

A Rare Cause of Myopathy and Paralysis in Crohn's Disease

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Abstract

Crohn's disease (CD) is a chronic inflammatory disease characterized by transmural and segmental involvement that can affect the entire gastrointestinal tract. Hypokalemic periodic paralysis (HPP) is an uncommon channelopathy marked by episodic bouts of acute muscle weakness accompanied by hypokalemia. While osmotic diuretics, insulin, cisplatin, amphotericin B, aminoglycosides, and infliximab are commonly associated drugs, steroids can also, albeit rarely, lead to this condition. Steroids may induce transcellular potassium shifts and resultant hypokalemia through various mechanisms, including increased sodium levels, steroid-induced hyperinsulinemia, and hyperglycemia. Through this case presentation, we aim to highlight a rare cause of myopathy and paralysis and contribute to the existing literature.

Keywords: Crohn's Disease, hypokalemic periodic paralysis, myopathy, paralysis, steroids

INTRODUCTION

Crohn's disease (CD) is a chronic inflammatory disease characterized by transmural and segmental involvement, potentially affecting the entire gastrointestinal tract.¹ The ileo-cecal region is the most commonly affected site in CD. About 70% of patients experience abdominal pain and diarrhea.² Isolated small intestine or colon involvement occurs in 20-30% of cases. CD can also present with extraintestinal manifestations, such as joint involvement (peripheral and axial arthropathy), skin conditions (erythema nodosum, Sweet's syndrome, aphthous stomatitis), ocular issues (episcleritis, uveitis), and hepatobiliary (cholelithiasis).³

Various agents are employed in the treatment of Crohn's disease. Systemic corticosteroids have proven effective for inducing remission in cases of moderate and severe CD.⁴ Thiopurines, serving as immunomodulators, are commonly used to maintain remission in CD.⁵ Biological treatments are utilized for both the induction and maintenance of remission, particularly in patients exhibiting complicated disease courses, such as those with fistulas.⁶

Hypokalemic periodic paralysis (HPP) is a rare channelopathy characterized by episodic bouts of acute muscle weakness accompanied by hypokalemia.⁷ The onset of hypokalemia and associated symptoms typically occurs when potassium is absorbed into cells, with clinical symptoms subsiding as potassium begins to exit the cells. Triggers for HPP include factors such as a carbohydrate-rich diet, intense exercise, stress, cold weather, alcohol consumption, and certain medications.⁸

CASE REPORT

A 37-year-old male patient presented with abdominal pain, diarrhea, and perianal discharge. He had no history of regular medication or allergy and did not use tobacco or alcohol. Physical examination revealed tenderness upon deep palpation in the periumbilical and right lower quadrants, along with perianal discharge. Laboratory tests showed leukocytes at $15.1 \times 10^3/\mu\text{L}$ (4-10), hemoglobin (hgb) at 13.1 g/dL (14-16), platelets at $720 \times 10^3/\mu\text{L}$ (150-400), C-reactive protein (CRP) at 8.4 mg/dL (0-5), erythrocyte sedimentation rate at 45 mm/h (0-30), urea at 5 mg/dL (17-43), creatinine at 0.99 mg/dL (0.6-1.2), albumin at 3.8 g/dL (3.5-5), aspartate aminotransferase (AST) at 17 U/L (5-50), alanine aminotransferase (ALT) at 22 U/L (5-50), sodium at 136 mmol/L (135-145), and potassium at 4.2 mmol/L (3.5-5). Thyroid function tests were normal, and stool microscopy showed no pathology. Colonoscopy revealed aphthous ulcers in the terminal ileum and colon. The patient was diagnosed with A2B3L3 CD according to the Montreal classification, based on typical CD pathology findings such as crypt abscess and crypt distortion in biopsy samples. MRI indicated a transsphincteric fistula and abscess at the 4, 6, and 11 o'clock positions. Treatment with ciprofloxacin (2x500 mg), metronidazole (3x500 mg), and mesalazine (3 g/day) was initiated, and a perianal seton was placed for the fistula. Azathioprine (2 mg/kg/day) and adalimumab were started, with radiological

imaging confirming abscess resolution. At 9 months, with clinical and endoscopic activation indicating secondary loss of response, infliximab treatment commenced. Premedication with 8 mg of dexamethasone and an antihistamine was administered due to potential allergic reaction.

