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SHORT REPORT

Mutation in the ATP7A gene may not be responsible for hypocupraemia in copper deficiency myelopathy

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The identified causes of copper deficiency in patients with copper deficiency myelopathy have included excessive consumption of zinc, a malabsorption syndrome, or a history of gastric surgery.¹ Not uncommonly the cause of copper deficiency has been unclear. We have recently reported on two patients with idiopathic hypocupraemic myelopathy who had increased copper content in biopsy specimens of the colonic mucosa.² This finding suggests impaired mobilisation of copper absorbed by intestinal epithelial cells as the probable defect in these patients. Increased copper content in the intestinal mucosa is well recognised in Menkes disease,³ the genetic basis for which are mutations in the ATP7A gene. Molecular defects at the ATP7A locus resulting in milder forms of the disease have also been described.⁴

To pursue the possibility that the hypocupraemia in idiopathic hypocupraemic myelopathy may relate to mutations in the ATP7A gene we undertook mutation analysis in one of our patients. Details of this patient have been reported elsewhere.^{2,5} She was a 48 year old woman with a myeloneuropathy who had a serum copper concentration at presentation of 0.11 µg/ml (normal: 0.75 to 1.45 µg/ml). Her 24 hour urine copper excretion was reduced to 6 µg/specimen (normal: 15 to 60 µg/specimen) and copper content in the colonic mucosa was 39 µg/g dry weight (normal: 6 to 13 µg/g dry weight). Her liver copper content was 71 µg/g dry weight (normal: 10–35 µg/g dry weight). With copper replacement and normalisation her neurological deficits stabilised and the spinal cord signal change seen by magnetic resonance imaging resolved.

DNA sequence analysis of the ATP7A gene did not show any abnormalities. All 22 coding exons and flanking introns were sequenced. Changes in the promoter or other non-coding regions as well as large intragenic deletions could not be ruled out. This finding suggests that hypocupraemia in

this subgroup of patients may not be related to ATP7A mutations. The understanding of copper homeostasis has become increasingly important and many different copper transporting proteins have been recognised.^{6,7} A primary absorption defect related to one of these copper chaperones may responsible for the hypocupraemia seen in copper deficiency myelopathy patients.

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