Alternatively, myocardial fibrosis could be a measure of the severity of CF, a concept supported by the observation of Oppenheimer and Esterly (1974) that acid mucopolysaccharide deposits in the media of the pulmonary artery and aorta were found only in severe cases. In our case abundant acid mucopolysaccharide was shown in heart and pancreas. As controls, 2 cases of cardiomyopathy, one cyanotic congenital heart disease with myocardial fibrosis and one myocarditis of undetermined origin, have been stained for acid mucopolysaccharide and negligible amounts were found.

The excessive amount of acid mucopolysaccharide in our case might have arisen from excessive production by fibroblasts along the lines of Danes’s (1969) experiment. The presence in the extracellular space of large amounts of acid mucopolysaccharides may possibly be the immediate cause of cardiac muscle cell damage and replacement fibrosis. It also supports the hypothesis of Johansen et al. of an abnormal distribution of acid mucopolysaccharides in the connective tissue in CF. CF may in future be regarded as a genetic acid mucopolysaccharidosis.

Summary

A case of cystic fibrosis with myocardial fibrosis and acid mucopolysaccharide deposits in the myocardium is described. The case supports the theory that cystic fibrosis may be a genetic acid mucopolysaccharidosis.

References


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Neonatal thyrotoxicosis is associated with transplacental passage of human thyroid stimulating immunoglobulin (HTSI)

Neonatal thyrotoxicosis accompanying or following maternal thyrotoxicosis was first described by White (1912) and is usually temporary. Mackenzie (1964) presented evidence that the disorder was related to transplacental passage of long-acting thyroid stimulator (LATS), an immunoglobulin-G, but Mahoney et al. (1964) described a case in which LATS was present in the mother but not in the child. Nutt et al. (1974) reported a case in which LATS was not found in mother or baby, but another immunoglobulin, LATS-P (now known as HTSI), was detected in the mother. We report a further case in which HTSI was detected in both maternal and cord blood, and sequential measurements of HTSI have been made in mother and baby. In the management of thyrotoxic pregnancy estimation of HTSI is helpful. A high value in the maternal serum may be an indication for giving propranolol treatment to the baby from birth.

Case reports

Mother. A 27-year-old teacher with an apparently uneventful first pregnancy until referred by her general practitioner at 34 weeks’ gestation because of thyrotoxicosis. Previous health had been good and there was no family history of thyrotoxicosis. She complained of malaise, vomiting, and intermittent weight loss throughout the pregnancy, and also sweating, nervousness, and irritability. On examination the classical features of thyrotoxicosis were apparent with goitre, bruit, exophthalmos, lid lag, tachycardia, sweating, and tremor. Investigations confirmed thyrotoxicosis with serum protein-bound iodine (PBI) >20 μg/ml (normal 3-0-8.0), T3 (tri-iodothyronine) resin uptake ratio 1·11 (normal range 0-82-1·28). She was treated with carbimazole 10 mg 8-hourly, and propranolol 40 mg 8-hourly. Her symptoms rapidly improved and at 38 weeks’ gestation she was euthyroid, with PBI 8·3 μg/100 ml. She remained on antithyroid drugs after delivery.

Baby. Labour started spontaneously at 39 weeks’ gestation, but delivery was by Haig-Ferguson forceps.
because of fetal bradycardia in the second stage of labour. The baby (female) required intermittent positive pressure ventilation at birth, but by 8 minutes the Apgar score was 9. Birthweight was 3.45 kg, length 53.5 cm; there were no abnormalities apart from splenomegaly. She was clinically euthyroid at birth and progress was uneventful until the 7th day when she was reported to be hyperactive, sweating profusely with temperature 38°C. On examination sinus tachycardia (220/min), tachypnoea (80/min), prominent eyes (Fig. 1), and a goitre were noted. Stool frequency had been 2 per day, but increased to 6 per day. Weight, which had increased to 3.5 kg on day 6, fell to 3.2 kg. She thus had a thyroid crisis. PBI was >20 μg/100 ml. Potassium iodide (5 mg 3 times daily) was started immediately and continued for 11 weeks. 12 hours after onset of symptoms the liver was enlarged three finger breadths, the tachycardia and tachypnoea continued, and digoxin therapy was started but was withdrawn after 72 hours. By 4 weeks of age thyroid function tests were normal. At 6 months psychomotor development was normal, and length, weight, and occipitofrontal circumference were on the 90th centile. Heart rate was 130/min and respiratory rate 30/min while the child was crying. There was no goitre or exophthalmos, though there was some asymmetry of the skull and face and the anterior fontanelle admitted only the tip of a finger.

