CASE REPORT

McKittrick–Wheelock syndrome: a rare etiology of acute renal failure associated to well-differentiated adenocarcinoma (G1) arising within a villous adenoma

LILIANA ANA TUTĂ1), MĂDĂLINA BOȘOTEANU2), MARIANA DEACU2), E. DUMITRU3)

1)Department of Nephrology
2)Department of Pathology
3)Department of Gastroenterology
Faculty of Medicine, “Ovidius” University, Constanta
Emergency County Hospital, Constanta

Abstract

Introduction: Large villous adenomas or adenocarcinomas of the rectum can determine secretory diarrhea, associated with a depleting syndrome of prerenal acute renal failure, hyponatremia, hypokalemia, and hypoproteinemia, with favorable prognosis if early detected and properly treated. The syndrome is rare, with approximately 50 cases reported in the literature.

Aim: Acute renal failure, caused by fluids and electrolytes hypersecretion, secondary to a malignant rectal villous adenoma is revealed in a 55-year-old patient, admitted with major hydro-electrolytic and acid-base disturbances to our Nephrology Department. Case Presentation: The 55-year-old male patient had a nine months history of mucous diarrhea, for which he was treated unsuccessfully by GP's and infectionists. The symptomatology aggravated progressively and the patient was admitted through ICU with oligoanuria, severe dehydration and hydro-electrolytic and acid-base disturbances. Rectosigmoidoscopy revealed a giant villous adenoma at the rectum. Conservative therapy initially improved, and finally normalized renal function and made possible surgical resection of the tumor, with an excellent evolution afterwards.

Conclusions: The McKittrick–Wheelock syndrome is a rare, life-threatening condition that requires interdisciplinary medical diagnosis and treatment, but has a good prognosis if renal function is recovered in time and makes possible curative tumoral resection.

Keywords: villous adenoma, hydro-electrolytic disturbances, acute renal failure.

Introduction

Villous adenomas causing secretory diarrhea and severe hydro-electrolytic and acid-base disturbances are known as the McKittrick–Wheelock syndrome, as it was first described in 1954 [1, 2]. The McKittrick–Wheelock syndrome classically describes secretory diarrhea associated with a depleting syndrome of dehydration, acute renal failure, hyponatremia, hypokalemia, and hypoproteinemia. Prognosis is usually good, especially after fluid and electrolyte replacement, with early recourse to definitive surgery. The syndrome is rare, with approximately 50 cases reported in the literature [3, 4]. We report a case of this uncommon syndrome and review the literature on the possible mechanisms.

Patient, Methods and Results

A 55-year-old male was admitted through ICU accusing in the last nine months mucinous diarrhea, followed in the last two weeks by nausea, vomiting, malaise and recently onset of oligoanuria. He was examined from the onset of the symptomatology by GP’s and infectionists and discharged for several times with presumptive diagnosis of infective gastroenteritis. Clinically, on this last admission, he was dehydrated (BP 85/60 mmHg, with sinusal tachycardia – pulse 112 beats/min.). Biological parameters: leukocytosis (18 600/mm³), severe nitrate retention (serum creatinine 9.18 mg/dL, urea 279.9 mg/dL), Na⁺ (108 mmols/L), K⁺ (2.39 mmols/L), Cl⁻ (50 mmols/L), bicarbonates (30 mEq/L), hypoproteinemia (4.6 g/dL), hyperuricemia (31.7 mg/dL), collected fecal specimens – negative for any infective cause. Abdominal ultrasound examination reveals a solid tumoral mass with a diameter of ~9 cm in the pelvic region. Rectosigmoidoscopy shows a large villous tumor until 7–8 cm from anal region; the rest of the sigmoid was normal (Figure 1). There was no evidence of metastatic disease.

After intensive therapy of fluids and electrolytes replacement, we obtained recovery of the renal function (creatinine 1.09 mg/dL, urea 40 mg/dL, Na⁺ 145 mmol/L, K⁺ 3.5 mmol/L, Cl⁻ 108 mmol/L) after seven days from admission. After the preoperative assessment, a low anterior resection of the rectum was carried out.

The pathological evaluation of the surgical specimen revealed peculiar features of the lesion. Gross examination of the segment of colon removed during specific surgical procedure identified an exophytic and infiltrative mass of 12×10 cm, localized at the distal extremity of the specimen and at 13 cm distance from...
the proximal surgical border. The external surface of the tumor had a papillary and irregular configuration, gray-reddish color with hemorrhagic areas, variable consistency. The proliferation completely obstructed the colic lumen (Figure 2).

Microscopic analysis evidenced histopathological features of villous adenoma, with its characteristic fingerlike projections composed of typical intestinal epithelium with apical secretion of mucin (Figure 3). This benign neoplasm was accompanied by the presence of glandular structures lined by multilayered cells with marked cyto-nuclear atypia, suggestive for diagnosis of well-differentiated adenocarcinoma (G1). Malignant features comprised increased nucleo-cytoplasmic ratio due to karyomegaly and decreased cytoplasmic volume, hyperchromatic or vesicular nuclei with prominent nucleoli and coarse chromatin; nuclei were stratified and reached luminal border (Figure 4).

