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COPPER DEFICIENCY MYELOPATHY: THE GREAT IMPERSONATOR PRESENTING AS LONGITUDINALLY EXTENSIVE TRANSVERSE MYELITIS

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ABSTRACT Copper deficiency myelopathy represents a rare but treatable cause of non compressive myelopathy. Nutritional deficiencies of copper in human adults are rare unless a condition is there that affects uptake or metabolism of copper, or dietary intake is markedly deficient in copper, such as with some parenteral feeding formulations. Longitudinally extensive transverse myelitis (LETM) represent extensive involvement of spinal cord, with abnormal T2 signal affecting three or more consecutive spinal cord segments which are typical of neuromyelitis optica spectrum disorder (NMOSD) but can be found in many other neurologic conditions. We are presenting a rare case of LETM secondary to copper deficiency in a teenager presenting with three months history of ataxic-spastic gait with proprioceptive deficits.

KEYWORDS : copper deficiency myelopathy, longitudinally extensive transeverse myelitis

INTRODUCTION:

Copper deficiency myelopathy (CDM) is a rare (exact incidence unknown, less than 100 cases reported till date [1]) acquired neurological syndrome clinically characterized by symptoms and signs of dorsal column dysfunction. The widely known causes of copper deficiency are excessive zinc ingestion, malabsorption, and gastrointestinal surgery; however, the exact etiology remains undetermined in about 20% of cases [1]. CDM must be suspected in cases who present with otherwise inexplicable subacute ataxic myelopathy and, in these cases, prompt supplementation of copper is strongly recommended. Here, we present a rare case of CDM which presented to us with a subacute neuropathy clinically involving anterior cord, posterior column and peripheral nerves, but radiologically LETM with exclusive posterior column involvement was found. Extensive investigations later revealed copper deficiency. Fortunately enough the patient showed a significant clinical, neuroradiological improvement after oral copper therapy. However, the cause of copper deficiency in this case remained elusive.

CASE REPORT:

A 17-year-old girl born out of non-consanguineous parentage with normal developmental history presented with history of progressive spastic gait disturbance for the past six months, asymmetrically starting first in the left lower limb, and three months later the right lower limb was involved. There is also a definite history of subacute onset ascending tingling and numbness starting from bilateral lower extremities. She did not have any complaint of any bowel and bladder dysfunction. No history of similar symptoms in either of the parents or other first and second degree relatives was present. No significant surgical history was obtained. No history of any addiction or denture cream use. Physical examination was normal except for a high stepping, spastic, ataxic, and predominantly tip-toe gait. She required assistance to ambulate. Speech and other higher mental functions were normal. She had mild wasting of all the muscles with spasticity of solely bilateral lower limbs. The power in lower limbs was grade IV in all groups of muscles. All the deep tendon reflexes in both the lower limbs were symmetrically brisk and plantar response was bilaterally extensor with prominent ankle clonus with positive Romberg sign. Sensory examination revealed impairment in vibration and position sense.

Her metabolic panel including Cerebrospinal fluid and MRI of brain was normal. We diagnosed it as a case of myelo-neuropathy with possible localization over cervical spine. Cervical spine MRI with contrast revealed there was T2 high signal intensity along the posterior aspect of the cervical cord extending from medulla to C4 level which fits the definition of LETM (figure 1, 2, 3: Sagittal T2W STIR images of the cervical spinal cord showing a linear hyperintensity extending from lower medulla to C4 in the posterior aspect of cord (green arrows) which is confirmed further by the same hyperintense signal in the axial images (purple arrows).