Immunological investigations. LATS and HTSI were measured as described by Dirmikis and Munro (1975). LATS was at the lower limit of detection in the

Figure 1.—Baby at the age of 2 weeks.

mother 16 days after delivery, but was not detected subsequently. LATS was not detected in the baby's blood at 1 day, 16 days, or 185 days. HTSI results of mother and baby are shown in Fig. 2. HTSI fell below the level of detection in the baby but did not fall in the mother.

Discussion

The incidence of hyperthyroidism in pregnancy is about 0.04% and can be difficult to diagnose as many of the clinical and laboratory abnormalities are reproduced by the metabolic changes of pregnancy. Radioactive iodine is clearly unsuitable for management and surgery, which should only be carried out on patients previously made euthyroid by drugs and was also not possible in our case. Carbimazole was used in moderate doses as the drug crosses the placenta and may make the fetus hypothyroid and induce a goitre. Propranolol was given with the carbimazole and though the use of this drug has not been reported in hyperthyroidism of pregnancy it has been used safely in pregnant women with hypertrophic obstructive cardiomyopathy.

Thyrotoxicosis in the baby is a well-known complication of hyperthyroidism in pregnancy and indeed may appear in the baby even if the thyrotoxicosis has occurred some time before the pregnancy. Until now there has been no reliable way to predict which babies will develop thyrotoxicosis. All those delivered from mothers with thyrotoxicosis, or with a history of the disorder, have had to be observed carefully. Thyroid function tests carried out soon after birth may be misleading and are best carried out after the 4th day of life (Davies, Lawton, and Waring, 1974). Dirmikis and Munro (1975) suggested that the level of HTSI in the mother near term may help to predict the development of thyrotoxicosis in the baby. If this is confirmed,
early treatment of the baby will be possible and it may also be possible to modify the drug regimen of the mother before delivery so as to delay the appearance of symptoms in the infant.

The management of the thyrotoxic neonate has usually included sedatives, potassium iodide, carbimazole, and digoxin, and recently propranolol has been used (Pemberton, McConnell, and Shanks, 1974). In view of the possibility of cardiac failure, many neonates may benefit from treatment with iodine and digoxin before propranolol is started. The long-term prognosis is good provided the initial thyroid crisis can be overcome, though Robinson, Hall, and Munro (1969) reported a baby who subsequently developed premature fusion of skull sutures. Long-term follow-up is therefore indicated.

The most important findings in this case were the high levels of HTSI in the mother and in cord blood. The level of HTSI has remained high in maternal serum, but the level in the baby has declined with time, with a half-life of approximately 10 days. In view of the results reported by Dirmikis and Munro (1975), HTSI should be estimated in the third trimester of a thyrotoxic pregnancy, or if there is a history of thyrotoxicosis. If the level of HTSI is high in the maternal serum, then the baby should be given propranolol from the time of delivery and the situation should be reviewed in the light of clinical progress and laboratory results obtained at the end of the first week of life.

Summary

A woman who developed thyrotoxicosis during pregnancy had a high level of HTSI at the time of delivery. The baby had high levels of HTSI initially but, unlike the mother, the levels fell, giving a half-life of HTSI of 10 days.

We are grateful to Dr. S. M. Dirmikis for immunological investigations, Professor J. A. Strong for helpful criticism and advice, and Mrs. M. Hamilton for secretarial help.

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Neonatal pyridoxine responsive convulsions due to isoniazid therapy

The control of neonatal fits after pyridoxine administration is well recognized. These may be either pyridoxine dependent (Hunt et al., 1954; Robbins, 1966), or secondary to pyridoxine deficiency. We report an infant born to a mother on antituberculous therapy, who was started on isoniazid therapy at birth. On the 13th day of life convulsions began which persisted for 4 days and only ceased after starting pyridoxine therapy. The pyridoxine deficiency was presumed secondary to the isoniazid medication.

Case report

An infant aged 17 days was referred with a 4-day history of frequent generalized convulsions. He was the first child of unrelated Indian parents. Active pulmonary tuberculosis was diagnosed in his 35-year-old mother by chest x-ray during the 19th week of pregnancy. She was treated with ethambutol 200 mg and isoniazid 100 mg three times daily, but stopped taking the drugs after 2 weeks because of nausea. The same therapy was started again 3 weeks before delivery. The pregnancy was otherwise uncomplicated; the infant was delivered by forceps under epidural block and weighed 2·9 kg at term. He was inoculated with isoniazid-resistant BCG after birth and started on oral isoniazid 20 mg twice a day. He was bottle fed (Cow and Gate full cream) and remained well, making normal progress until the onset of convulsions.

On admission he was convulsing. He had generalized, multifocal clonic fits that lasted for 60 to 90 seconds and occurred every 15 to 30 minutes. Between convulsions no abnormalities were detected on examination. Investigations for an infective or biochemical cause were