syndrome may develop well after the treatment of syphilis has been initiated.

Scott and Clark (1946) reported what they believed to be a possible renal Herxheimer reaction in an adult with an acquired syphilis. Their patient had a febrile reaction after the initiation of penicillin therapy and then developed the nephrotic syndrome 14 days later. Our patient had no known initial manifestations of the Herxheimer reaction. One can only speculate as to whether Scott and Clark’s case and our case may indeed represent renal Herxheimer reaction.

The pathogenesis of the nephrotic syndrome in syphilis is obscure. However, the morphological studies of others may afford a clue. Electron dense deposits in the area of the glomerular basement membrane have been described in adults with syphilis and the nephrotic syndrome (Falls et al., 1965). Braunstein et al. (1970) have identified these as complement-fixing \( \gamma \)-G2 heavy chains and \( \lambda \)-light chains. Churg (1968) has also identified electron dense deposits in the glomerular capillary wall of an infant with syphilis and the nephrotic syndrome. Pollner (1966), utilizing light microscopy, reported glomerular basement membrane thickening in a similar case. Thus the nephrotic syndrome in congenital syphilis appears to be associated with what are ordinarily considered ‘immune deposits’ in the region of the glomerular basement membrane: these apparently regress with clinical improvement (Falls et al., 1965).

Summary

A 3-month-old infant with congenital syphilis developed the nephrotic syndrome 14 days after having been adequately treated with penicillin. This case is believed to be the first reported instance of nephrotic syndrome occurring in congenital syphilis after treatment with an adequate dose of penicillin.

REFERENCES


Severe cutaneous reactions to phenytoin

Since the first reports of the effectiveness of phenytoin in the treatment of epilepsy (Merrit and Putnam, 1938), it has established itself as the drug of choice in many of the forms of epilepsy. The many side effects reported are usually attributed to blood levels in excess of 20 \( \mu \)g/ml (Kutt and McDowell, 1968). Signs such as gingival hypertrophy and skin rashes are not usually related to phenytoin blood levels but indicate a sensitivity to the drug.

The purpose of this paper is to describe a child who developed a fatal skin reaction to the drug when only therapeutic blood levels of the drug were reached, and another case where a severe sensitivity reaction was associated with toxic blood levels of the drug.

Case reports

Case 1. A 10-year-old boy was admitted with a history of six generalized seizures within 1 year. There was no previous history of illness in himself or his family. He had received no anticonvulsant therapy. Physical examination was normal. EEG indicated an active epileptogenic focus in the right midtemporal region, involving the cortex. He was given phenytoin 200 mg daily. He had no further convulsions, but 10 days after starting phenytoin he developed a morbilliform rash. Blood phenytoin level on this day was 18-3 \( \mu \)g/ml. Phenytoin was stopped. By the next day the rash had extended and became more intense. Bullous formation occurred and he became ill and toxic. Rupture of the bullae and leak of serous fluid occurred. Intravenous fluids, antihistamines, and analgesics were given. Dermatological opinion confirmed a diagnosis of Stevens-Johnson syndrome, the rash being confluent, sheets of skin desquamating, and the oral mucosa, by now, being affected.
Tetracycline and prednisolone 60 mg/day were given. 600 ml whole blood followed by plasma were then required. He was confused and restless, and became incontinent.

Continuous serous fluid loss occurred. By this stage the trunk and abdomen were totally desquamated and areas of the upper and lower limbs were involved. He became dysnpoeeic and cyanosed, and radiology confirmed an extensive bronchopneumonia. 13 days after the onset of the rash he died. At no stage during the illness were there biochemical changes to suggest hepatitis. Terminally, blood urea rose to 180 mg/100 ml. Necropsy permission was refused.

Case 2. This 10-year-old girl was admitted with uncontrolled centrocephalic epilepsy. Numerous anticonvulsants had been tried before admission, all with little effect. Phenytoin had not been used previously. A further EEG showed a greater frequency of discharges and she was given phenytoin. On the first day she received 400 mg and this was reduced to 300 mg/day on the following day. She rapidly developed signs of toxicity with nystagmus and ataxia. The blood phenytoin level reached 35-7 µg/ml. 9 days after starting phenytoin a macular rash developed on the trunk and face. Phenytoin was stopped. The rash progressed rapidly and became confluent over the face. She was pyrexial and confused, with periorbital oedema and a severe erythematous morbilliform rash over her face, trunk, and abdomen and, to a lesser degree, the limbs. She was treated with antihistamines, steroids, and local therapy. A further 3 days elapsed before the rash showed any improvement. 8 days after the onset, the rash had almost cleared. The child was apyrexic and alert. Convulsions were partially controlled at this time by diazepam.

Discussion

Skin reactions occur in about 5% of patients receiving phenytoin. Reactions usually occur 10 to 14 days after the start of treatment. The classical reaction is a morbilliform rash, but occasionally scarlatiniform or urticarial rashes occur (Livingston, 1956).

Fatal cases are extremely rare, two cases only having been reported, both in adults. Gropper (1956) described a 29-year-old man who developed jaundice, exfoliative dermatitis, eosinophilia, and lymphadenopathy; terminally ulceration extended to include lips, eyes, oral cavity, and genitalia. Ritchie and Kolb (1942) described a fatal case of haemorrhagic erythema. Necropsy showed extensive haemorrhagic changes in the skin, mouth, and gastrointestinal tract, and pulmonary oedema and oedema of the brain. The only child mentioned in the literature is a nonfatal case of erythema bullosum malignans in a 9-year-old (Heller and Sloane, 1950).

None of these reports gave blood phenytoin levels at the time of the onset of the rash. The child with the fatal reaction reported here had therapeutic blood levels of phenytoin throughout the period when the rash began, phenytoin being measured by the method described by Dawson and Jamieson (1971). On the other hand, the child with the less severe reaction had grossly raised blood levels and the toxic signs of ataxia and nystagmus. The initial dosage of phenytoin in this child was excessive. An initial dosage of 100 mg twice daily (10 mg/kg) should have been prescribed, then a probable reduction to 5 mg/kg monitored by blood phenytoin levels.

The differing severity and outcome of these two cases suggest that skin reactions are indeed a sensitivity reaction to the drug and not a toxic reaction associated with raised phenytoin levels. Immediate cessation of the drug is indicated. These two children fit into the described pattern in which the rash develops 8 to 10 days after ingestion of the drug and tends to be morbilliform. Both children had negative antibody titres to measles, in that no rise in titre developed over the period of their illnesses.

Summary

Two 10-year-old children are described who were treated with phenytoin for epilepsy, both of whom developed a severe cutaneous reaction, which proved fatal in one child. The severer reaction was accompanied by therapeutic blood levels of phenytoin, while the milder reaction was associated with grossly raised levels. It is suggested that such skin reactions to phenytoin are a sensitivity response, rather than a toxic reaction.

References


K. P. DAWSON

Paediatric Unit, Law Hospital, Carlute, Lanarkshire.