The McKittrick-Wheelock syndrome: A rare case with a complex acid-base disorder

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Abstract

McKittrick-Wheelock syndrome is a rare condition characterized by secretory diarrhea due to villous adenoma of the colon, acute renal failure, dehydration, electrolyte and acid-base disorders. Diagnosis requires high suspicion especially when the presentation is unusual. Although potentially fatal for its complications, if promptly diagnosed and treated it is completely reversible. We present a case of a 67-year-old man who presented with symptoms and to point out a correct diagnosis.

Introduction

Since its first description in 19541 only a few cases of McKittrick-Wheelock syndrome (MWS) have been described in literature. This rare syndrome is characterized by secretory diarrhea, often without pain, caused by a secretory colorectal tumor, most notably villous adenomas.2,3 Adenomas of the colon are usually asymptomatic or cause mild gastrointestinal symptoms, but a range from 0.76-2.4% of them could become secretory4 leading, potentially, to a severe loss of fluid and electrolyte due to a mucinous diarrhea. The consequences are severe dehydration with acute renal failure, significant electrolyte abnormalities and acid-base imbalance, making MWS a potentially lethal condition.2,3 Over 100 cases of MWS have been reported in literature,4 despite that some authors believe it is not rare as often thought.5 Considering that MWS is a potential life-threatening condition it’s essential to include it in the work up of a patient with diarrhea, depletion syndrome, electrolyte and acid-base abnormalities. Sometimes acid-base imbalance can provide precious information for the diagnosis as in our case of MWS with a triple acid-base disorder.

Case Report

A 67-year-old man presented to our Emergency Department with head trauma, secondary to orthostatic syncope. His recent medical history showed watery diarrhea for the previous 3 days (5-6 times per day) without fever nor abdominal pain. His past medical history was not relevant apart from a cholecystectomy, a previous perianal abscess and lower back pain. He was not taking medications. Vital signs were normal (BP 120/80 mmHg, HR 96/min, SpO2 on room air 97%, apyretic). On physical examination the patient showed evidence of fluid depletion with dry mucous membranes and obtundation. Abdomen examination was normal. Electrocardiogram revealed U waves. Chest-radiograph and head CT scan were unremarkable. Arterial blood gas test highlighted mild alkalemia (pH 7.491; pCO2 19.6 mmHg; pO2 116 mmHg; HCO3- 14.8 mEq/L; Anion Gap 35.2 mEq/L; lactate acid 6.4 mmol/L; Na+ 116 mEq/L; Cl- 66 mEq/L). Blood tests demonstrated hemoconcentration, neutrophilic leukocytosis, renal failure, hyponatremia, hypokalemia and hypochloremia. Serum biochemistry is shown in Table 1. A contrast-enhanced CT scan of the abdomen put on view a pseudo-nodular thickening of the rectosigmoid colon with narrowing of the lumen and upstream dilatation. After admission renal failure and electrolyte disorders improved with intravenous fluids and electrolyte replacement. A colonoscopy showed a voluminous polyoid mass with villous appearance in the rectum at 10 cm from the anal orifice, extending to the rectosigmoid junction and involving the 50% of the bowel lumen. The histopathological examination diagnosed a tubulovillous adenoma with areas of high-grade dysplasia. The final diagnosis was hypovolemia, acute renal failure, electrolyte and acid-base imbalance in patient with mucous diarrhea and tubulovillous adenoma. On hold of surgical treatment, the persistence of diarrhea with severe fluid loss and hyponatremia required hospital re-admission for hydroelectrolytic replacement. Therefore, anterior resection of the rectum was performed. Postsurgical recovery was
Discussion

MWS is classically characterized by a triad: i) chronic secretory diarrhea due to a colorectal tumor; ii) severe dehydration with acute renal failure; iii) electrolyte abnormalities and acid-base imbalance. According to literature most of reported cases are due to villous adenoma, with some cases secondary to adenocarcinoma or neuroendocrine tumor. Only a little percentage (0.76-2.4%) of villous adenomas become secretory and the etiopathogenesis of this process is not completely clear. Secretory and nonsecretory villous adenomas show differences on microscopic and ultrastructural examinations. Secretory adenomas are characterized by abundant and atypical mucin-filled goblet cells that produce exaggerated mucus amount with abnormal composition. Furthermore, evidences support the hypothesis of a secretagogue mediated diarrhea, due to the activation by tumor of PGE2 and adenylate cyclase pathways, that are responsible of water and electrolyte depletion from adenoma cells. Despite many authors suggest a strict dichotomy between secretory and non-secretory villous adenomas some evidences support the hypothesis of a secretory continuum, making cases of MWS the extreme end. The loss of results can reach to 1.5-3.5 L of fluid/day with large amount of electrolyte, leading some author to use the expression neoplastic cholera. Characteristically in early stages these losses can be compensated by renal adaptation and oral intake, but as tumor size increases compensatory mechanisms become exhausted. Moreover, this is the reason why almost only distal tumors are implicated in MWS genesis, preventing adequate water and electrolyte reabsorption.

Clinical picture may change from patient to patient and symptoms are usually related to electrolyte depletion and acute renal failure. First of all, diagnosis requires a high index of suspicion. Choi et al suggest that in case of prerenal failure, electrolyte abnormalities and diarrhea, the existence of an intestinal adenoma should always be considered. Despite aggressive hydroelectrolytes disorders correction can be consider the cornerstone of successful management, definitive treatment requires endoscopic or surgical excision of the tumor. Some studies have shown the usefulness of indomethacin and somatostatin especially for poor surgical candidate.

The case we described meets the diagnostic criteria of MKS, such secretory diarrhea due to villous adenoma, acute renal failure and electrolyte and acid-base disorders. Clinical features were similar to those already reported in literature. Despite above, our patient shown a complex and rare acid-base disorder. Choi et al suggest that in case of prerenal failure, electrolyte abnormalities and diarrhea, the existence of an intestinal adenoma should always be considered.

Table 1. Serum biochemistry on admission.

| Parameter               | Value  |
|-------------------------|--------|
| Hb (g/dL)               | 18.7   |
| WBC [×10^9]/μL          | 23.2 (90.1) |
| CRP (mg/dL)             | 0.19   |
| Na⁺ (mEq/L)             | 119    |
| K⁺ (mEq/L)              | 3.1    |
| Cl⁻ (mEq/L)             | 59     |
| Mg²⁺ (mEq/L)            | 3.71   |
| Bilirubin (μg/dL)       | 2.16   |
| Albumin (g/dL)          | 5.4    |
| Creatinine (mg/dL)      | 6.13   |
| Glycemia (mg/dL)        | 279    |

between alkalosis (metabolic and respiratory) and metabolic acidosis. Therefore, as Pucci et al suggest, even if the most common acid-base balance feature in MWS is metabolic acidosis, the presence of metabolic alkalosis in a patient with mucous diarrhea and renal failure should raise the suspicion of a chloride-excreting villous adenoma.

Conclusions

To our knowledge only a few cases with MWS and metabolic alkalosis have been reported. Moreover most of authors have focused on electrolyte disorders giving less importance to the acid-base imbalance. MWS syndrome is a rare condition that may develop life-threatening complications, but if promptly diagnosed and treated is completely reversible. Complex acid-base disorders are the outcome of the interplay between different pathophysiological mechanisms and the accurate interpretation of acid-base balance can provide precious information to the clinicians. The coexistence of metabolic alkalosis and mucous diarrhea (with or without renal failure) should raise the suspicion of a chloride-excreting villous adenoma leading to an early diagnosis.

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