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Nutritional Vitamin D Deficiency Presenting as Hemichorea

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The authors describe a pediatric patient with repaired hypoplastic left heart syndrome developing protein-losing enteropathy, hypocalcemia, vitamin D deficiency, and hemichorea. After correction of nutritional vitamin D deficiency with calcium and vitamin D supplementation, the chorea resolved. Hypoalbuminemia also improved after the correction of vitamin D deficiency without requiring albumin infusions. This report also raises the possible role of calcium or vitamin D in the intestinal loss of albumin in protein-losing enteropathy.

Keywords: hypocalcemia; hemichorea; protein-losing enteropathy; vitamin D deficiency; hypoalbuminemia

Choreiform movements are quick, random movements that can involve all extremities, including the trunk and face. The differential diagnosis for the causes of chorea in children is diverse: congenital/familial, genetic, infectious, autoimmune, neoplastic, trauma, toxic, drug induced, or vascular. Protein-losing enteropathy is a recognized complication of the Fontan corrective cardiac surgical procedure, with a median time interval between surgery and diagnosis of 2.7 years.[1,2] It is thought to result principally from chronically elevated systemic venous pressure causing intestinal lymphangiectasia and hemodynamic derangement of the intestinal circulation. There is a consequent loss of albumin, protein, lymphocytes, fat, and immunoglobulin into the gastrointestinal tract. Eventually, this leads to edema, ascites, weight loss, chronic diarrhea, hypocalcemia, effusions, infections, and thromboembolism.[2] We describe a child with protein-losing enteropathy and electrolyte abnormalities presenting with hemichorea.

Case Report

A 5-year-old boy presented with acute onset of slurred speech, fidgetiness of the right upper and lower extremities, facial grimacing, and uncontrollable irregular movements of the right extremities, face, and tongue. A detailed review of systems revealed diarrhea for more than a month with 2 to 3 large, bulky loose stools per day and minimal exercise tolerance. There was no history of vomiting, headache, fever, sore throat, weight or appetite loss, or any weakness.

The patient had a complex past medical history: hypoplastic left heart syndrome was diagnosed at birth, and he underwent subsequent corrective heart surgeries, including Norwood procedure at 4 days of life, hemi-Fontan procedure with diaphragmatic plication at 4 months of age, complete Fontan procedure at 1.5 years of age, and subsequent fenestration procedure. At 3 years of age, he was diagnosed with protein-losing enteropathy based on an elevated fecal α-1-antitrypsin level of 441 mg/dL (normal ≤54 mg/dL) and hypoalbuminemia. There was no history of chylothorax or chylous ascites. After the diagnosis of protein-losing enteropathy, the patient was started on diuretic therapy, a high-protein and low-to-absent long-chain triglyceride fat diet along with medium-chain triglyceride fat supplementation (1 tablespoon of medium-chain triglyceride oil 3 times a day). Past medical history also included a right cerebrovascular accident occurring at 3 years of age with residual mile left hemiparesis. The patient's medications were hydrochlorothiazide, spironolactone, lasix, digoxin, coumadin, heparin, magnesium 400 mg 3 times daily, calcium carbonate 300 mg daily, and ergocalciferol 400 IU daily.

Physical examination at the time of admission revealed a weight of 21 kg (75th-90th percentile), height of 104.5 cm (10th-25th percentile), body mass index of 19.4 kg/m^2, pulse rate of 90/min, blood pressure of 90/58 mm Hg, O_2 saturation of 86% in room air, and respiratory rate of 26/min. He was comfortable at rest except for spontaneous chorea, affecting the right arm and leg. The patient had normal facial strength and minimal weakness of the left arm and leg. Sensation was normal in all modalities. The Chvostek sign was positive, and Trousseau sign was negative. The cardiovascular examination was significant for a 2 of 6 continuous murmur and central cyanosis. The abdomen

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Table 1. Laboratory Characteristics of the Case

Serum Values	Nov 18, 2002	Jul 24, 2004	Jul 25, 2004	Jul 30, 2004	Aug 9, 2004
Serum calcium (8.5-10.0 mg/dL)	7.2	4.2	6.3	7.9	8.9
Ionized calcium (1.12-1.30 mmol/L)		0.70	0.90	1.11	
Serum phosphorous (4-5.4 mg/dL)	5.2	3.9	4.4	4.7	5.9
Serum albumin (3.2-5.2 g/dL)	1.4	1.2	1.2	2.1	3.6
Corrected calcium, mg/dL	9.28	6.44	8.54	9.42	8.92
Serum magnesium (1.5-2.4 mg/dL)		0.6	1.7	1.9	2.2

NOTE: The table depicts the significant hypocalcemia in 2004 at the time of presentation with hemichorea. The normal values are in parentheses.

was distended with minimal ascites, and there were bilateral hydroceles. He had no evidence of rickets or peripheral edema.

