Stump the Consultants: Case Presentation

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Background

• 20 year old young woman with ESRD of unknown etiology
• Progressed to ESRD by 9 years of age, maintained on PD for 2-3 years
• Received a deceased donor transplant in 2009 (11 years old)
• Course complicated by multiple rejection episodes and graft failure, with initiation of HD in 2015
• One year later, received a second deceased donor renal transplant at Boston Children’s Hospital
• Again developed multiple episodes of ACR in the setting of non-adherence, initiated HD in November 2018 at age 19
Presenting History

• In May 2019 presented to our ED with bilateral lower extremity weakness x 2 weeks
• Difficulty standing up and walking
• Several falls because “legs were giving out”
• Numbness in her lower abdomen and perineal area
• Pain along bilateral medial thighs
• Anuric at baseline, no changes in bowel movements
• Reports feelingfatigued and intermittently nauseated
• Review of Systems: otherwise negative
Past Medical History

- ESRD of unknown etiology
- s/p two deceased donor renal transplants
- Pseudotumor cerebri
- Severe obesity
- Gastric bypass surgery (laparoscopic Roux-en-Y) in March 2019
Medications

- Azathioprine 150 mg daily
- Epogen 6000 units 3x/week with dialysis
- Calcitriol 0.5 mcg daily
- Calcium carbonate (calcium supplement) 1500 mg daily
- Ergocalciferol 8,000 units daily
- Nephro-Vite 1 tablet daily
- Kphos Neutral 250 mg BID
- Pantoprazole 40mg daily
- Ursodiol 300 mg BID
Physical Examination

- Vitals: T 36.3, HR 102, BP 138/85, RR 20, SpO2 100% RA
- Weight: 88.6 kg (EDW ~87.8 kg)

- Well-appearing, cooperative
- Neuro:
  - Alert, oriented x3. CNs 2-12 normal.
  - Motor: 4+/5 strength in bilateral iliopsoas and hamstrings. 5/5 strength in all other muscle groups.
  - Sensory: Decreased sensation to pinprick and light touch below umbilicus extending to anterior and medial aspects of bilateral legs. Sensation in posterior and lateral aspects of upper and lower legs intact. Proprioception intact.
  - Reflexes: Absent patellar and Achilles reflexes.
Summary of Neurological Manifestations

- Proximal muscle weakness
- Sensory loss
- Hyporeflexia

Polyneuropathy

- Generalized process affecting peripheral nerves
- Typically affects distal nerves
- Symptoms include: symmetric distal sensory loss, paresthesias, and weakness
What is your differential diagnosis for polyneuropathy in this patient?
Differential Diagnosis

- Guillain-Barre Syndrome (AIDP)
- Autoimmune (SLE, amyloidosis, vasculitis)
- Infection (e.g. HIV, Lyme disease)
- Inherited (e.g. Charcot-Marie-Tooth)
- Uremic polyneuropathy
- Diabetic neuropathy
- Hypothyroidism
- Drug-induced/Toxins
- Malignancy
- Nutritional causes
- Idiopathic

Spinal Cord Lesions:
- Compression fracture
- Tumor
- Abscess
What initial studies would you want to obtain?
Laboratory and Imaging Studies

- AST: 27
- ALT: 24
- Albumin: 2.9
- Ca: 9.0
- Phos: 3.0
- Mg: 1.8
- TSH: normal
- ESR: normal
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Guillain-Barre Syndrome

Risk Factors:
- Possibly Autoimmune
- Association with Immunizations
- Frequently preceded by mild respiratory or intestinal infection
- Progresses over hours to days
- Minimal Muscle Atrophy

• AIDP is most common subtype
• CSF studies with albuminocytologic dissociation
  - Elevated protein
  - Normal WBC
• Rx: Plasmapheresis, IVIG

Symmetrical Paralysis

Causes Problems With
- Respiration
- Talking
- Swallowing
- Bowel & Bladder Function

http://www.emdocs.net/guillain-barre-syndrome-third-times-charm/
Uremic Polyneuropathy

• First described in 1963
• Can occur amongst non-dialysis and dialysis CKD patients, typically once GFR falls to < 10-12 mL/min/1.73m²
• Distal, symmetric mixed sensorimotor neuropathy
• Symptoms include:
  – Paresthesias -> pain -> weakness
  – On exam: reduced deep tendon reflexes, loss of vibration and proprioception
  – Progresses distally to proximally
• Thought to be due to accumulation of toxic metabolites although precise etiology unknown
Uremic Polyneuropathy

• Studies in adult dialysis patients report a prevalence of 50-100%, but prevalence in pediatric patients is unknown

• Symptoms typically progress despite dialysis, and only known treatment is renal transplantation

• Prior Boston Children’s Hospital Case:
  • 16 year old girl with FSGS who presented with muscle cramping, weakness, and dropped reflexes
  • Received plasma exchange and IVIG (for presumed CIDP) without improvement
  • Subsequently received a kidney transplant with rapid improvement in symptoms within 1-2 weeks post-transplant

