LETTER TO THE EDITOR

To The Editor

A 'Fixing' Explanation for Neurological and Haematological Disturbances

Keywords: Toxicology, Copper deficiency, Myeloneuropathy, Haematological disease, MRI

We present a case of a 47-year-old male who came to the neurology clinic with a 1-year history of weakness in the lower limbs and numbness with a proximally progressive pattern in the four limbs, walking imbalance and urinary symptoms. His previous medical history encompassed a 2-year long anaemia and leukocytopenia with an unremarkable thorough investigation by Hematology. He had started treatment with granulocyte colony stimulating factor (GCSF) with no clear benefit.

His neurological examination showed a mild paraparesis with decreased distal pinprick perception to the wrist in the upper limbs and to the hips in the lower limbs, hypopalestesia to T10 level, hyporeflexia in the upper limbs and lower limbs hyperreflexia, positive Romberg sign and ataxic gait (Figure 1).

The patient was hospitalized and underwent diagnostic workup. His blood tests revealed an anaemia with an Hb level of 7.5 g/dL (reference value: 13.0–18.0 g/dL) and leukocytopenia of 2.88×10^9/L (reference value: 4.0–11.0 $\times 10^9$/L). Noteworthy, his analytical study revealed a low ceruloplasmin of <2.6 mg/dL (reference value: 18.0–45.0 mg/dL) and a low urine level of copper associated with elevated serum and urine levels of zinc (106, 1 µmol/24 h; upper limit: 18, 4 µmol/24 h). Nerve conduction studies depicted a severe axonal sensorimotor polyneuropathy in the lower limbs, and the spinal cord MRI showed a symmetrical increased signal lesion located in the posterior columns between the cervical segments C2–C6 (Figure 2). Other analytical measurements including vitamin B9, B12, anti-MOG and anti-AQP4 antibodies were unremarkable.

After inquiring for environmental exposures, the patient revealed the use of denture fixative containing zinc for 5 years. He was advised to switch to a zinc-free denture cream and started on oral copper supplementation – 2.5 mg three times daily in the first week, twice daily in the second week and once daily in the following weeks.

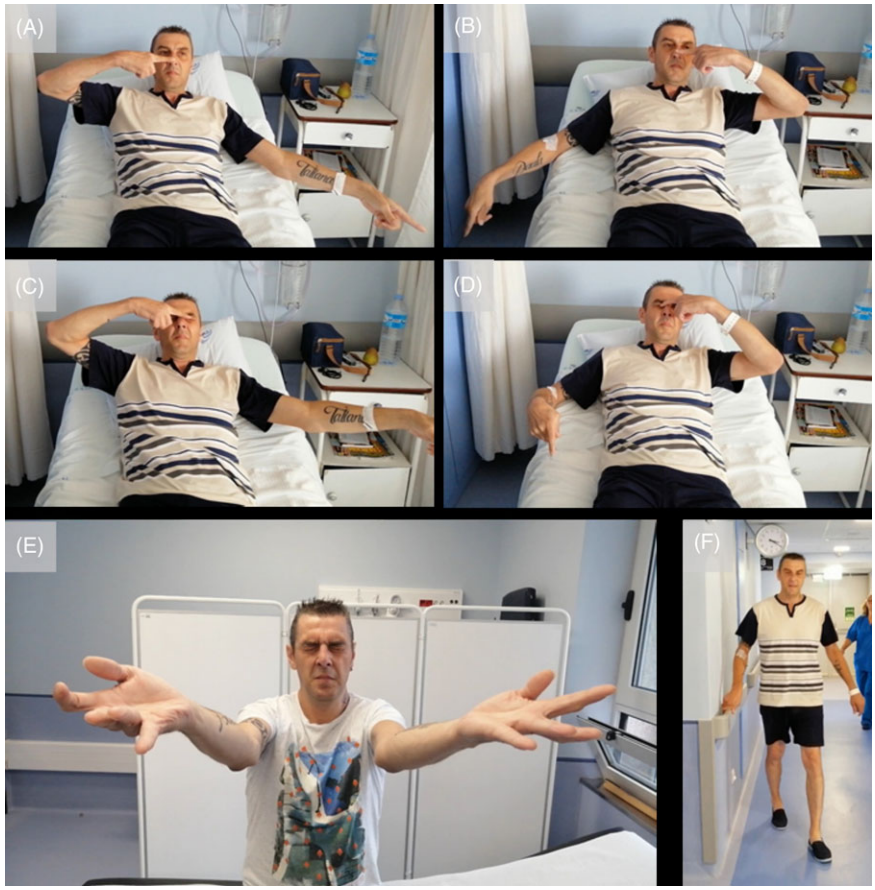

Figure 1: *Neurological examination. Finger-to-nose exam displaying accurate upper limbs movement with eyes open (A, B) but dysmetria with target deviation during eyes closure (C, D); pseudoathetosis of the upper limbs with writhing movements of the fingers exacerbated during eyes closure (E) and unsteady and stumbling gait with a wide base of support (F).*

