JGH Open An open access journal of gastroenterology and hepatology
JGHF
doi:10.1002/jgh3.12635

CASE REPORT

Rare case of advanced rectal cancer with multiple liver and bone metastases presenting with McKittrick–Wheelock syndrome

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Key words
electrolyte depletion syndrome, McKittrick–Wheelock syndrome, rectal cancer, signet ring cell carcinoma.

Accepted for publication 31 July 2021.

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Declaration of conflict of interest: None.
Author contribution: Hirofumi Fukushima, Takashi Murakami, and Nobuyuki Suzuki mainly contributed to this work and wrote the manuscript; Tomoyoshi Shibuya and Akihito Nagahara provided support and made amendments; Takashi Yao pathologically reviewed the cases. All authors read and approved the final manuscript.

Abstract

McKittrick–Wheelock syndrome (MWS) is a rare entity that has been described as electrolyte and fluid depletion secondary to secretory diarrhea caused by a large villous tumor in the colon or rectum. Most tumors associated with MWS are large but benign villous adenomas. Advanced cancers are seldom reported. We report a rare case of advanced rectal cancer with multiple liver and bone metastases presenting with MWS. A 59-year-old man was admitted to our hospital with a more than 3-year history of chronic mucous diarrhea. Laboratory data revealed hyponatremia, hypokalemia, hypochloremia, and renal failure. Based on the findings on colonoscopy, computed tomography, and magnetic resonance imaging, he was diagnosed with advanced rectal cancer with liver and bone metastases, and MWS. Following intravenous fluid treatment, abdominoperineal resection of the rectum with lymph node dissection was performed. The surgically resected specimen was a circumferential villous tumor measuring 110 × 80 mm. Histological examination of the resected specimens revealed signet ring cell carcinoma with villous adenoma and metastasis in regional lymph nodes. The renal dysfunction and electrolyte abnormalities that were present before surgery improved. Two courses of capecitabine were administered as adjuvant chemotherapy after the surgery. However, approximately 2 months after surgery, he died of poor general condition due to progression of the liver metastases.

Introduction

Electrolyte depletion syndrome is a rare entity that has been described as electrolyte and fluid depletion secondary to secretory diarrhea caused by a large villous tumor in the colon or rectum. In 1954, McKittrick and Wheelock first described colorectal villous adenoma, which caused secretory diarrhea associated with severe electrolyte and fluid depletion[1]; consequently, it is also often referred to as McKittrick–Wheelock syndrome (MWS). Most tumors associated with MWS are large but benign villous adenomas,[2–5] and advanced cancers are seldom reported.[6] Proper endoscopic or surgical resection of tumors causing MWS could improve electrolyte balance and often have a good prognosis.[5] Here, we report a rare case of advanced rectal cancer with multiple liver and bone metastases, presenting with MWS, in a patient who died of cancer progression approximately 2 months after surgery.

Case report

A 59-year-old man was admitted to our hospital for chronic mucous diarrhea (more than 10 times a day), which had been ongoing for more than 3 years. His physical examination findings and vital signs were normal. His medical history was unremarkable. Laboratory data revealed hyponatremia (sodium, 130 mEq/L), hypokalemia (potassium, 3.2 mEq/L), hypochloremia (chloride, 77 mEq/L), and renal failure (creatinine, 1.63 mg/dL; blood urea nitrogen, 53 mg/dL). The blood leukocyte count was 11 600/μL, hemoglobin level was 17.7 g/dL, and platelet count was 32.7 × 10^4/μL. Regarding tumor markers, the carcinoembryonic antigen level was elevated (28.4 ng/mL). His endocrine functions including free thyroxine and thyroid-stimulating hormone were normal. There were no significant features in the stool microscopy or culture. A contrast-enhanced computed tomography scan of the abdomen and pelvis revealed a lobulated mass from the rectosigmoid colon to the lower