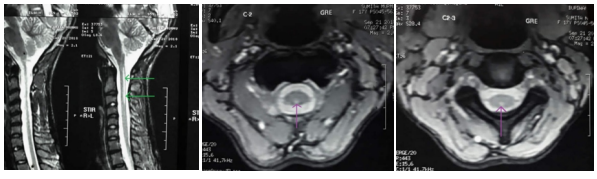

FIGURE 1: Sagittal T2W STIR images of the cervical spinal cord showing a linear hyperintensity extending from lower medulla to C4 in the posterior aspect of cord (green arrows)

FIGURE 2, 3: Hyperintensity on axial sections at C2 C3 level on T2W STIR images of cervical spinal cord as shown by the purple arrows

Nerve conduction studies were suggestive of early large fiber involvement predominantly axonal sensory neuropathy. A list of differential diagnoses was made including deficiency states (vitamin B12, vitamin E, Copper), neurosyphilis (tabes dorsalis), HIV-vacuolar myelopathy, neuromyelitis optica (NMO), anti-MOG associated encephalomyelitis, Multiple sclerosis, Connective tissue disorders, systemic illness with cervical spinal cord involvement (i.e. neurosarcoidosis, Sjögren syndrome, systemic lupus erythematosus (SLE), Behçet's disease, paraneoplastic myelitis), hereditary spastic paraplegia, idiopathic (aquaporin 4 negative) LETM, post-infectious demyelination, Friedreich's ataxia related spinal cord atrophy and lastly vascular phenomenon i.e.(spinal cord infarction, dural arteriovenous fistula).

However with the aim to narrow down our differentials rationally, after amalgamating history, physical examination and neuro-radiological findings, subacute myelo-neuropathy with predominant posterior cord signal changes we kept five or six leading possibilities i.e., Vitamin B12 deficiency, Vitamin E and Copper deficiency, neurosyphilis, NMO (Aquaporin positive or negative) and anti-MOG associated myelitis.

Hence, serum vitamin B12 level along with serum homocysteine and urine methymalonic acid, Serum vitamin E, plasma and CSF VDRL and FTA-abs tests, MS profile, NMO and MOG profile, VEP (visual evoked potential) and OCT(optical coherence tomography), Vasculitis Screen & autoimmune profile, HIV, Anti-HCV, HBsAg and HTLV serologies were done and were negative. Serum ACE level was normal. Interestingly serum copper level came 45µg/dl (normal: 70-140 µg/dl) alongside serum Ceruloplasmin and 24 hours excretory

urine copper levels. However, the etiology of copper deficiency in this case remained unclear as serum zinc level, 24 hour urinary zinc excretion, celiac disease profile (anti-ttg, anti gliadin, anti-ema and HLA for celiac disease) were all negative and intestinal and duodenal biopsy ruled out any malabsorption syndromes.

DISCUSSION:

Copper is an essential trace element. Nutritional inadequacy of copper in human adults are seldom unless there is a defect that affects the uptake or metabolism of copper, or dietary intake is markedly deficient in copper, such as with some parenteral feeding formulations.[2]

Effects on the nervous system have been characterized in the past decade;[3] they include myeloneuropathy with spastic gait, distal parasthesias and sensory ataxia, which closely mimic the symptoms and radioimagings in patients with subacute combined degeneration associated with vitamin B12 deficiency.[4] Reflexes can be increased or depressed, and bladder symptoms can be present. Rarely, copper deficiency is associated with isolated demyelination of the optic nerve and in the CNS, peripheral neuropathies, or myopathy. [4]

High concentration of zinc is linked to copper deficiency, sideroblastic anemia and neutropenia for long, [5] but has only been implicated in copper-deficiency myeloneuropathy in the past few years. Zinc impedes absorption of copper from food. Excessive urinary excretion of copper represents another cause of deficiency and has been reported in patients with glomerulonephritis[6]. Malabsorption of copper can occur in patients who have chronic gastrointestinal diseases or those who have previously undergone gastrointestinal surgery to treat such diseases or to attain weight loss.[3] Gastric-bypass surgery is linked to multiple nutritional deficiencies that can lead to neurological symptoms, including myeloneuropathy associated with low serum levels of copper, vitamin B12, or both[7].

Copper deficiency is an uncommon cause of myeloneuropathy presenting as LETM. Given the insidious clinical presentation of the progressive myeloneuropathy, diagnosis can be delayed for years. Therefore, investigation and treatment of copper deficiencies should not be detained because, once present, the neurological symptoms of copper deficiency can be stabilized but are generally indelible.

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