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Case Report

Rectal Tubulo-Villous Adenoma and Mckittrick-Wheelock Syndrome

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Abstract

The fluid depletion and severe electrolyte disorders due to mucorrhea is a result of rectal villous adenomas hypersecretion. Its evolution in acid-base disorders and renal failure was described by McKittrick and Wheelock in 1954. The medical literature comprises only 257 such cases worldwide by the year 2018. We report the case of a 68-year-old female who presented McKittrick Wheelock syndrome with persistent mucorrhea, severe electrolyte depletion, asthenia with cramps in legs and depressive syndrome. A large rectal tubulovillous adenoma was discovered on colonoscopy. Further investigation (pelvic TAC and MR) confirmed diagnosis. The abdominal resection second to Miles's procedure with laparoscopy in abdominal time was achieved by removal of the tumor. Histology was tubulovillous adenoma with mostly low-grade glandular dysplasia and the finding of isolated high-grade apical foci. A follow up was started and after 24 months the patient has not relapsed.

The pathophysiology of McKittrick Wheelock is still unclear and it is linked to the secretion for a long time of electrolyte-rich mucin by adenomas with villous component. Goblet cells with the production of mucin MUC2 are involved in the process of formation of the mucous skeleton and its epithelial lining. In adenomas with a villous component this process is altered with loss of mucus rich in electrolytes. From a therapeutic standpoint medical therapy with electrolyte infusion and surgery is the treatment of choice.

Keywords: McKittrick wheelock syndrome; Rectal villous adenomas; Mucorrhea; Glandular dysplasia

Introduction

The polyp with a tubulovillous glandular structure is one of the three varieties of rectal dysplastic sessile adenomas with possible malignant transformation. It is a mixture of two patterns: tubular and villous. It can reach very large dimensions and even affect the entire circumference of the bowel. In a small percentage villous adenoma (<3%) can shows hypersecretory function with thin and clear mucous in rectal fluid containing electrolytes (K+, Na+, Cl-) and inflammatory mediatory (PGE2) [1]. The secretory mucinous diarrhea for long period can cause a particular condition with electrolyte depletion and possible renal failure described by McKittrick and Wheelock in 1954 [2]. Its incidence is unclear but recently reviews consider it not as rare as hypothesized so far [3,4].

Medical therapy can address electrolyte imbalance and prevent hypovolemic shock or cardiac and renal injury but surgery plays a fundamental role in resolving the pathology. This report adds one case to literature for pathology still unclear.

Case Presentation

A 68-year-old woman was hospitalised for recurrent asthenia with cramps in legs, depressive syndrome, persistent mucorrhoea (>5 stools/24 h), oligoanuria and severe electrolyte depletion. On clinical examination the patient appeared dehydrated, disoriented with hypotension (85 mmHg /60 mmHg) and moderate tachycardia (84 beats/min). No abdominal pain or palpable mass were detected. The manual exploration of the rectum highlighted a large swelling with a multiple polypoid surface in the circumference of the rectum, 3 cm from the anal verge. The protrusion of the finger revealed a transparent gelatinous substance.

Laboratory tests revealed a severe hyponatremia (Na level of 111 mEq/L, normal 136-145), hypokalemia (K level of 2.5 mEq/L, normal 3.5 - 5.1) hypochloremia (Cl level of 76.9 mEq/L, normal 98-107), high values of creatinine and urea nitrogen (Cre level of 3.91 mg/dl, normal 0.51 - 0.95) (BUN level of 368 mg/dl, normal 16-49). The peripheral blood leukocyte count was 13.23 × 10 ^ 3/ul, haemoglobin was 13.3 g/dL, and platelet count was 308 × 10 ^ 3/uL.

The electrolytes were aggressive corrected with intravenous saline 0.9% and daily potassium supplementation (80 mgEq/l). After fluid therapy the patient started to pass urine, her blood pressure increased to normal values (125 mmHg/80 mmHg), and her renal function was recovered with normal values in six days (Cre level of 0.97 and BUN level of 40). Sodium values increased rapidly (135 mEq/L) while potassium remained below the threshold value, returning to the range only after 10 days (3.8 mEq/L). Symptoms disappear but after ten days, due to sudden double rectal bleeding, a severe anemia occurred (Haemoglobin level of 7.8 g/dl) and it required transfusions.

Colonoscopy demonstrated huge conglomerated sessile polyps in the whole circumference of the rectal ampulla starting to dentate line up to 13 cm. Pathology of multiple biopsy reported adenomatous tissue with tubulovillous architecture and low-grade glandular

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dysplasia (Figure 1). An abdominal and pelvic Computed Tomography (CT) scan and Magnetic Resonance (MR) were performed to check the lesion; they confirmed colonoscopy and revealed a huge mass throughout the rectal wall, without abnormal lymph nodes of mesorectal (Figure 2). The patient underwent Miles' procedure with laparoscopic abdominal time, high ligation of the inferior mesenteric artery, total mesorectal excision and a left colostomy (Figure 3).

