septum produced the clinical features of hydatid embolization of both pulmonary and systemic circulations.

I am grateful to Dr. R. T. Jenkins and the many members of staff who were involved with this patient for advice and encouragement.

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Wiskott-Aldrich syndrome associated with idiopathic infantile cortical hyperostosis (Caffey’s disease)

The Wiskott-Aldrich syndrome is an X-linked recessive disorder characterized by thrombocytopenia, purpura, eczema, and recurrent infections (Wiskott, 1937; Aldrich, Steinberg, and Campbell, 1954). Infantile cortical hyperostosis is a well-recognized clinical and radiological entity of unknown cause which usually resolves spontaneously (Caffey and Silverman, 1945). We report briefly the details of two unrelated male infants with the Wiskott-Aldrich syndrome who developed cortical hyperostosis.

Case reports

Case 1. A male born 15 September 1967 is the only child of his mother's second marriage. By her first marriage she had two children, one of whom, a boy, died at the age of one year from bronchopneumonia having suffered from thrombocytopenia, purpura, eczema, and recurrent infections since early infancy.

Our patient developed purpura and a low platelet count within a few days of birth, and later had fresh blood in the stools and eczema. On the ninth day of life the serum immunoglobulins were IgG 1050 mg/100 ml, IgA 248 mg/100 ml (greatly raised, Stiehm and Fudenberg, 1966), IgM none detected. Marrow aspiration from a tibia at the age of 4 weeks was normal apart from defective budding of megakaryocytes. He continued to have thrombocytopenia (platelets usually <10,000/mm³), anaemia, and occasional epistaxes. In early life he had several infections, notably gastroenteritis (Esch. coli O55), otitis externa, skin sepsis, bronchitis, and lobar pneumonia.

At the age of 3 months spontaneous swellings of the left scapula and lower jaw appeared; x-rays showed hyperostosis (Fig. 1). Surgical biopsy of the scapula showed oedema of the perichondrium, but no evidence of neoplasm or infection. The soft tissue and bone changes subsided slowly, and later x-rays were normal.

At 6 months he was transferred to The Hospital for Sick Children, Great Ormond Street. The bone marrow contained plentiful megakaryocytes which had ragged cytoplasm, peripheral vacuolation, and defective budding. No antibodies to platelets were found in the serum. The blood group was A rhesus positive with very weak anti-B titre. No antibodies to pathogenic Esch. coli were found. At one stage there was a weakly positive Coombs test. The lymphocytes transformed normally with phytohaemagglutinin. A thymic shadow was present on x-ray. Serum immunoglobulins have been measured on several occasions, usually showing raised IgA, with normal IgG, and IgM near the lower limit of the normal range. Results of the most recent measurement, at the age of 5 years, were IgG 800 mg/100 ml, IgA 500 mg/100 ml, IgM 54 mg/100 ml.

Three inoculations of diphtheria and tetanus toxoids in the third year of life produced no detectable antibodies. During the last year this patient has been reasonably well apart from persistent wide-spread eczema.

The boy's mother said that at the age of 15 years she herself had developed a swelling of the mandible and her doctor diagnosed Caffeys disease. No medical details are available.

Case 2. A male born 20 May 1970. On the first day of life this infant, an only child of unrelated parents, had a petechial rash and a platelet count of less than 10,000/mm³. The thrombocytopenia persisted and, at the age of 2 months serum immunoglobulins were IgG 370 mg/100 ml, IgA 88 mg/100 ml, IgM 14 mg/100 ml, indicating a raised IgA level with IgM at the lower limit of normal.

At the age of 4 weeks attempts to obtain bone marrow from both tibiae were unsuccessful. Later (aged 6 weeks) open biopsy from an iliac crest yielded only hypocellular marrow. At 7 weeks (3 weeks after the initial attempt at marrow examination) tender swellings developed over both tibiae and the soft tissues became brawny and oedematous. Blood cultures were negative but, since the possibility of osteomyelitis could not be eliminated, he was treated with cloxacinil and fucidic acid intravenously. Pyrexia with neutrophil leukocytosis continued throughout this episode. Surgical exploration of the right tibia (aged 2 months) revealed only swelling of the subperiosteal, periosteal, and overlying tissues. There was no pus or altered blood.

