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An Unusual Case of Thiamine Deficiency in a Total Parenteral Nutrition-Dependent Child Secondary to Munchausen by Proxy

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INTRODUCTION

Factitious disorder imposed on another, or Munchausen by proxy (MSP), is the fabrication of symptoms by a caregiver imposed on another to promote medical interventions for self-fulfillment (1). Thiamine deficiency (TD) in total parenteral nutrition (TPN)-dependent children has only been seen in the United States during intravenous multivitamin infusion (MVI) shortages (2), outside of the United States where MVIs were not administered with TPN (3), and unintentional human error corrected with caregiver reeducation (4,5). We present the first known case of TD in a TPN-dependent child as evidence for MSP.

CASE REPORT

A 9-year-old female was exclusively TPN-dependent due to caregiver-reported feeding intolerance and presumed dysmotility. Her complex medical history included chronic pain with opioid dependence. She had previous extensive diagnostic workup at 8 different facilities, including unremarkable endoscopies, whole exome/mitochondrial sequencing, and immunodeficiency testing. No motility studies were performed. She had several surgeries: gastrojejunostomy tube placement, diverting end ileostomy for frequent fecal impactions, splenectomy, thymectomy, and cholecystectomy. She had recurrent hospitalizations for unexplained acute loss of ambulation with wheelchair dependence and episodes of severe lactic acidosis with coagulopathy attributed to infectious etiologies despite negative pan-cultures. These episodes resolved with hydration, TPN, vitamin K, and antibiotics.

She presented with minimal responsiveness and shock physiology. She had severe lactic acidosis, hyperglycemia, hypokalemia, hyperammonemia, and elevated international normalized ratio. Renal function, thyroid function, toxicology, infectious evaluation, and lumbar puncture were unremarkable (Table 1). Electrocardiogram demonstrated prolonged QT interval (530 milliseconds). Echocardiogram was normal; electroencephalogram did not identify subclinical seizures. Brain magnetic resonance imaging with spectroscopy demonstrated signal abnormalities in the bilateral frontal cortex, hippocampus, putamen, and thalamus (Fig. 1). Single-voxel brain magnetic resonance spectroscopy demonstrated no lactate doublet (typically seen at 1.3 parts per million chemical shift); a nonspecific slightly elevated choline level was identified in the left internal capsule/basal ganglia junction (3.2 mm chemical shift) (Fig. 2) (6).

When her neurological status improved, she was noted to have intermittent vertical nystagmus/saccadic eye movements and abnormal gait, prompting discovery of a low thiamine level.

Diagnosed with TD, she improved with fluid resuscitation, electrolyte repletion, vitamin K supplementation, and a 5-day course of intravenous thiamine (100 milligrams daily). Her thiamine levels remained stable within normal limits 1 month after replacement; her eye/gait abnormalities resolved. Her coagulopathy resolved with

TABLE 1. Laboratory Values at Presentation

Laboratory Markers (Units)	Normal Range	Laboratory Value at Presentation
pH	7.320–7.420	7.052
Partial pressure of carbon dioxide (mm Hg)	40–50	27.1
Lactate (mmol/L)	<2.0	30
Thiamine (nmol/L)	70–180	32
White blood cell (thousand [k]/uL)	4.5–13.5	46.8
Hemoglobin (g/dL)	11.5–15.5	12.9
Platelets (thousand/uL)	150–400	380
Procalcitonin (mg/mL)	<0.5	1.08
Sodium (mmol/L)	135–145	142
Potassium (mmol/L)	3.5–5.5	2.8
Magnesium (mg/dL)	1.7–2.1	2.2
Phosphorous (mg/dL)	3.1–5.5	4.3
Calcium (mg/dL)	8.8–10.8	10.4
Bicarbonate (mmol/L)	22–29	8
Anion gap (mmol/L)	5–15	31
Glucose (mg/dL)	70–100	229
INR (none)	0.9–1.2	1.9
Ammonia (umol/L)	11–35	52
Urinalysis		1+ blood, rare bacteria
Blood urea nitrogen (mg/dL)	7–20	32
Creatinine (mg/dL)	0.2–0.73	0.34

INR = international normalized ratio; PCO_2 = partial pressure of carbon dioxide.