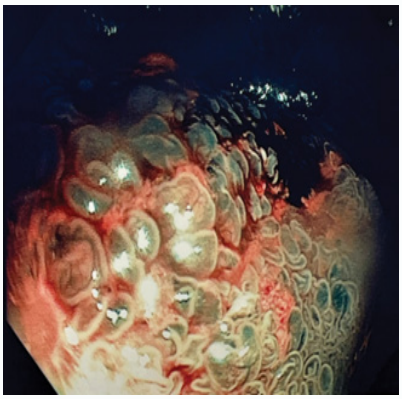

Figure 1: Colonoscopy show soft vegetating lesion with papillary configuration and friable tissue.

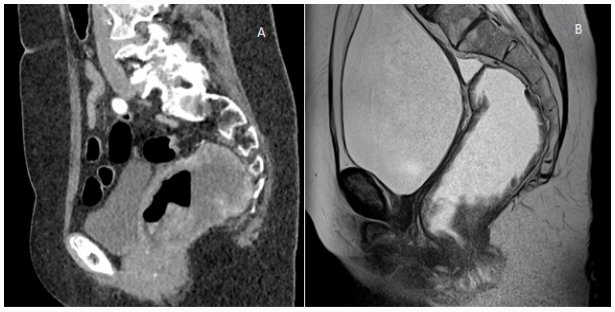

Figure 2: A) The CT scan (sagittal view) shows dilated rectum and the endoluminal large circumferential adenoma. B) A pelvic magnetic resonance shows the huge rectal adenoma near the anus.

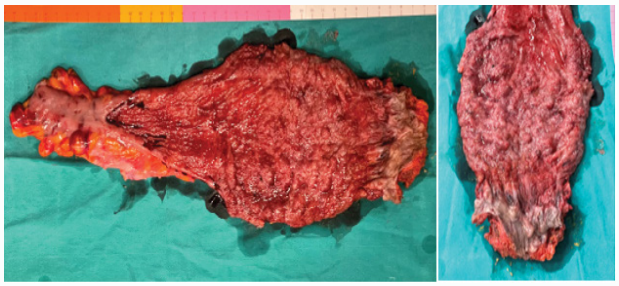

Figure 3: Resected specimen with large neoplasm that involving all circumference of the rectum.

Postoperatively there was a dehiscence of the perineal wound which required the use of topic negative pressure with good results. The patient was discharged 15 days postoperatively and it followed both at home with nursing medications and in the clinic for medical checks.

After fixation the operative specimen was seen to measure a total length of 30 cm, including colorectal tract of 25 cm and anal canal of 5 cm. Flat neoformation, with a spongy surface, measured 13 cm × 8.5 cm which reaches the pectinate line and 3.5 cm from the anal verge. Mesorectum measured 4 × 3.5 cm from which 24 lymph node structures were isolated. Histologically the extensive sampling showed the characteristics of tubulovillous adenoma with mostly low-grade glandular dysplasia and the finding of isolated high-grade apical foci with frequent mitotic figures (Figure 4). Muscolaris mucosae were unscathed. All 34 isolated lymph nodes were the site of chronic reactive lymphadenitis. An oncological follow up was started and after 24 months the patient has not replaced.

Discussion

Although the first description of a villous tumour of the rectum dates back to 1899 [5], the first attempts of classification of polypoid tumours of the rectum was addressed in the middle of the last century. From 1938 to 1948 was identified a villous papilloma (specific type of adenoma) that can become very large [6,7]. After 1948 it was treated as a separate entity usually broad, flat, and sessile with velvety and glistening surface [8-10].

These particular adenomas were associated from the beginning with secretory diarrhoea and prerenal uremia [10], but the first detailed description of conspicuous electrolyte losses with subsequent uremia date back to 1954 by Mc Kittrick and Wheelock. They reported an 82 years old patient with history of diarrhoea, oliguria, weakness, fainting for 10 years [11,12]. Subsequently other reports described a rectal fluid to contain a high concentration of sodium, potassium and chloride which resulted in severe hyponatremia (included shock) [13-17] and the syndrome took the name of Mckittrick and Wheelock syndrome. Characteristically, the patient passes a considerable amount of thin and clear mucus upon arising in the morning but which continues throughout the day until it reaches considerable quantities (it described as up to 4 liters per day containing up to 11 gm of sodium daily) [18]. The volume of mucous and electrolyte depletion was correlated to volume of tumour. A hypersecretory activity is reported in about 2% to 3% of villous adenomas that are greater than 3 to 4 cm [19]. The secretory diarrhea of 500 mL/24 to 3000 mL/24 hours is caused by villous adenomas that are ranging from 4 cm-18 cm [20].