Eight hours post-treatment, the patient, experiencing generalized weakness and muscle cramps, presented to the emergency department. Tests revealed leukocytes at $11.9 \times 10^3/\mu\text{L}$, hgb at 12.1 g/dL, platelets at $322 \times 10^3/\mu\text{L}$, urea at 55 mg/dL, creatinine at 0.76 mg/dL, sodium at 140 mmol/L, potassium at 2.54 mmol/L, and calcium at 9 mg/dL. Vitamin D and parathormone levels were normal. Differential diagnosis investigations including CT, MRI, and electromyography (EMG) revealed no pathology explaining the paralysis. After neurology and nephrology evaluations, hypokalemic periodic paralysis was suspected. Potassium replacement improved the patient's condition, with potassium levels at 3.89 mmol/L on the third day. Subsequent hypokalemia (K: 2.31 mmol/L) post-second infliximab dose and improvement (4.34 mmol/L) post-potassium replacement suggested infliximab-related hypokalemia. However, hypokalemia with muscle weakness and cramps also occurred following vedolizumab treatment, administered with steroids as premedication. This led to the consideration that the hypokalemic periodic paralysis was due to steroid treatment, not the biological therapy. No steroid was administered before the second dose of vedolizumab, and the patient exhibited no symptoms or hypokalemia. After a challenge test, a diagnosis of steroid-induced hypokalemic periodic paralysis was confirmed.

DISCUSSION

Crohn's disease (CD) is a chronic and progressive condition that can present with diverse clinical manifestations, including fistulas, obstructions, fever, perianal disease, and metabolic disorders. Approximately 30% of individuals with inflammatory bowel disease (IBD) exhibit at least one extraintestinal manifestation, with common occurrences including arthritis, aphthous stomatitis, axial arthropathy, and uveitis.³ Additionally, hepatobiliary, pulmonary, and vascular manifestations are also observed.⁹ Rarely, patients may present with symptoms like muscle weakness and cramps, which can also develop due to malnutrition and vitamin D deficiency.

Hypokalemic periodic paralysis is a condition characterized by episodic attacks, with serum potassium levels dropping over hours to days, leading to muscle weakness.¹⁰ Typically affecting proximal muscles, hypokalemic periodic paralysis can, in rare cases, be life-threatening if it impacts crucial muscle groups such as those in the respiratory and cardiac systems. This type of paralysis can result from autosomal dominant genetic disorders as well as acquired causes like thyrotoxicosis, renal diseases, and certain medications.¹¹ Drugs more commonly associated with this condition include osmotic diuretics, insulin, cisplatin, amphotericin B, aminoglycosides, and infliximab, although steroids can also be a rare cause.¹² Steroids may induce transcellular potassium shifts and consequent hypokalemia through various mechanisms, including an increase in sodium, steroid-induced hyperinsulinemia, and hyperglycemia.¹³ Most reactions occur within 24 hours of exposure. Men are more likely to experience symptoms than women due to differences in penetrance. The likelihood of hypokalemic periodic paralysis varies with the type of glucocorticoid used (dexamethasone, methylprednisolone, prednisolone), the route of administration (oral, intravenous, intramuscular), and the dosage.¹⁴

In our case, the patient developed hypokalemic periodic paralysis following the administration of steroids, which were given as premedication prior to a biological agent for Crohn's disease treatment. Although

the precise mechanism by which steroids trigger hypokalemia remains unclear, it is thought that this effect could be due to an increase in NA-K ATPase activity in the muscles, which is stimulated by glucose and insulin secretion.¹⁵ Additionally, no definite correlation was identified between the dosage and duration of steroid administration and the occurrence of hypokalemic episodes.¹⁶

CONCLUSION

While muscle weakness and cramps can be extraintestinal manifestations of Crohn's disease (CD), it is important to consider that they may also be indicative of hypokalemic periodic paralysis. This condition, which can lead to life-threatening symptoms, should be recognized as a potential consequence of steroid use, a treatment frequently employed in managing CD.

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