

## Case Report

# Villous Adenoma Depletion Syndrome: Case Report

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### ABSTRACT

Villous recto-sigmoidal tumors with severe fluid and electrolyte loss are rare. We report the case of a 90-year-old man with a 10 year history of mucous diarrhea. On admission he had pre-renal uremia, severe hyponatremia and hypokalemia. Colonoscopy showed a large rectal villous adenoma. Conservative treatment was followed

by a complete, though temporary, recovery of the renal function. The McKittrick-Wheelock syndrome is a condition of severe water and electrolyte depletion due to colonic secretory villous adenoma. It can be a diagnostic challenge. Sodium loss may be the dominant feature.

KEYWORDS: acute renal failure, depletion syndrome, villous adenoma

### INTRODUCTION

Villous adenomas of the colon comprise approximately 10% of all colonic adenomas and tend to occur in patients more than 60 years old. The incidence of invasive carcinoma in villous adenomas < 2 cm in size is about 10%, whereas villous adenomas > 2 cm in size have > 50% chance of having invasive carcinoma<sup>[1]</sup>. Villous adenomas are generally large and bulky and tend to be distal in location, resulting sometimes in constipation and rectal prolapse<sup>[2]</sup>.

In 1954, McKittrick and Wheelock described a subset of patients with villous adenoma who had profuse watery diarrhea leading to excessive losses of fluid and electrolytes, dehydration, circulatory collapse, pre-renal azotemia and metabolic acidosis<sup>[3]</sup>. Since then several reports have described a syndrome with severe dehydration, hyponatremia, hypochloremia, hypokalemia and metabolic acidosis occasionally resulting in cardiovascular collapse, renal insufficiency and death.

The clinical picture results from the chronic fluid and electrolyte depletion in the watery mucous rectal discharge occasionally associated with these tumors.

To highlight the importance of the metabolic disturbance that may develop and the high index of suspicion required for diagnosis, a case of recurrent acute renal failure due to a large rectal villous adenoma is reported. The pathophysiology and management of the villous adenoma depletion syndrome are discussed.

### CASE REPORT

A 90-year-old man presented to our emergency department with generalized weakness, drowsiness and vomiting for the previous seven days. He had no abdominal pain, but suffered from intermittent diarrhea (described as loose jelly-like stools occasionally streaked with blood) for the past 10 years.

Physical examination was unremarkable except for moderate signs of dehydration and mild disorientation. He had a heart rate of 80/min and a blood pressure of 100/60 mmHg. His abdominal examination was unremarkable. Rectal examination revealed mucous discharge with blood streaks, but no masses were felt.

Aggressive but meticulous fluid and electrolyte replacement was started. His electrolytes almost normalized over the next seven days. The results of the initial serum electrolytes and the ones done a week later after treatment are shown in Table 1.

At this stage the family members were informed about the importance of performing a colonoscopy. However, they refused to give consent. Hence the patient was discharged home. He was readmitted three weeks later with a similar picture and he was in acute renal failure.

Consent was obtained during this admission and a flexible colonoscopic examination was performed. This revealed a large friable polypoid mass that oozed out a mucinous solute; the mass extended from the first rectal valve to at least 15 cm. The rest of the colon was normal.

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Fig. 1: Histopathologic examination of sections from colonoscopic biopsy material on light microscopy showing villous adenoma morphology with mild dysplasia

Histopathologic examination of sections from colonoscopic biopsy material on light microscopy revealed villous adenoma morphology with mild dysplasia (Fig. 1). These pathological findings in a patient with severe fluid and electrolyte loss are consistent with a secretory villous adenoma.

Surgical resection was refused by the family; therefore a trial of nonsteroidal anti-inflammatory drug therapy (using diclofenac sodium 50 mg twice daily) was given. This had to be discontinued after a few days as the patient developed a severe allergic reaction. Since then the patient has required frequent admissions for the same problem with severe metabolic disturbances requiring intensive fluid and electrolyte management.

## DISCUSSION

Colonic villous adenomas have a tendency to occur 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<sup>[4]</sup>. Secretory villous adenomas differ from non-secretory villous adenomas on light microscopic and ultra structural examination. These differences may to some extent clarify the secretory diarrhea associated with these villous adenomas. In non-secretory villous adenoma, mucous secretion is diminished, while in secretory villous adenoma, there is exaggerated mucous production. In these lesions, most of the adenomatous epithelium is composed of prominent, clear mucin-filled goblet cells. In addition, ultrastructural study of villous adenomas shows that secretory villous adenomas are hypersecretory, with atypical goblet cells that produce a mucin of abnormal composition<sup>[5]</sup>.

