Acrocyanosis due to imipramine

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SUMMARY An 11 year old girl who was being treated for enuresis with imipramine developed acrocyanosis of the hands and feet. All biochemical and haematological investigations gave normal results. When imipramine was stopped the girl recovered within three days.

Imipramine, the oldest of the tricyclic anti-depressants, is widely used to treat nocturnal enuresis in children. We describe an unusual side effect of imipramine that has not been previously reported in children with enuresis and suggest a new hypothesis for the pathogenesis of this phenomenon.

Case report

An 11 year old girl was admitted for investigation of persistently cyanosed hands. The problem started seven weeks before admission with sudden painful swelling of the medial two metacarpophalangeal joints of her left hand. The pain lessened but both hands became increasingly blue and swollen. Her feet also became persistently cold, blue, and moist, although not painful. There was no history of cold injury nor of Raynaud's phenomenon.

Her only medication was imipramine 25 mg nightly for primary nocturnal enuresis. This had been started 10 weeks before admission, three weeks before the onset of symptoms.

She was the product of a healthy term pregnancy and normal delivery and had weighed 3760 g at birth. Her growth and development were normal, and her only hospital admission had been for a tonsillectomy and adenoidectomy at age 10. Her father had maturity onset diabetes, and her mother was enuretic until age 16. She had a brother who was also enuretic.

Physical examination showed a slender afebrile girl. Her hands and feet were noticeably cold, blue, and moist, and blanched on pressure. Her forearms showed livido reticularis. Her blood pressure was 120/80 mm Hg, pulse was 80 beats/minute, and all peripheral pulses were palpable. The remainder of the examination was normal.

On admission her haemoglobin concentration was 133 g/l, white blood cell count 7.7×10⁹/l with a normal differential, and her erythrocyte sedimentation rate was 3 mm in the first hour. The urinalysis gave normal results. A coagulation screen (activated partial prothrombin time, prothrombin time, thrombin clotting time) gave normal results. Cold agglutinins were absent. Rheumatoid factor was absent, as were autoantibodies. Immunoglobulin concentrations were normal. Radiographs of the chest and hands were normal, and barium swallow showed normal oesophageal peristalsis.

During her hospital stay the imipramine was discontinued because her enuresis had not improved. No new drugs were started. Three days later her hands and feet were warm, pink, and dry. At follow up two months later she reported that apart from one brief episode of cyanosis of the hands on a cold day, her hands and feet had remained normal. She remains enuretic.

Discussion

The diagnosis in this case was acrocyanosis, a condition seen most often in female adolescents and defined as 'a symmetric persistent coldness and cyanosis of the distal ... extremities'. Acrocyanosis is a vasospastic disorder related to Raynaud’s phenomenon, which is intermittent but more severe than acrocyanosis and often leads to trophic changes and ulceration. Childhood Raynaud's phenomenon is rare and is usually associated with a collagen vascular disease. There was neither clinical nor laboratory evidence of collagen vascular disease in this case. There was, however, a strong temporal relation between imipramine use and the occurrence of acrocyanosis.

There are sparse reports of digital vasospasm attributable to imipramine. Coldness of hands and feet has been observed in two of 52 hyperkinetic children and in two psychotic children treated with imipramine. Appelbaum and Kapoor have also described an adult treated for depression with 150 mg/day of imipramine who developed digital vasospasm.

A mechanism by which this may have happened is related to the neurohormonal effects of imipramine. Imipramine inhibits reuptake of monoamine neurotransmitters at both central and peripheral recep-
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Transient neonatal hyperthyroidism and maternal thyroid stimulating immunoglobulins

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SUMMARY Serum thyroid stimulating hormone binding inhibitor immunoglobulins (TBII) and thyroid stimulating antibody (TSAb) concentrations were measured in three pregnant women with hyperthyroidism and then in their infants. The results suggested that TBII concentrations in infants in the neonatal period or from mothers during the third trimester of pregnancy showed a good correlation with the development of neonatal hyperthyroidism.

It is now widely believed that the transient thyroid overactivity in infants born to mothers with hyperthyroidism is a result of the placental transfer of thyroid stimulating immunoglobulins from the mother to the infant. The immunoglobulins in the sera from some patients with Graves’ disease were shown, by the radioreceptor assay system, to inhibit the binding of thyroid stimulating hormone to its receptor sites and were designated as thyroid stimulating hormone binding inhibitor immunoglobulins (TBII). It was also shown that immunoglobulins in the patient’s sera stimulated the production of cyclic AMP in human thyroid tissues and were known as thyroid stimulating antibodies (TSAb).

We studied three unrelated infants who were born to women with hyperthyroidism, and one of them developed typical transient neonatal hyperthyroidism. We measured serum TBII and TSAb concentrations in these infants and their mothers.

Case report

Family 1 The mother developed hyperthyroidism at 26 years old when she was in her 32nd week of pregnancy. From the 34th week until delivery she had been maintained euthyroid with methimazole. A girl (3330 g) was born at 39 weeks’ gestation. On the 8th day of life she was noted to be hyperactive and had developed diarrhoea. Tachycardia was noticed on the 10th day when her body weight was 3100 g. Thyroid studies on day 8 showed that she had hyperthyroidism; she had serum concentrations of triiodothyronine, thyroxine, free thyroxine, and...
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