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CASE REPORT

Solitary extramedullary plasmacytoma of the rectum complicating ulcerative colitis

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Abstract

Solitary extramedullary plasmacytoma (EMP) arising in the rectum is an extremely rare clinical entity. Only ten cases have been reported in the English-language literature. We experienced a case of an EMP in the rectum of a 55-year-old man with an 8-year history of proctitis-type ulcerative colitis (UC). The plasmacytoma appeared as an 8-mm semipedunculated polypoid lesion in the actively inflamed rectal mucosa when the remittent UC flared. The tumor was treated using endoscopic mucosal resection. This is the second case of rectal EMP associated with UC after a similar report was published in 2004. Both patients had a chronic history of proctitis-type UC and were taking no immunosuppressive agents that could cause Epstein–Barr virus-associated plasmacytoma, such as thiopurines. The UC activity seemed to correspond well with the development of the rectal EMP. Therefore, we herein discuss a possible association between rectal EMP and UC and review the past literature of rectal EMP.

Keywords Extramedullary plasmacytoma · Ulcerative colitis · Endoscopic mucosal resection

Introduction

Plasma cell neoplasms are a group of lymphoproliferative disorder (LPD) characterized by monoclonal accumulation of terminally differentiated B cells. Most plasma cell neoplasms are multiple myeloma (MM). In contrast, plasmacytoma is an infrequent form characterized by localized proliferation of neoplastic plasma cells without evidence of systemic involvement. Plasmacytoma can be classified into two groups according to location: solitary plasmacytoma of the bone and extramedullary plasmacytoma (EMP) [1]. EMP, which develops outside of the bone marrow, is very infrequent, accounting for 4% of all plasma cell neoplasms [1, 2].

Although EMP can develop in any part of the body, approximately 90% of cases involve the head and neck, especially the upper respiratory tract; only a small percentage involve the gastrointestinal (GI) tract [2, 3]. While the stomach and intestine are the most commonly affected GI sites, EMP is extremely rare in the colon, particularly in the rectum. To our knowledge, only ten cases of rectal EMP have been reported in the English-language literature to date [4–12].

We herein present a case of an EMP arising from the inflammatory rectum of a patient with proctitis-type ulcerative colitis (UC). This is the second report of a rectal EMP that appeared as remittent UC flare-up; the first case was reported by Hashiguchi et al. [9] in 2004 and was very similar to the present case. Although the pathophysiology of rectal EMP is unclear, a possible association with UC is herein discussed with regard to the literature.

Case report

A 55-year-old man presented in January 2015 with a 1-month history of bloody diarrhea. He had an 8-year history of proctitis-type UC. An initial diagnosis of mild proctitis (Mayo 1) had been made in our hospital by colonoscopy

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when the patient developed occasional bloody diarrhea in 2007. Rectal salazosulfapyridine was administered with subsequent remission. Shortly thereafter, however, he discontinued treatment and took no medications for UC for about 5 years, when the bloody diarrhea recurred in 2013. He visited our hospital again, and a mild to moderate (Mayo 1–2) flare-up of proctitis-type UC was confirmed by colonoscopy. Oral mesalazine was initiated at 3.6 g/day, resulting in a rapid clinical response. Mucosal healing (Mayo 0) was verified on follow-up colonoscopy 10 months before the current presentation, and the patient thereafter remained in clinical remission with mesalazine until the resumption of bloody diarrhea 1 month before the current presentation.

Colonoscopy revealed recurrence of proctitis-type UC (Mayo 1–2), and an 8-mm semipedunculated polypoid tumor with a wide area of superficial erosion was newly detected on the inferior transverse fold of the rectal anterior wall (Fig. 1). The surface mucosa of the polypoid tumor was the same as that of the surrounding inflamed UC, and the erosive area of the tumor showed a regular surface pattern with no abnormal vessels by narrow band imaging. Our preliminary clinical diagnosis was a benign inflammatory polyp associated with UC, although the possibility of a neoplastic tumor could not be eliminated considering its rather sudden appearance.

Because the polypoid tumor was only 8 mm in size and semipedunculated with a relatively narrow base, the patient was treated by endoscopic mucosal resection (EMR) after providing informed consent. The resected specimen contained massive infiltration of atypical plasmacytoid cells nearly occupying the whole polyp from submucosa to mucosa (Fig. 2). The area with disappearance of the rectal glands corresponded to the erosive surface of the polyp.