The depletion syndrome characterized by cardiovascular collapse, acute renal failure,

Table 1: Biochemical parameters before and after treatment along with the normal values

	Biochemistry on presentation	Biochemistry after fluid and electrolyte repletion	Normal range
Sodium	108 mmol/l	133 mmol/l	134 - 144 mmol/l
Potassium	3.0 mmol/l	3.9 mmol/l	3.60 - 5.10 mmol/l
Chloride	62 mmol/l	104 mmol/l	94 - 115 mmol/l
Bicarbonate	20.9 mmol/l	19.6 mmol/l	17.0 - 35.0 mmol/l
BUN	66.5 mmol/l	13.9 mmol/l	2.5 - 7.2 mmol/l
Creatinine	303 mmol/l	96 mmol/l	53 - 97 mmol/l
Serum osmolality	94 mosm/kg	284 mosm/kg	280 - 300 mosm/kg
Urate	1013 mmol/l	-	150 - 450 mmol/l

hyponatremia and a hypokalemic, hypochloremic metabolic acidosis is a rare complication of a rectal villous adenoma<sup>[3]</sup>. Characteristically there is watery, mucinous diarrhea with bowel actions as frequent as 20 times a day, not uncommonly for up to 15 years prior to the recognition of the cause<sup>[6]</sup>. At the onset the fluid and electrolyte losses are easily compensated by increased oral intake and renal regulation. As the tumor size increases these losses overwhelm compensatory mechanisms and the patient may seek medical attention<sup>[7]</sup>. One must keep in mind that digital examination of the rectum might miss even large tumors in many cases due to their soft, mucin-covered surface, often described as velvet-like. The mechanism of fluid and electrolyte loss is unclear. In a series of reported cases, secretory villous adenomas associated with the depletion syndrome were large, ranging from 7 to 18 cm in greatest dimension and were situated primarily in the rectum and occasionally in the sigmoid colon<sup>[8]</sup>. The large size allows for more surface area for secretion and their distal location limits the colon's ability to reabsorb fluid resulting in the depletion syndrome<sup>[9]</sup>. Locally released prostaglandin E2 has been suggested as the secretagogue responsible for salt wasting<sup>[10]</sup>. Steven *et al* compared the rectal effluents from a secretory villous adenoma and infectious diarrhea. They discovered that immunoreactive prostaglandin E2 level were three-folds higher in the patients with a secretory villous adenoma. In an attempt to further categorize the presence of a secretagogue in the villous adenoma depletion syndrome, Jacob and colleagues had compared the cyclic nucleotide metabolism of a large secretory villous adenoma with a non-secretory villous adenoma, a solid carcinoma and their normal mucosa. The adenylate cyclase, cyclic AMP content, and acyclic AMP-dependent protein kinase ratios in the secretory tumor were increased as compared to these values in the non-secretory tumors and normal mucosae. They suggested that increased adenylate cyclase activity might be responsible for the massive

secretory diarrhea in patients with a secretory villous adenoma<sup>[11]</sup>.

Whilst the mechanism remains unclear, its consequences are dramatic. Resultant losses can amount to 1.5 - 3.5 liters of fluid containing sodium 40-160 mmol/l (mean = 120 mmol/l), potassium 15-105 mmol/l (mean = 60 mmol/l) and chloride 30-165 mmol/l (mean = 123 mmol/l)<sup>[12]</sup>. This results in a characteristic presentation with circulatory collapse, pre-renal uremia, hyponatremia, hypochloremia, hypokalemia and metabolic acidosis. The latter is particularly severe and often underestimated due to the co-existent metabolic acidosis<sup>[7]</sup>. Rectal losses of sodium chloride are isotonic, whereas potassium losses are well in excess of plasma concentration with active secretion in the stool accounting for up to 150 mmol/day<sup>[7]</sup>. This is crucial to the clinical presentation as chronic hypokalemia not only contributes to the patient's symptoms, but also inhibits the normal compensatory mechanisms of electrolyte and water conservation.

A state of nephrogenic diabetes insipidus develops due to more than one mechanism; these include an inability to generate maximal medullary tonicity, impaired cellular responsiveness to antidiuretic hormone (ADH) and possible impaired release of ADH from the neurohypophysis<sup>[7]</sup>. Reversal of the biochemical derangement is the cornerstone of successful management. Once resuscitated, immediate surgical resection of the tumor is the treatment of choice. Steven *et al*<sup>[10]</sup> concluded that prostaglandin E2 is the mediator of fluid and electrolyte secretion by villous adenomas of the rectum. They suggested that the use of PG synthetase inhibitor (indomethacin) may facilitate the correction of severe fluid and electrolyte deficits in patients with large villous adenomas of the rectum. Another study<sup>[13]</sup> on rabbit ileum demonstrated that indomethacin inhibited secretion of potential secretagogues, including cholera toxin and dibutyryl - cyclic adenosine monophosphate at sites that included the prostaglandin synthetic pathway. In 1989, Waddell *et al*<sup>[14]</sup> reported regression of polyps in patients with familial polyposis using a nonsteroidal anti-inflammatory drug, sulindac. This observation has been confirmed in two subsequent studies by Labayle *et al*<sup>[15]</sup> and Giardiello *et al*<sup>[16]</sup>. Gowen, in 1996<sup>[17]</sup> also showed a similar response in a patient with two villous adenomas of the colon using a long acting NSAID, piroxicam.

## CONCLUSION

The reported case highlights the serious metabolic disturbances that occur in patients with villous adenomata. Lack of awareness of this complication might lead to a fatal outcome, as energetic replacement is required in the management of these patients. Treatment with NSAIDs would not eliminate the attendant risk of cancer and should not replace surgery as the mainstay of therapy.

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