A supplementary argument for the malignant character of this glandular proliferation consisted in the evidence of the infiltrative pattern of the malignant glands that invaded desmoplastic stroma and induced the appearance of an inflammatory response (Figure 5).

The use of PAS special stain revealed the mucosecretant nature of the glandular structures, with both intra- and extraluminal accumulation of mucin (Figure 6).

Histopathological diagnosis: well-differentiated adenocarcinoma (G1) arising within a villous adenoma.

Figure 1 – Rectosigmoidoscopy: large villous tumor.

Figure 2 – Macroscopic aspect of the lesion: protrusive and infiltrative character.

Figure 3 – Villous adenoma: branching papillary projections with preserved nuclear polarity (HE stain, ×200).

Figure 4 – Malignant glandular structures lined by multilayered epithelial atypical cells, with karyomegaly, conspicuous nucleoli, coarse chromatin (van Gieson stain, ×400).

Figure 5 – Malignant glandular structures with infiltrative pattern into a desmoplastic stroma (van Gieson stain, ×40).

Figure 6 – Mucosecretant nature of the neoplastic structures (PAS stain, ×200).
Discussion

Colonic villous adenomas occur usually in the rectum and rectosigmoid regions. These adenomas are generally sessile and may be up to 10 cm in diameter. The malignant potential of adenomatous polyps increases with size, villous configuration, and degree of dysplasia. Secretory villous adenomas are different from non-secretory villous adenomas on light microscopic and ultrastructural examination. In secretory villous adenoma, there is an exaggerated mucous production, explaining secretory diarrhea [5, 6]. Ultrastructural study of villous adenomas shows that secretory villous adenomas are hypersecretory, with atypical goblet cells that produce a mucin of abnormal composition [5, 7].

The depletion syndrome characterized by cardiovascular collapse, acute renal failure, hyponatremia and a hypokalemic, hypochloremic metabolic acidosis is a rare complication of a rectal villous adenoma. Characteristically there is watery, mucinous diarrhea with increased bowel action. As the tumor size increases the enteral losses overwhelms compensatory mechanisms and the patient may seek medical attention. Digital rectal examination might miss sometimes even large tumors in many case, due to their soft, mucin-covered surface, often described as velvet-like [7, 8].

The mechanism of fluid and electrolyte loss is unclear. The theoretical explanation for this is that the more distal and larger the lesion, the more likely the bowel is unable to subsequently absorb the large secretory output of the tumour. Jacob et al found that in a patient with a secretory villous adenoma that there was increased adenylate cyclase activity compared to patients with non-secretory tumors [9].

Steven K et al. discovered that immunoreactive prostaglandin E2 level were three-folds higher in the patients with a secretory villous adenoma compared with infectious diarrhea [10]. Locally released prostaglandin E2 has been suggested as the secretagogue responsible for salt wasting [9, 11]. After indomethacin or somatostatin administration in patients with the secretory rectal villous adenoma, the stool concentration of PGE2 markedly decreased, as did the patient’s stool volume, combined with a similar reduction in the stool sodium excretion. When the indomethacin was stopped, the stool PGE2, sodium, and volume once again increased [11]. This study suggests that the use of prostaglandin synthetase inhibitors can be used to reduce the stool output in patients with secretory distal tumors, but caution should be taken with this treatment when the patient has dehydration and renal failure. Still, our option is for fluid and electrolyte replacement, even in high levels of nitrate retention, better, if possible, than hemodialysis, with early recourse to definitive surgery [10, 11]. Secretory diarrhea should not be always equated with the development of metabolic acidosis. Alkalosis is most likely to develop when the stool electrolytes (Na+ + K+) - Cl- are less than plasma HCO3-. Hydro-electrolytic balance is required before radical therapy [9, 12], which may be: endocavitary irradiation (recurrence rate of ~32% of rectal adenomas), endoscopical resection (high risk of recurrence), surgical resection of the tumor [12, 13].

Our patient underwent rectal amputation with permanent ileal stoma and the postoperative evolution was favorable until the time being, with maintenance of normal levels of renal function and electrolytes and no local recurrence of the carcinoma, almost four years after tumoral resection followed by chemotherapy.

Conclusions

The McKittrick–Wheelock syndrome arises from the severe dehydration and electrolyte depletion that occurs as a complication of colonic villous adenoma. These adenomas exude large quantities of electrolyte-rich fluid. Severe orthostatic hypotension and prerenal acute renal failure may occur. A key diagnostic feature is greatly elevated blood urea nitrogen with proportionately lesser elevation of serum creatinine. This syndrome is a rare, life-threatening condition that requires multidisciplinary cooperation for diagnosis and treatment, but has a good prognosis if renal function is recovered in time, and makes possible curative tumoral resection.

References


**Corresponding author**
Liliana Tuță, Associate Professor, MD, PhD, Department of Nephrology, Emergency County Hospital, Faculty of Medicine, “Ovidius” University, 145 Tomis Avenue, 900591 Constanța, Romania; Phone +40722–300 505, Fax +40241–662 071, e-mail: tutaliliana@yahoo.com

*Received: February 2nd, 2011*

*Accepted: October 25th, 2011*