Remission of progressive renal failure in familial Mediterranean fever during colchicine treatment

T HERLIN, K STORM, AND B HAMBORG-PETERSEN

Department of Paediatrics, Aarhus Kommunehospital, University of Aarhus, Denmark

SUMMARY Colchicine was administered to a 12 year old girl with familial Mediterranean fever and progressive renal insufficiency. There was immediate resolution of abdominal attacks together with a dramatic fall in the serum creatinine concentration and the degree of proteinuria. At the same time her severely impaired growth was stimulated.

Familial Mediterranean fever is an inherited disease with recurrent inflammation of the joints and the pleural and peritoneal cavities. Development of amyloidosis in this disease is fairly common and is seen in one third of patients during the first two decades of life.\(^1\) Onset of familial Mediterranean fever amyloidosis in childhood indicates a poor prognosis, with only 20% survival 5 years after proteinuria has developed,\(^2\) and no spontaneous regression of renal failure has been reported.\(^1\)

Colchicine has been shown to reduce the severity and frequency of attacks.\(^3\) We describe the course of progressive renal failure in a 12 year old girl with familial Mediterranean fever which remitted during colchicine treatment.

Case report

This girl was the first of three children of Turkish parents. From 5 years of age she had suffered recurrent attacks of abdominal pain. She was admitted to our department when 11 years old, shortly after arriving in Denmark as an immigrant. She was chronically disabled with oedema of hands and feet, anaemia (haemoglobin 9.6 g/dl), hepatomegaly, height 107 cm (less than –3 SD), weight 18 kg (less than –3 SD), and erythrocyte sedimentation rate 97 mm in the first hour. Proteinuria was present (10 g/day), but her renal function was normal (creatinine clearance 94 ml/minute, serum creatinine value 33 \(\mu\)mol/l). The fibrinogen value was considerably raised at 10.5 g/l. Blood pressure and liver function were normal. At first, nephrotic syndrome was suspected but a trial with prednisone produced no effect. Rectal biopsy showed amyloid infiltration and the clinical picture was consistent with familial Mediterranean fever (recurrent polyserositis). This disorder has subsequently been diagnosed in a cousin. Her abdominal symptoms partly subsided and she was treated with diuretics only. During autumn 1983 the abdominal attacks

References

intensified and progressive renal failure was observed. The serum creatinine concentration rose to 290 μmol/l (Figure), creatinine clearance fell to 7 ml/minute, and the erythrocyte sedimentation rate increased. Secondary hypoparathyroidism and hypotonicity of both legs were observed.

Treatment with colchicine was instituted with 0.5 mg twice daily for one week and thereafter 0.5 mg daily. After this treatment began the spontaneous attacks abated immediately. A gradual fall in the serum creatinine concentration was observed during the next seven months (now 58 μmol/l) (Figure) and creatinine clearance increased to 68 ml/minute. Although proteinuria declined rapidly it is still considerable (4–8 g/day) (Figure). In addition an increase in haemoglobin, a fall in the erythrocyte sedimentation rate (44 mm in the first hour) and parathyroid hormone values, and a reduction in liver size were observed as well as resolution of the neurological symptoms. Growth, which had been arrested for at least one year, was again stimulated and within the past 7 months her height has increased by 4 cm. During treatment with colchicine no adverse side effects were observed, not even changes in bowel habits.

Discussion

The well known effect of colchicine of reducing the frequency and severity of abdominal attacks was observed dramatically in this patient. A steady fall in the serum creatinine value, proteinuria, and the erythrocyte sedimentation rate were seen immediately after treatment began, together with the relief of uraemic symptoms. Normal renal function returned after seven months, but proteinuria has persisted.

