

Short reports

Menkes's syndrome

Report of a patient treated from 21 days of age with parenteral copper

Menkes *et al.* first described the steely hair syndrome in 1962 and since then there have been several reports of it. The disturbance in copper metabolism in this condition leads to widespread changes, particularly in the skin, brain, and blood vessels. Wheeler and Roberts (1976) described dilatation of the urinary tract in three unrelated children with Menkes's syndrome in Norfolk. We report a further abnormality, namely emphysema, in a child with Menkes's syndrome, and we describe the ineffectiveness of early treatment of the syndrome with parenteral copper.

Case report

This boy was the second child of unrelated healthy parents whose first son had had Menkes's steely-hair syndrome and had died at age 6 months. This second child was born at term weighing 2.63 kg after an uneventful pregnancy during which the mother had declined an offer of amniocentesis. He was a thin

hypotonic infant with abnormal facies, low set ears, high arched palate, and a wrinkled skin. He did not feed well and had poor temperature control with one episode of severe hypothermia (rectal temperature 29°C) at 16 days.

Serum copper and caeruloplasmin levels are shown in Fig. 1. At 3 weeks he was started on regular IM injections of copper-EDTA, receiving on average 600 mg/kg weekly in divided doses without complications.

Other investigations showed normal blood urea, electrolytes, calcium, and liver function tests. Apart from an episode of iron deficiency anaemia at 2 months, which responded to oral iron, blood counts were also normal. An intravenous urogram at 10 days was unremarkable but a micturating cystogram at 8 weeks showed severe bilateral reflux. Skull x-rays showed wormian bones.

During the first 3 months the baby's feeding improved and he gained weight. He smiled at 7 weeks. Hypothermia did not recur and he had no convulsions. Subsequently, however, in spite of continuing treatment with copper he deteriorated with marked muscle wasting, microcephaly, and mental regression. Sternal recession, first noticed at 3 months, became progressively more obvious. Copper treatment was abandoned after one year.

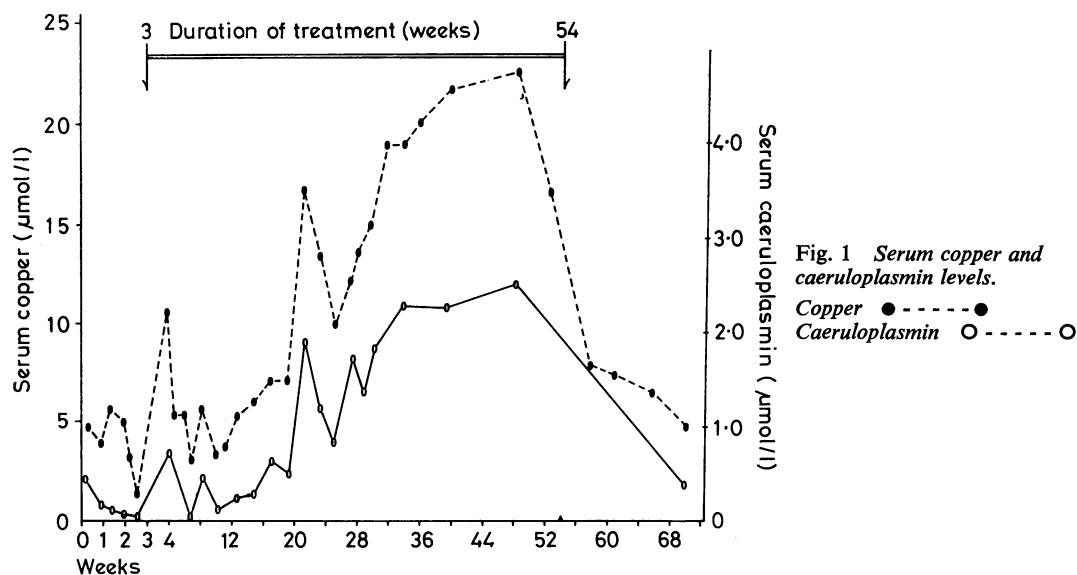


Fig. 1 Serum copper and caeruloplasmin levels.

Copper ● - - - ●
Caeruloplasmin ○ - - - ○

At age 19 months he was admitted in a terminal state of severe dehydration and collapse after 10 days of profuse vomiting.