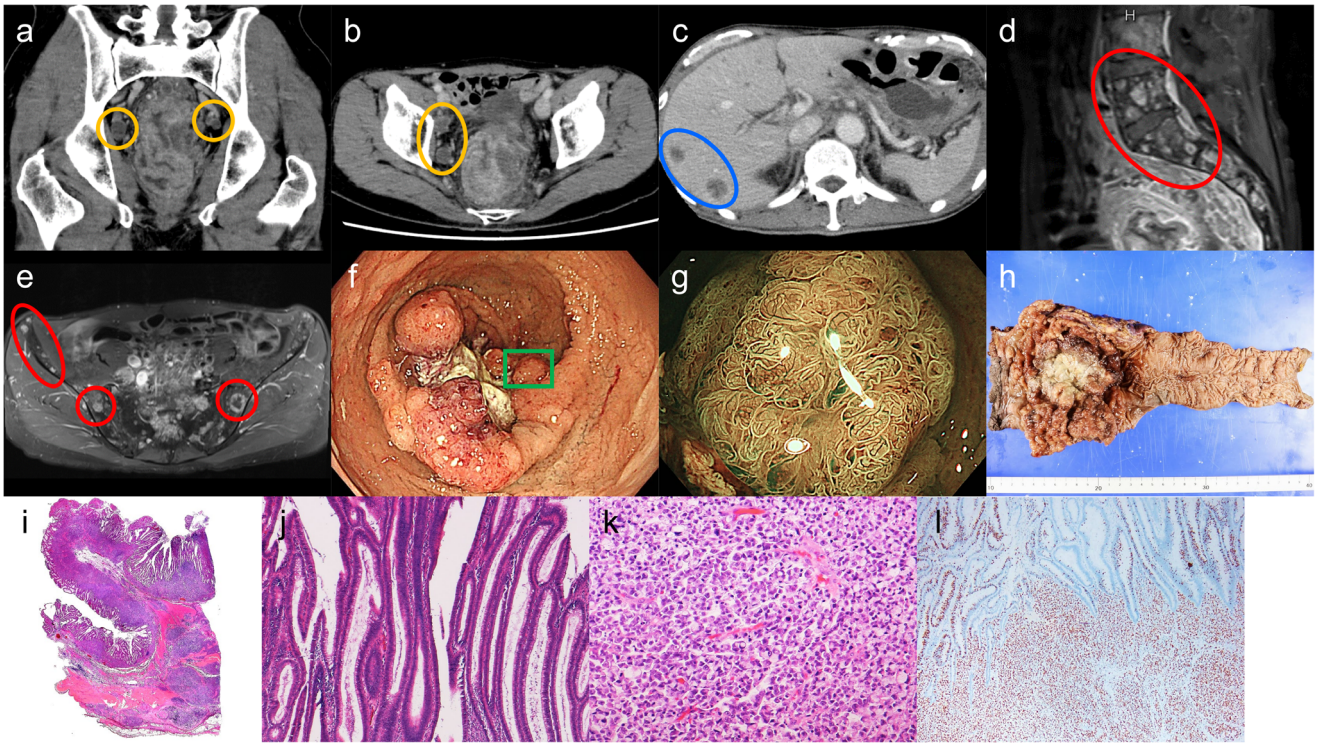

Figure 1 (a–c) Coronal (a) and axial (b, c) computed tomography images show a lobulated mass from the rectosigmoid colon to the lower rectum with associated adenopathy (yellow frame) and metastatic liver lesions (blue frame). (d, e) Sagittal (d) and axial (e) T2-weighted magnetic resonance images demonstrate multiple well-defined lesions in the lumbar vertebrae, sacrum, and ilium (red frame). (f) Conventional colonoscopy using white light imaging reveals a large villous mucus-rich tumor with ulcer, spreading circumferentially along the rectal wall. (g) Magnifying narrow band imaging of green frame in (f) show a regular villous structure on the tumor surface. (h) The surgically resected specimen is a circumferential, soft villous tumor measuring 110 × 80 mm. (i) Low-power field view of the resected specimen. (j, k) Higher power field view of the surface area (j) and invasive area (k) in tumor shows a villous adenoma and signet ring cell carcinoma, respectively. (l) Ki-67 (MIB-1) immunohistochemistry shows estimated 20% proliferation index in villous adenoma area, while the index in the carcinoma area is 100%.