Laboratory evaluation revealed hypocalcemia, hypomagnesemia, and hypoalbuminemia (see Table 1). The serum 25-hydroxyvitamin D level was 6 ng/mL (reference range, 13-67 ng/mL); 1,25 dihydroxy vitamin D was 78 pg/mL (normal, 27-71 pg/mL), parathyroid hormone level was 73 pg/mL (reference range, 10-65 pg/mL), and alkaline phosphatase level was low at 75 u/L (normal, 134-346 u/L). Vitamin A and K levels were normal, and the vitamin E level was low at 3.8 mg/L (5.5-11.8 mg/L). Antistreptolysin O titer was negative (<6 IU/mL). Magnetic resonance imaging (MRI) of the brain revealed the findings of right hemispheric encephalomalacia related to the prior right middle cerebral artery distribution stroke. No new intracranial findings were identified. A magnetic resonance angiogram result was consistent with the prior right middle cerebral artery infarction, demonstrating a markedly small caliber of right middle cerebral artery with decreased arborization of the right middle cerebral artery distribution. No focal stenosis, occlusion, or vascular malformation was seen. No acute changes were observed on the imaging studies.

Hypocalcemia was initially managed with intravenous calcium supplements and subsequently by oral supplementation of 8 g of oral calcium 3 times a day, resulting in a corrected serum calcium level of 8.54 mg/dL (see Table 1). Hypomagnesemia was corrected immediately by magnesium supplementation. The patient received 50 000 U of ergocalciferol intramuscularly. With correction of the serum calcium, the patient's chorea began to resolve. The child was subsequently discharged from the hospital, and upon follow-up, the patient had improved exercise tolerance and no chorea, and his ascites and hydroceles were reduced. Surprisingly, his serum albumin level normalized at follow-up without receiving albumin infusions.

Discussion

Hypocalcemia has been described to be causative in movement disorders.[3-7] The limitation of the chorea to the right side of the body is consistent with the lack of contralateral cortical input to the basal ganglia as a result of the prior stroke. In this case, the cause of the patient's hemichorea was hypocalcemia secondary to nutritional vitamin D deficiency. Although the patient was hypomagnesemic upon presentation, hemichorea persisted even after his magnesium was corrected, making hypomagnesemia an unlikely etiological factor of hemichorea in this case. The patient had clearly improved after correcting his hypocalcemia. The MRI of the brain did not reveal any acute changes noted on the diffusion-weighted series, thus eliminating a new acute cerebral vascular event. He did not have a presentation suggesting a febrile syndrome, an infectious process, or a history of seizures. His antistreptolysin O titer was normal, making Sydenham chorea unlikely. Wilson disease also could be excluded in the absence of clinical or biochemical characteristics. Multiple sclerosis was excluded given the lack of suggestive history and radiological evidence. Drug-induced chorea was not likely. This case, as well as others mentioned, reinforces the fact that electrolyte abnormalities should be searched as a cause of chorea.

Laboratory findings of hypocalcemia, low serum phosphate, and low 25(OH) vitamin D confirmed the diagnosis of hypocalcemia secondary to hypovitaminosis D. The etiology of vitamin D deficiency in this patient is multifactorial. Attenuated intake of fat along with malabsorption resulting in lower vitamin D absorption, low ultraviolet exposure (decreased exercise tolerance and parental concerns for sun exposure), and low serum albumin contributed to the development of vitamin D deficiency. Another compounding factor could be low vitamin D–binding protein, as most of the 25(OH) D circulates bound to the vitamin D–binding protein and some to albumin.[8] Intestinal absorption of calcium is determined by vitamin D status, intestinal calcium-binding protein, calbindin induced by vitamin D, availability of bile salts, absorption of free fatty acids, and the presence of gastric acid.[9] Severe magnesium deficiency can also cause parathyroid deficiency, and in that scenario, secondary hyperparathyroidism fails to develop. This most likely was operational in our case, as evidenced by the low alkaline phosphatase level. In this case, hypomagnesemia could have been secondary to diarrhea. This again reinforces the fact that hypomagnesemia should be looked for and corrected in scenarios with hypocalcemia. It is common knowledge that fat restriction will contribute to malabsorption of fat-soluble vitamins, and hence, constant

monitoring with careful attention to the fat-soluble vitamin levels is important in children with protein-losing enteropathy.

A fascinating observation we made is that hypoalbuminemia corrected on its own upon correcting the serum calcium and vitamin D levels. One tenable explanation is that with improved cardiac contractility, output and exercise tolerance upon correction of hypocalcemia resulted in a drop in systemic venous pressures and hence remission of protein-losing enteropathy. Similar observation was also noticed by Kim et al[10] proposed the direct action of Ca^{++} on the cellular membrane of the enteric epithelium, allowing covalent binding with the negative charge (COOH tail) of the 2 protein chains, thus preventing enteric loss of proteins.

The interesting observations in this case are the spontaneous disappearance of hemichorea after normalization of hypocalcemia and the correction of serum albumin levels upon rectification of vitamin D status. This unique finding needs further evaluation as to how vitamin D or calcium affects the serum albumin levels.

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