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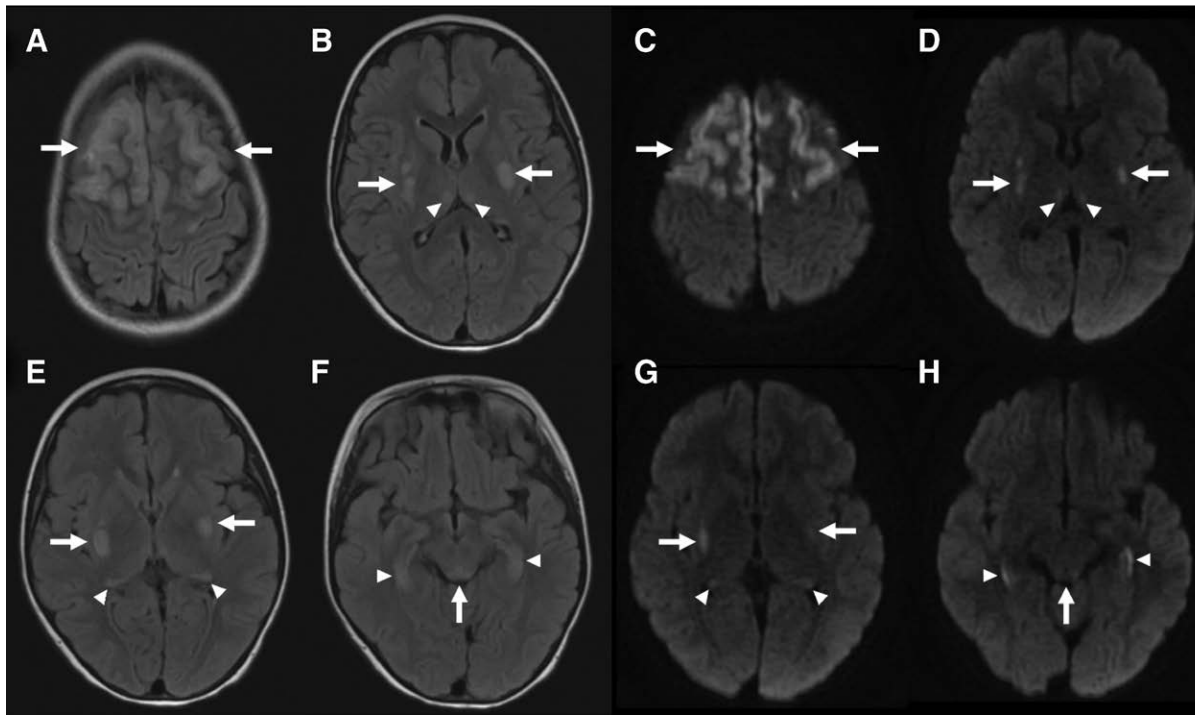

FIGURE 1. MRI brain imaging of patient. Multiple axial T2 FLAIR-weighted brain MR images demonstrate symmetric areas of signal abnormality in the frontal cortical (A, white arrows), putamen (B–C, white arrows), posteromedial thalami (B–C, white arrowheads), hippocampi (D, white arrowheads), and tectum/periaqueductal gray (D, white arrow). Multiple axial diffusion-weighted brain MR images demonstrate symmetric areas of restricted diffusion corresponding to T2 FLAIR signal abnormalities in the frontal cortical (E, white arrows), putamen (F–G, white arrows), posteromedial thalami (F–G, white arrowheads), hippocampi (G–H, white arrowheads), and tectum/periaqueductal gray (H, white arrow). FLAIR = fluid-attenuated inversion recovery; MR = magnetic resonance.

vitamin K. Comprehensive vitamins and trace minerals levels 2 weeks after presentation were unremarkable.

Retrospective review of prior hospitalizations for recurrent lactic acidosis and coagulopathy were attributed to thiamine and vitamin K deficiency despite prescribed MVI with her home TPN. Given her unusual symptoms and extensive unremarkable workup, a multidisciplinary team of pediatricians, pediatric gastroenterologists, neurologists, psychiatrists, social workers, nurses, and a child abuse expert relayed concern of MSP and provided expert testimonial to child protective services. This led to the patient's removal from the caregiver's custody. The patient's symptomatology resolved after separation. She no longer requires TPN, ambulates well without a wheelchair, and has no active clinical concerns.