rectum with associated adenopathy and liver metastatic lesions (Fig. 1a–c). Furthermore, T2-weighted magnetic resonance images demonstrated multiple well-defined lesions in the lumbar vertebrae, sacrum, and ilium (Fig. 1d,e). Colonoscopy revealed a large villous mucus-rich tumor with ulcer spreading circumferentially along the rectal wall (Fig. 1f,g). Based on these findings, he was diagnosed with advanced rectal cancer with liver and bone metastases, which caused MWS. With intravenous fluid treatment, abdominoperineal resection of the rectum with lymph node dissection (miles resection) was performed. The surgically resected specimen was a circumferential, soft villous tumor measuring 110 × 80 mm (Fig. 1h). Histological examination of the resected specimens revealed signet ring cell carcinoma with villous adenoma, which invaded through the muscularis propria into the subserosa and metastasized to regional lymph nodes (Fig. 1i–l). Fifteen of the 21 lymph nodes resected with the specimen were positive for adenocarcinoma. Renal dysfunction and the electrolyte abnormalities that were present before surgery gradually improved. Two courses of capecitabine were administered as adjuvant chemotherapy after the surgery. However, approximately 2 months after surgery, he died of poor general condition due to progression of the liver metastases.

Discussion

MWS is a condition that leads to secretory diarrhea with severe electrolyte and body fluid depletion caused by a loss of large amounts of mucus secreted by a villous adenoma.[1] The frequency of electrolyte disorders caused by villous tumor is 2%, and the condition is relatively rare.[2] The mechanism responsible for promoting potassium and water excretion has been suggested to involve increased secretion of potassium and water from cells caused by elevated intracellular levels of cyclic adenosine monophosphate and prostaglandin E2 released from tumor cells. Initial treatment consists of correcting the hydroelectrolyte imbalance, and definitive treatment is extirpation of the tumor. Treatment is usually surgical with targeted resection of the tumor, which leads to near resolution of symptoms in the majority of cases.[2] In the systematic review by Orchard *et al.*, MWS was associated with a prolonged history of disease, villous tumors located in the rectum or sigmoid colon, tumor diameter ≥10 cm, severe mucous diarrhea, electrolyte abnormalities, and concurrent presence of cancer.[5] Our patient's symptom of mucous diarrhea lasted for more than 3 years. He presented with a villous tumor of the rectum, and the tumor diameter exceeded 10 cm, spreading circumferentially in the rectum, and partially extending into the anal canal.

The majority of villous tumors associated with MWS consist mainly of adenomatous elements, with a shallow depth of invasion, even in the presence of carcinoma.[2] Their development into advanced cancers is very rare.[6] Therefore, except for cases with severe complications caused by renal impairment and hydroelectrolyte imbalance, the prognosis is relatively good if properly treated. In this case, histopathological examination revealed a signet ring cell carcinoma with villous adenoma, and the patient already had multiple liver metastases and bone metastases at the time of diagnosis. In general, colorectal primary signet ring cell carcinoma is a rare entity accounting for nearly 1% of all colorectal carcinomas.[7] It is an independent prognostic factor associated with less favorable outcomes. In this case, it was considered that a rare signet ring cell carcinoma showing high malignancy arose from villous adenoma, which led to a poor prognosis and high probability of death early after surgery.

In conclusion, a patient with a large rectal carcinoma leading to MWS had multiple liver and bone metastases and died approximately 2 months after surgery. MWS is rare and potentially lethal.

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