Necropsy findings

The body was that of a baby boy weighing 5.1 kg with crown-heel length 740 mm. The scalp hair was blond with a steely texture. The teeth were poorly formed and showed a concave deformity on the occlusal surface. The meninges were not thickened. The brain (weight 850 g) showed mild cortical atrophy. The thymus was atrophic (weight 4 g). There were small effusions in both pleural sacs and there was a pectum excavatum deformity of the chest wall. The upper respiratory tract was patent. Both lungs were pink and voluminous, the cut surfaces showing a diffuse, fine panlobular type of emphysema. The heart was normal but the aorta and pulmonary arteries were thickened and dilated. There were no aneurysms of the arteries or veins, although the elastica was deficient. In the urinary tract there was gross dilatation and trabeculation of the bladder with diverticula but no urethral obstruction. There was mild dilatation of the left ureter. The right ureter and pelvis were markedly dilated and there was pus in the right kidney. The other abdominal viscera, the endocrine glands, and the skeleton were normal.

Discussion

This is the first time that panlobular emphysema has been demonstrated in detail in association with Menkes's syndrome (Fig. 2). It seems likely that the two conditions are causally related since copper is an important element in the formation of connective tissue, particularly elastin. The morphological abnormalities of elastin are well seen in the walls of blood vessels in Menkes's syndrome. These weakened vessels may undergo aneurysmal dilatation. The lung contains abundant elastin in the walls of alveoli, alveolar ducts, bronchioles, and bronchi as well as in the lung vessels. Fig. 3 shows that the pulmonary artery elastin is also affected in this patient. It is reasonable to suppose, therefore, that any abnormality in quantity or quality of elastin would lead to the development of emphysema.

Our case has shown that the level of serum copper is normal on the first day of life in a child with Menkes's syndrome and that it falls during the neonatal period. Early confirmation of the diagnosis could be made on the basis of two or three decreasing serum copper levels; this contrasts with the rising levels found in the normal neonate (Henkin *et al.*, 1973). Parenteral copper treatment raises the serum copper and caeruloplasmin levels, but even when started early in life it does not prevent the inexorable

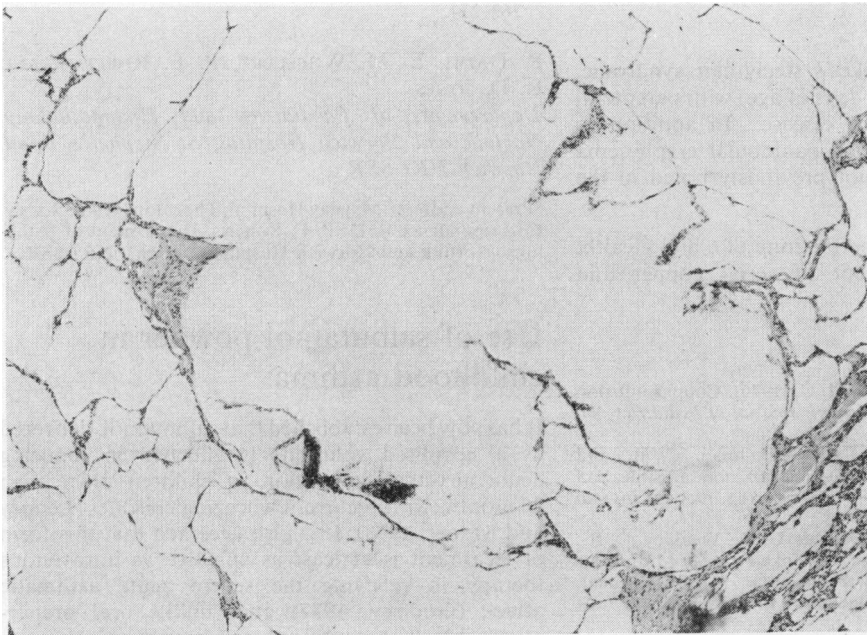


Fig. 2 Emphysematous space in section of lung. (H and E $\times 40$).