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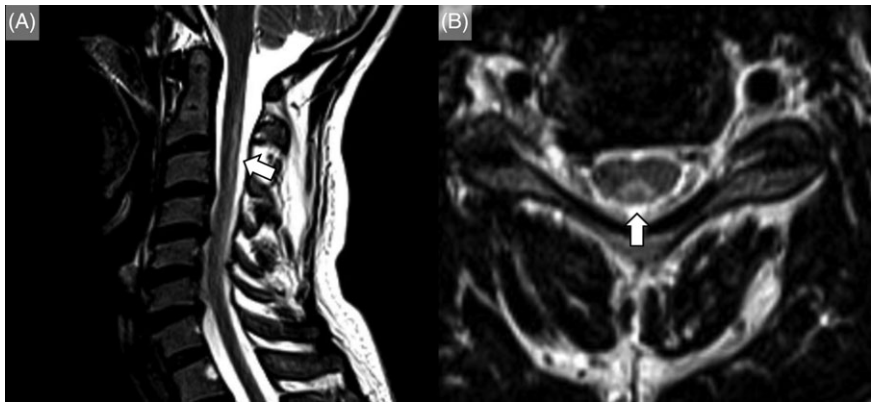

Figure 2: *Cervical spinal cord MRI. Sagittal (A) and axial (B) T2-weighted MRI demonstrates a contiguous, non-enhancing, increased signal lesion in the posterior columns between the cervical segments C2–C6 (inverted 'V' sign).*

Revaluation after 6 months showed a normalization of the haematological abnormalities, a subtle improvement in pinprick sensation and gait stability with no significant recoveries regarding other overt neurological deficits. Treatment with GCSF was suspended and copper supplementation was continued.

It is estimated that 7%–15% of denture wearers use adhesives, many of which contain zinc in significant concentrations, leading to potentially excessive zinc intake.[1] Elevated zinc ingestion causes a decreased copper absorption due to an upregulation of chelator metallothionein in enterocytes.[2] This copper imbalance might lead to haematological disturbances such as sideroblastic anaemia, leukopenia and neutropenia as well as neurological effects with peripheral neuropathy and myelopathy.[3–5] Previously reported cases in the literature reveal a peak of incidence in the fifth and sixth decades with a marked female predominance (3:1).[6] Symptoms and radiographic findings of this condition can closely mimic those of subacute combined degeneration of the spinal cord, an acquired condition caused by vitamin B12 deficiency as a result of nutritional deficit, reduced absorption or intake of certain drugs. Likewise, copper deficiency might be caused by malabsorption (e.g. gastrointestinal surgery, coeliac disease) or due to impairment of its metabolism with zinc overload or supplements of iron.[7] MRI is the imaging choice for the evaluation of this disease, with a signal change in the spinal cord, particularly in the cervical segments, being the most consistent neuroimaging finding in patients with myelopathy.[8]

While copper supplementation usually causes prompt and full resolution of haematological abnormalities, recovery of neurologic signs and symptoms is variable, often limited to improvement of the sensory symptoms and halting of further neurological deterioration.[6,7] It is known that the duration and severity of symptoms prior to treatment inversely correlates with the functional prognosis.[9]

Unexplained cytopenia associated with neurological manifestations should prompt clinicians to look for causes of copper deficiency, namely excessive zinc intake. This case illustrates the diagnostic challenge and typical insidious clinical manifestations of an unusual cause of myeloneuropathy with a potentially unfavourable outcome.

Conflicts of Interest

None.

Statement of Authorship

DF was responsible for the design, concept and draft of the manuscript. ALC and AC provided significant input for early and final drafts of the manuscript. PA was responsible for the design, supervision and critical revision of manuscript.

Supplementary Material

To view supplementary material for this article, please visit https://doi.org/10.1017/cjn.2021.80

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