Nutritional Causes

• **Vitamin Deficiencies**
  - Vitamin B1 (Thiamine)
  - Vitamin B6
  - Vitamin B12
  - Vitamin E
  - Copper

• **Vitamin Excess:**
  - Vitamin B6
How would you determine our patient’s diagnosis? What would you do next?
Hospital Course

- B-vitamin, vitamin E, and copper levels sent
- Empirically treated with IV thiamine, folate, and multivitamin
- Dextrose-containing fluids avoided
- LP planned for the following day

Vitamin B1: 40 nmol/L [ref: 70-180]

Vitamin B6: 8.6 nmol/L [ref: 20-125]

Folate (B9): 2.6 ng/mL [ref: 4.2-20]

Vitamin B12: 1,051 pg/mL [ref: 190-778]

Vitamin E: 8.8 mg/dL [ref: 5-23]

Copper: 105 mcg/dL [ref: 85-150]
Hospital Course

- Rapid improvement in neurological symptoms the following day
- Continued to receive IV thiamine, folate, and multivitamin with dialysis, and then transitioned to oral high-dose B-complex vitamins once B1 levels normalized

Supplement Facts

<table>
<thead>
<tr>
<th>Supplement</th>
<th>Amount Per Serving</th>
<th>% Daily Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiamin</td>
<td>25 mg</td>
<td>1667 %</td>
</tr>
<tr>
<td>Riboflavin</td>
<td>25 mg</td>
<td>1478 %</td>
</tr>
<tr>
<td>Niacin</td>
<td>75 mg</td>
<td>375 %</td>
</tr>
<tr>
<td>Vitamin B6 (Pyridoxine Hydrochloride)</td>
<td>51.5 mg</td>
<td>2575 %</td>
</tr>
<tr>
<td>Folic Acid</td>
<td>200 mcg</td>
<td>50 %</td>
</tr>
<tr>
<td>Vitamin B12 (Cyanocobalamin)</td>
<td>100 mcg</td>
<td>1667 %</td>
</tr>
<tr>
<td>Biotin</td>
<td>100 mcg</td>
<td>33 %</td>
</tr>
<tr>
<td>Pantothenic Acid (Calcium Pantothenate)</td>
<td>125 mcg</td>
<td>1250 %</td>
</tr>
<tr>
<td>Choline Bitartrate</td>
<td>125 mg</td>
<td>*</td>
</tr>
<tr>
<td>Inositol</td>
<td>50 mg</td>
<td>*</td>
</tr>
<tr>
<td>RABA (ParaAminobenzoic Acid)</td>
<td>50 mg</td>
<td>*</td>
</tr>
</tbody>
</table>

* Daily value not established.
What is Thiamine (B1)?

• One of many water-soluble vitamins

• Dietary thiamine from cereals, wheat bread, brown rice, legumes, yeast, and fresh meats

• Does not have large functional tissue depot • half-life 10-20 days

• Co-enzyme in carbohydrate and amino acid metabolism

• Important for nerve impulse propagation

• Beriberi first described in ancient Chinese texts from the 3rd century BC
Thiamine Deficiency – Dry Beriberi

Common early manifestations:
- Loss of tendon reflexes
- Paresthesia
- Numbness of feet
- Foot drop
- Painful, tender muscles (pain on compressing calf)

Dry beriberi:
- Emaciation
- Wrist drop
- Marked weakness
- Aphonia may appear (poor prognosis; vagus nerve involved)

Thiamine Deficiency – Wet Beriberi

How does bariatric surgery affect things?

- **Roux-En-Y Gastric Bypass (RYGB):** duodenum and first portion of jejunum are bypassed.

  - Paper in *Pediatrics* 2016 found 9 reported cases of adolescent Wernicke encephalopathy after RYGB.

  - Due to combination of malabsorption, bacterial overgrowth, and poor nutritional intake.
Learning Points

• Consider thiamine deficiency (dry beriberi) in any dialysis patient with polyneuropathy

• Bariatric surgery is an independent risk factor for vitamin deficiencies

• Dialysis patients who undergo bariatric surgery or have other malabsorption syndromes may require higher doses of B-vitamin supplementation

• Early and empiric therapy with IV thiamine is safe and can be diagnostic, as symptoms typically improve within hours to days
References


• Young W., Netter F., et al. *The Netter Collection of Medical Illustrations. Volume 2, Endocrine*
Thank You

Stop Your Kidneys Being Irate
Pause Risky Meds & Re-Hydrate!
Guillain-Barre Syndrome

- Immune-mediated, rapidly progressive polyneuropathy
- Acute inflammatory demyelinating polyradiculoneuropathy (AIDP) is the most common subtype
- Autoantibodies against nerve gangliosides (GQ1b) thought to play a role in the pathogenesis
- CSF findings typically demonstrate “albuminocytologic dissociation” — elevated CSF protein but normal CSF WBC
- Brighton Diagnostic Criteria provide guidelines for therapy
- Treatment includes plasmapheresis and IVIG
Dialysis Adequacy

BUN

KT/V: 1.27
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![Image of Water-soluble vitamins absorbed in the jejunum](image-url)