DISCUSSION

The differential diagnosis for severe lactic acidosis includes metabolic disorders, tissue hypoperfusion, infection, and rarely TD (7). Our patient's TD diagnosis was based on abnormal neurologic symptoms, brain imaging, low serum thiamine level, and clinical status improvement after restarting prescribed MVI with additional thiamine. Nystagmus, gait disturbances, and altered mental status comprise the classic triad of Wernicke encephalopathy, which is seen in 21% of children with TD, and was demonstrated in our patient (3). Our patient did not have cardiac manifestations of TD (wet beriberi), such as dilated cardiomyopathy and high-output congestive heart failure. Her laboratory workup was consistent with abnormalities observed in TD: severe lactic acidosis, hyperglycemia, electrolyte disturbances (3), and hyperammonemia (2). An erythrocyte transketolase activation assay, which can aid in diagnosis, was not obtained. Our patient's brain imaging was consistent with previously reported cases of TD (Fig. 1). Encephalitis/infection and to a lesser extent hypoxic-ischemic encephalopathy may demonstrate overlapping magnetic resonance features, although this was not supported by the clinical presentation (6). Most importantly, our patient's clinical condition stabilized with thiamine replacement and correct use of prescribed TPN.

TD in TPN-dependent children has been reported in patients with a known lack of MVI, such as nationwide shortages (2), and in global areas where MVI is not used as standard of care (3). There have been 2 reported cases of TPN-dependent (with prescribed MVI) children who developed TD, attributed to human error and corrected with caregiver reeducation (4,5). Our patient's TD and vitamin K responsive coagulopathy with prior similar presentations were suspicious for purposeful avoidance of MVI administration.

This case highlights red flags that should raise suspicion for MSP: unusual symptoms, extensive medical history without validation from diagnostic procedures, frequent changes of medical locations due to caregiver's dissatisfaction, and illnesses with no identifiable cause (1). Our patient's caregiver had characteristics of an MSP perpetrator: female gender, knowledgeable of the medical system, seldom away from the abused child, and close connections with staff (1). A multidisciplinary team reviewed the patient's clinical history and provided effective guidance for acute therapeutic intervention. The team was essential in providing expert testimonial,

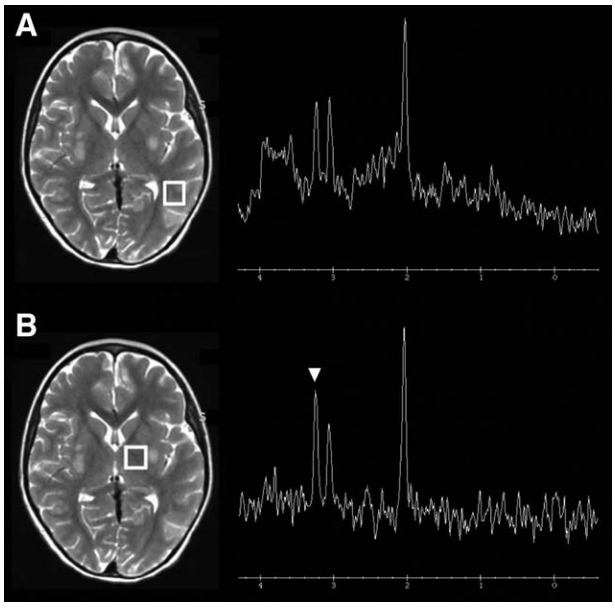

FIGURE 2. Axial T2-weighted brain MR images with single-voxel ^{1}H-MRS. A, Spectroscopy voxel centered at the left temporal white matter shows a normal spectrum, which includes the progressively ascending metabolites choline (3.2 mm ppm chemical shift), creatine (3.0 mm ppm chemical shift), and NAA (2.0 mm ppm chemical shift). B, Spectroscopy voxel centered at the left internal capsule/basal ganglia junction shows an elevated choline level at 3.2 mm chemical shift (white arrowhead). ^{1}H-MRS = proton magnetic resonance spectroscopy; MR = magnetic resonance; NAA = N-acetyl aspartate; ppm = parts per million.

resulting in the patient's removal from caregiver's custody and subsequent resolution of symptoms.

Pediatric gastroenterologists are consulted in up to two-thirds of MSP cases (8). Common MSP presentations in gastroenterology are nausea, abdominal pain, and TPN dependence (1). The development of TD in a TPN-dependent child with prescribed MVI is unusual and should raise suspicion for noncompliance or MSP. Prompt recognition of MSP is essential and should be addressed swiftly by a multidisciplinary team, which can aid with faster evidence discovery, earlier therapeutic intervention, and improved patient outcomes.

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