Colchicine seems to prevent amyloid deposits in experimental mice by blocking the release of amyloid A precursors from the neutrophils. Long term colchicine treatment in familial Mediterranean fever amyloidosis is followed by a gradual decrease in the degree of proteinuria. Remission of renal failure in this disorder, however, has not been reported, even during colchicine treatment. The rapid fall in serum creatinine (halved within one week) and in the degree of proteinuria after beginning this drug, without any other medication, makes it probable that colchicine is responsible for the improvement of renal function in our patient. Although renal biopsy was not undertaken, renal amyloidosis is extremely probable since our patient had Mediterranean fever with nephrotic syndrome, renal failure, and a positive rectal biopsy. The clinical picture and the time related colchicine response argue against the possibility that the improvement in renal function was due to resolution of a renal venous thrombosis often associated with this disease.

In a review describing the course of 35 children with amyloidosis and familial Mediterranean fever, growth retardation was not observed. Although growth arrest is known in uraemic patients, this girl presented with very short stature even before severe renal impairment was found. The onset of growth after beginning colchicine may indicate a relation between growth retardation and systemic amyloidosis. Relief of peripheral neuropathy symptoms and reduction of liver enlargement may further indicate the systemic effect of colchicine. Our results show that colchicine, in the treatment of familial Mediterranean fever, besides its preventive effect on acute spontaneous attacks, may also cause regression of amyloidosis which otherwise progresses relentlessly.

References

Prognosis for babies born with fused eyelids

G CROSS, M BECKER, AND P CONGDON

Regional Neonatal Intensive Care Unit and University of Leeds, Department of Paediatrics and Child Health, Leeds General Infirmary

SUMMARY The overall mortality for babies referred to our unit with fused eyelids was 68.7%; but when severe skin bruising was present only one of 18 babies survived (5-6%). This compares with a survival rate of 75% for those not bruised at or soon after birth. Skin bruising invariably indicates a very poor prognosis in babies born with fused eyelids.

The idea of a `cut off' weight below which intensive care could be withheld for babies born at the extremes of viability has been suggested. 1 Although mortality increases with decreasing birthweight, survival rates of 40% have been reported for babies born between 501 and 750 g. 2 Birthweight cannot, therefore, be used as the sole criterion when deciding whether to initiate or withdraw intensive care. Although each unit develops its own criteria in the light of previous experience, paediatricians often find the outcome for babies treated in other units helpful when counselling parents. For this reason we report our findings for a group of babies born with fused eyelids (gestation 24 to 27 weeks).

Patients

Between June 1981 and November 1983, 319 babies were admitted to our neonatal intensive care unit for respiratory support. The neonatal unit in our hospital at this time was atypical in that there was no maternity unit on site and all babies requiring ventilatory support were transferred. Retrospective analysis of case notes showed that 32 (10%) of these babies had fused eyelids, and in all but two this was bilateral. Their birthweights ranged from 500 to 970 g (mean 755 g) with estimated gestational ages of 24 to 27 weeks (calculated from the mother's menstrual dates). Only 10 of these 32 (31%) babies survived to be discharged from the unit. Of the 19 with birthweights equal to or less than 800 g, four survived (21.5%) but six of the 14 (43%) with birthweights greater than 800 g survived. Bruising, noticeable within the first hours of life (usually affecting both legs, the lower abdomen, or the head), was present in 18 of 30 (no record was made in two cases). Only 1 (5-6%) of these 18 survived compared with nine of 12 (75%) without bruising. There were no survivors in 11 newborns with bruising, fused eyelids, and a birthweight under 800 g. The Table summarises these findings. A full necropsy was available in only 14 of the 32 babies with fused eyelids. Twelve of these 14 were bruised at birth and seven had an associated intraventricular haemorrhage (59%). Twelve babies died within 24 hours (mean birthweight 765 g) and eight died within the next seven days (mean birthweight 690 g). Of the two remaining babies, one died aged 39 days with gross hydrocephalus secondary to a large intraventricular haemorrhage and the other died at 3 months from severe bronchopulmonary dysplasia. Two of the 10 survivors subsequently died unexpectedly as cot deaths when aged 5 and 15 months. Follow up examinations have been completed for all the others, and while none has a profound handicap, as the oldest is still only 23

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