So, the salient symptomatology consists of an excessive watery mucous secretion and or rectal bleeding for a long period. It is also true, how-ever, that the exact pathophysiological mechanism is not yet clear. Goblet cells derived from pluripotent stem cells at the base of the intestinal crypts produce mucus and have an immune function [21]. Morphological alterations in the epithelial layer and biochemical alterations in the transport of ions, not yet perfectly identified, cause abnormal mucorrhea [22,23]. Some processes appear to be mediated by cAMP and PGE2 but they are still being defined and watery diarrhea is a common presentation (approximately one-third of cases) in villous adenomas not associated with McKittrick Wheelock syndrome [24-26]. In any case, the crux of the problem is represented by mucorrhea. The formation of mucous is influenced by the immune system and in particular by interleukins which by regulating *MUC* gene expression stimulate mucin production. The mucous skeleton is composed of mucin MUC2 secreted by globet cells [27]. It is conceivable that in adenomas with a villous component the subversion of the epithelium determines the lack of attachment of the internal mucous layer to the epithelium itself, leading to its loss and expulsion. Therefore, it is possible that the already continuous secretion of MUC2 is reinforced with the production of further mucin by the goblet cells of the crypt, responsible for the emergency secretion [27]. This may be reflected in the fact that McKittrick-Wheelock syndrome may represent the

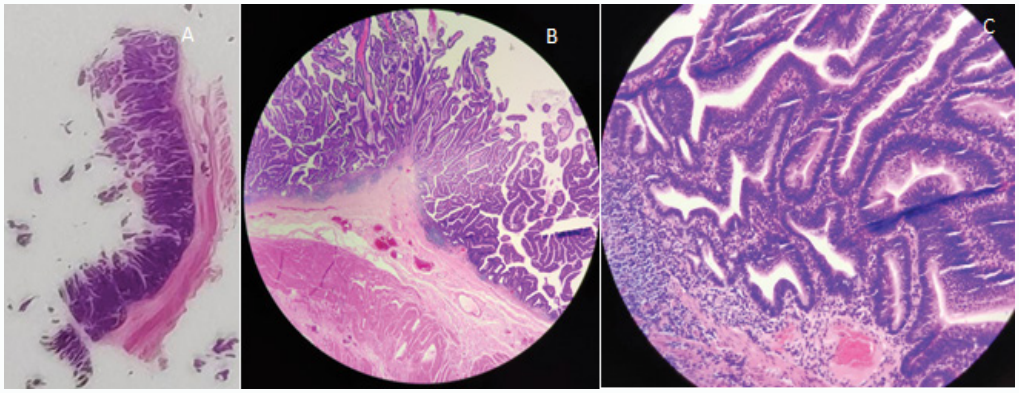

Figure 4: A) Microscopic specimen with profile of the lesion; B) Villous architecture, E/E × 2.5. The yellow circle indicates the detail; C) E/E × 20 and shows dysplasia with mitotic figures.

extreme of a normally distributed continuum of secretory activity in colorectal villous adenomas [28]. In any case the secretion of mucin is a multifaceted phenomenon, regulated by a number of different factors. Therefore, further and in-depth genetic studies in pathophysiological determinism are necessary.

Mucorrhoea causes a continuous loss of non-reabsorbed electrolytes. The hyponatremia and the volume depletion led to altered mental status, and hypokalemia was responsible for electrocardiographic repolarization abnormalities and rhabdomyolysis. Upon admission, our patient appeared disoriented and hypotensive with clear signs of dehydration. The hydroelectrolyte imbalance is associated with acute renal failure and metabolic acidosis, the latter mediated both by the focal loss of bicarbonate and by the renal failure itself. The immediate saline infusion quickly restoresd the blood share of sodium ions and more slowly that of potassium. Therefore, adeguate infusion therapy is necessary and azotemia is reversible in the absence of renal disease [16].

Obviously, the electrolyte depletion caused by mucorrhoea is only a secondary effect but the main pathology is represented by the adenoma with its dysplasia. Therefore, according to our current knowledge, the main therapy cannot do without surgery.

Nowadays, tubulovillous polyps of the rectum are classified among those potentially neoplastic together with tubular and villous adenomas with a frequency percentage varying between 10% and 25% and a villous surface between 25% and 75% of tissue, unlike villous adenomas whose frequency is equal to 5% and with a villous tissue varying between 75% and 100%. Tubular adenomas with a low villous component (<25%) are much more frequent, with a percentage varying between 70% and 85% [29]. In multiple adenomas and with a diameter greater than 1 cm, the villous component determines a high risk of malignant transformation, equal to 22% for tubulovillous adenomas and up to 50% in villous adenomas [28]. The size and extension of the adenoma are the main factors associated with high-grade dysplasia. The villous architecture, the large size and degree of dysplasia increase the risk percentage of neoplastic transformation [30].

The size and distance from the anal verge also affect the surgical strategy. Giant adenomas are not amenable for endoscopic or transanal resection. The anterior resection of the rectum or the abdominoperineal amputation seems to guarantee a complete cure of the disease especially in high grade of dysplasia. In the literature, for McKittrick-Wheelock syndrome the data relating to the percentage of mortality after radical resective surgery are equal to 0% [31]. On the other hand, incomplete resection can lead to a recurrence of the disease and even death [16].

For this reason, possible malignancy and recurrence, we absolutely consider surgery essential in case of tubulovillous adenoma of the rectum with McKittrick-Wheelock syndrome even in the presence of low-grade dysplasia.

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