 24 hours prevented further hypoglycaemia. (The mother did not have glycosuria during pregnancy.)

Serum bilirubin was 140 µmol/l (8 mg/100 ml) at age 40 hours and maximum bilirubin 190 µmol/l (11 mg/100 ml). Phototherapy was given for 8 days. The jaundice was prolonged and continued until age 6 weeks. Bilirubin was mainly unconjugated and there was no evidence of haemolysis, infection, hepatocellular dysfunction, hypothyroidism, or metabolic defect to account for this prolonged jaundice. Unconjugated hyperbilirubinaemia persisted for 2 weeks after stopping breast feeding at age 4 weeks, and the possibility of an enzyme deficiency—such as Gilbert's disease—must be considered.

Progress

Maternal breast milk was given for 30 days; thereafter (as maternal milk production was inadequate) artificial feeds were given. The infant thrived and discharge weight was 2.44 kg on day 35. Maternal desferrioxamine was restarted 5 weeks after delivery, after breast feeding had stopped.

Discussion

Puberty is often delayed in nontransfusion-dependent thalassaemia, but subsequent fertility is usually unaffected.⁴ This case is unique in that no other transfusion-dependent thalassaemic woman has been known to have undergone successful pregnancy. In addition, our patient continued desferrioxamine during the first trimester because pregnancy was not overt until 16 weeks. Experiments in pregnant rabbits and mice have shown minor teratogenic effects with large doses of desferrioxamine (retardation of bone ossification, vertebral aplasia, bifurcation, and fusion of ribs) (R Bruckner, 1965, CIBA unpublished report). Regular administration of high-dose desferrioxamine to fully-grown dogs, cats, and rats causes subcapsular cataracts, and 3 cases of cataract formation in adult humans have been recorded since the drug became available in 1963 (R Bruckner, 1965, CIBA unpublished report). These 3 patients were not thalassaemic, but were receiving desferrioxamine for treatment of chronic

iron overload secondary to multiple transfusions for hypoplastic anaemia. Two patients were receiving corticosteroids in addition to desferrioxamine, and corticosteroids have also been reported to cause posterior subcapsular cataracts. However, the cataracts cleared partially when desferrioxamine was withdrawn in these patients, and increased in density in the one patient who was later re-exposed to the drug (thus implicating desferrioxamine in a causative role). Our infant exhibited no obvious abnormality. We were also concerned about the possible excretion of desferrioxamine in breast milk, although since this chelating agent is little absorbed from the adult human gut, the presence of desferrioxamine in breast milk seems unlikely to have been harmful to the infant.

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Correspondence to Dr R M Thomas, Department of Paediatrics, University College Hospital, Gower Street, London WC1E 6AU.