3 weeks after the operation tender swellings appeared in both forearms, the mandible, and in several ribs. These
Case 1. X-ray showing cortical hyperostosis of left scapula and slight thickening of left clavicle also.

Case 2. X-ray showing cortical hyperostosis involving the mandible.
swellings were accompanied by the radiological changes of cortical hyperostosis (Fig. 2) which gradually resolved.

This patient is now just over 2 years old and has been remarkably well, though thrombocytopenia with episodes of purpura have continued. Eczema first appeared at the age of 4 months and has persisted. Serum immunoglobulins have been measured on several occasions and, in general, a high IgA level has persisted and the IgM value has been at the lower end of the normal range for his age. On 7 June 1972, (aged 2 years) the immunoglobulins were IgG 590 mg/100 ml, IgA 300 mg/100 ml, IgM 20 mg/100 ml.

Discussion

The combination of thrombocytopenia, appearing very early in life, and eczema in these two male infants strongly suggests a diagnosis of the Wiskott-Aldrich syndrome, particularly in Case 1 whose half-brother died of a similar disorder. This diagnosis was supported in both children by the subsequent findings of raised serum IgA, with IgM values low in the normal range (as given by Stiehm and Fudenberg, 1966), together with defective antibody responses to active immunization. In the third month of life (Case 1) and in the second month (Case 2) these infants developed multiple bony swellings with tender induration of the overlying soft tissues, the jaw being involved in both. The clinical and radiological features and, in Case 1 the histology, are those of infantile cortical hyperostosis as described by Caffey and Silverman (1945).

The aetiology of idiopathic infantile cortical hyperostosis is unknown, but the concurrence of these two unusual disorders in the same individuals may not be fortuitous. The Wiskott-Aldrich syndrome is inherited in an X-linked recessive manner, whereas idiopathic cortical hyperostosis usually occurs sporadically and affects both sexes. Nevertheless, examples of the latter disease have occurred in a family pattern affecting adults and children (Gerrard et al., 1961); the mother of our first case possibly had the disease in adolescence. There is no firm evidence for a genetic basis to these familial cases, which are of both sexes, so that concurrence with the Wiskott-Aldrich syndrome cannot be ascribed to genetic factors.

The presence of fever, raised sedimentation rate, neutrophil leucocytosis, and bone swellings occurring in two infants with immune deficiency suggests an infective disorder, particularly as one infant had recently had narrow punctures in two of the affected bones. Caffey (1973) has postulated an infective basis (either prenatal or postnatal) for infantile cortical hyperostosis. A recent case report (Temperley, Douglas, and Rees, 1972) gives this some support, but unlike our patients this child had persistently raised IgG and IgM, as well as IgA. Surgical exploration showed no evidence of infection in either of our patients, but the possibility of previous infection cannot be excluded. If the occurrence of these two rare diseases is not fortuitous, one is tempted to suggest that Caffey's disease might be the result of an immunological defect associated with infection.

The thrombocytopenia in our patients we ascribe to the Wiskott-Aldrich syndrome. We are not aware that it has been previously reported in infants with cortical hyperostosis; on the contrary, thrombocythaemia is not rare in the latter disease (Pickering and Cuddigan, 1969) and was present in one of Caffey's original patients. Subperiosteal haemorrhages may occur in the Wiskott-Aldrich syndrome (Rivera and Biehusen, 1960), but the findings at operation in our patients showed no haemorrhage. In Case 2 the bone changes began in both tibiae 3 weeks after marrow puncture in these bones. Though subsequent changes appeared spontaneously in other bones, it is possible that trauma may have initiated the process.

Finally, it is worth commenting on the IgA levels. A rise in IgA is common in the Wiskott-Aldrich syndrome, but the extremely high level in Case 1 at the age of 9 days appears to be unique.

Summary

Two infants with the Wiskott-Aldrich syndrome developed infantile cortical hyperostosis in early infancy. The association of these two disorders, not previously reported, raises the possibility that immunological defect may play a part in the pathogenesis of idiopathic cortical hyperostosis.

We thank Dr. June Lloyd and Dr. Betty Wallace for help with the investigation of the two children, and Professor J. Soothill for helpful comments.

References


Short reports


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Arch Dis Child 1973 48: 818-821
doi: 10.1136/adc.48.10.818

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