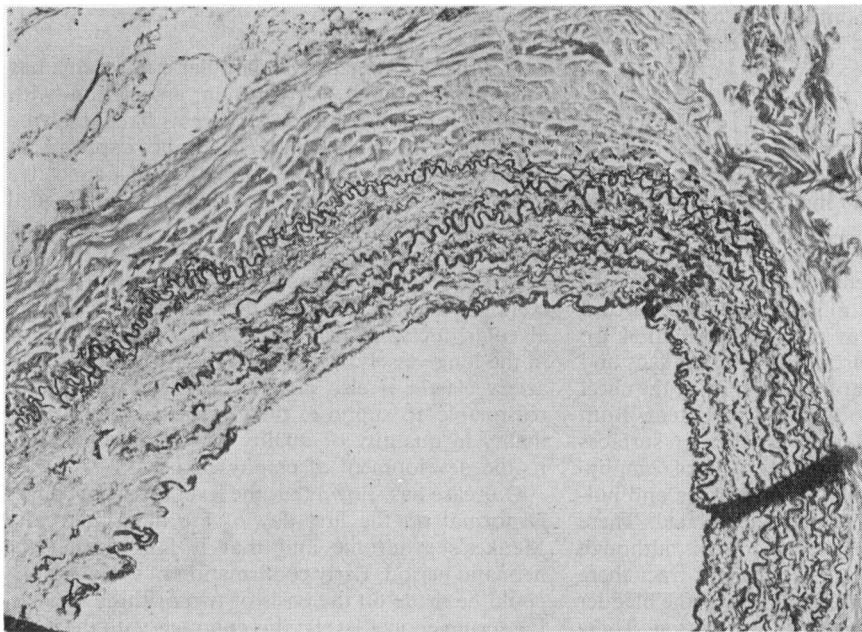


Fig. 3 *Deficiency in elastin in conducting pulmonary artery branch. (Elastin Van Gieson $\times 100$).*

mental and physical deterioration, leaving unfulfilled the hopes previously expressed by Walker-Smith *et al.* (1973) and Grover and Scrutton (1975).

Summary

In an infant with Menkes's steely-hair syndrome, early treatment (from 21 days of age) with parenteral copper failed to halt the disease. In addition to urinary tract abnormalities, panlobular emphysema was present, a finding not previously noted in the syndrome.

We thank Dr Delves, The Institute of Child Health, London for measurement of serial copper and ceruloplasmin levels.

References

Grover, W. D., and Scrutton, M. C. (1975). Copper infusion therapy in trichopoliodystrophy. *Journal of Pediatrics*, **86**, 216-220.
 Henkin, R. I., Schulman, J. D., Schulman, C. B., and Bronzert, D. A. (1973). Changes in total, nondiffusible, and diffusible plasma zinc and copper during infancy. *Journal of Pediatrics*, **82**, 831-837.
 Menkes, J. H., Alter, M., Steigleder, G. K., Weakley, D. R., and Sung, J. H. (1962). A sex-linked recessive disorder with retardation of growth, peculiar hair, and focal, cerebral, and cerebellar degeneration. *Pediatrics*, **29**, 764-779.
 Walker-Smith, J. A., Turner, B., Blomfield, J., and Wise, G. (1973). Therapeutic implications of copper deficiency in

Menkes's steely-hair syndrome. *Archives of Disease in Childhood*, **48**, 958-961.
 Wheeler, E. M., and Roberts, P. F. (1976). Menkes's steely-hair syndrome. *Archives of Disease in Childhood*, **51**, 269-274.

P. DAISH, E. M. WHEELER*, P. F. ROBERTS, AND R. D. JONES
Departments of Paediatrics and Histopathology, Norfolk and Norwich Hospital, St Stephen's Road, Norwich NRI 3SR

*Present address: Mayday Hospital, Thornton Heath, Surrey. Correspondence to Dr P. F. Roberts, Department of Pathology, Norfolk and Norwich Hospital, Norwich NR1 3SR.

Use of salbutamol powder in childhood asthma

It has now been established that salbutamol, delivered as a nebulised solution, is effective in reducing acute airways obstruction in children older than 20 months with recurrent wheezing episodes (Lenney and Milner, 1978). It is also accepted that this form of treatment is at least as effective as intravenous therapy in relieving the severe acute asthmatic attack (Godfrey, 1977) and, unlike oral preparations, blocks exercise-induced bronchoconstriction (Anderson *et al.*, 1976). Unfortunately nebulising