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Copper Deficiency Myeloneuropathy: An Atypical Presentation of Guillain-Barré Syndrome

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Copper (Cu) deficiency myeloneuropathy due to acquired Cu deficiency is both rare and debilitating. More women than men are affected, with patients aged 60–80 years. Cu deficiency is a consequence of the inability to store Cu, including Cu deficiency anemia, Cu deficiency protein, Cu deficiency neuropathy, intermittent deficit, catecholamine synthesis, and xerostomia. Affected patients usually present with anemia and leukopenia, along with subacute gait disorder with prominent sensory symptoms, along with an MRI of the cervical spine and evidence of hypomyelination.

Copper (Cu) deficiency myeloneuropathy (human swayback) is both rare and debilitating. It is important to consider this diagnosis in patients with ascending motor paralysis, gait issues, and unexplained sensory ataxic ganglionopathy. Copper (Cu) deficiency myeloneuropathy produces a clinical picture like subacute combined degeneration.

We present the case of an 83-year-old woman with a history of limited stage small cell lung cancer in complete remission for 6 months. Copper deficiency can be present years before symptoms. Copper deficiency presented as subacute sensory ataxic ganglionopathy with profound ascending motor paralysis and weakness, maintenance of bladder and bowel functions, and subacute sensory ataxic ganglionopathy. Subacute sensory ataxic ganglionopathy is more common in women. Copper deficiency and hypomyelination are more common in women.

Copper deficiency results in abnormalities in normal Cu-dependent enzymes, affecting the growth and development of the central nervous system. Abnormalities in Cu-dependent enzymes include copper transporting ATPases, dopamine, and serotonin. Copper deficiency is associated with degeneration of the central nervous system in patients with limited stage small cell lung cancer in complete remission.

The patient had anemia and leukopenia, along with subacute gait disorder with prominent sensory symptoms, along with an MRI of the cervical spine and evidence of hypomyelination.

Introduction

- Copper (Cu) deficiency myeloneuropathy (CDM) is rare and debilitating, with a predilection for middle-aged females.
- Presentation: anemia and leukopenia, along with subacute gait disorder with prominent sensory ataxia/spasticity, impaired vibration/position sense, and a positive Romberg sign.
- Etiologies: gastric surgery (50%), excess zinc (Zn) exposure, dietary overconsumption and replacement of other deficient vitamins (B, C, D, E, K, Omega-3), cow’s milk protein allergy, celiac disease, Wilson’s disease, cystic fibrosis, and IBS.
- Early recognition is difficult, especially when CDM from Guillain-Barré Syndrome (GBS) and vitamin B12 deficiency are considered.

Case Description

- 63 y.o. woman with PMH of limited stage small cell lung cancer in complete remission, COPD, hypertension, and bullous changes.
- Presented with a 2-month history of shortness of breath and weakness, numbness and paresthesias of bilateral upper/lower extremities.
- ROS: Patient reported increasing difficulty grasping objects, increasing difficulty breathing, and falling.
- Hospital Course:
  - Hospital Day 1: CXR: Negative for PE or cancer (see Fig. 2).
  - Hospital Day 2: CBC: WBC 5.7 K/µL, Hgb 9.9 g/dL, Hct 28.8%, Plts 312 K/µL.
  - Echocardiogram: EF 47.9%, no heart failure.
  - Hospital Day 3: Plasmapheresis performed given concerns for B variant.
  - No IVIG given the patient’s history of cancer.
  - Hospital Day 4: LP: clear, colorless, glucose 77 mg/dL, protein 649 mg/dL, RBC >55 mm, WBC < 3 cells, 11% neutrophils, CSF culture negative.
  - Paraproteinemia labs: comprehensive autoimmune workup negative.
  - Hospital Day 5:
    - Unresponsive to plasmapheresis, repeat EMG: worsening neuropathy with greater axon loss and motor unit dropout in proximal lower extremity muscles, with demyelinating features.
    - Copper (Cu) level of 473, and Neurology recommended lifelong elemental Cu supplements, 6 mg elemental Cu/kg body weight.
  - Hospital Day 19:
    - Copper (Cu) level 473 ug (reference range 810 - 1,990 ug/L).
    - Patient started on Cu replacement, vitamin B6 supplementation, Cu avoidance with 6 weeks expected recovery time.
  - Hospital Day 20:
    - Discharged: rehabilitation facility, strength/sensation improved with a plan to follow up with Neurology for outpatient care.

Case Images

Table 1. Summary of lab findings at outside hospital (OSH)

<table>
<thead>
<tr>
<th>CT-PE (see Fig. 1)</th>
<th>Negative for PE/lobar consolidation</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI Brain, C-Spine, T-Spine, L-spine</td>
<td>Normal findings</td>
</tr>
<tr>
<td>Lumbar Puncture</td>
<td>Normal cell count and protein level. CSF cytology negative for malignancy.</td>
</tr>
<tr>
<td>Paraneoplastic Labs: AChR-antibody and VGCC-antibody</td>
<td>Negative for AChR-antibody and VGCC-antibody</td>
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</tbody>
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Table 2. Enzymes utilizing Cu for electron transfer

<table>
<thead>
<tr>
<th>Cytochrome-c-oxidase</th>
<th>Electron transport and oxidative phosphorylation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Copper/Zinc superoxide dismutase</td>
<td>Antioxidant defense</td>
</tr>
<tr>
<td>Tyrosinase</td>
<td>Melanin synthesis</td>
</tr>
<tr>
<td>Dopamine b-hydroxylase</td>
<td>Catecholamine biosynthesis</td>
</tr>
<tr>
<td>Monooxidase</td>
<td>Sulfotransferase</td>
</tr>
<tr>
<td>Ceruloplasmin</td>
<td>Brain iron homeostasis</td>
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References