Immunohistochemical staining showed that the tumor cells were diffusely positive for CD138, CD79a, and IgG

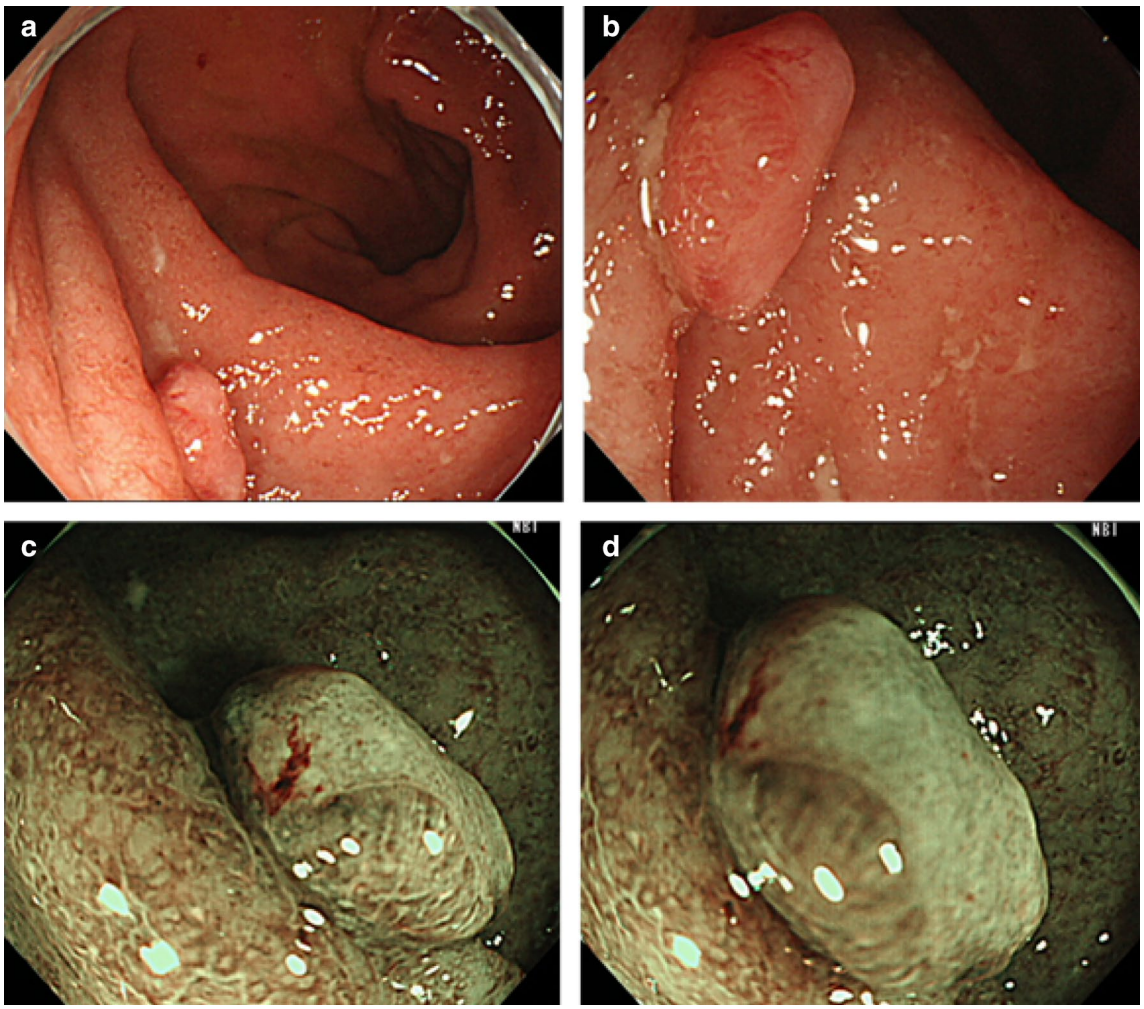

Fig. 1 Rectal colonoscopic findings. **a** A flare-up of proctitis-type ulcerative colitis (Mayo 1–2) was observed. **b** An 8-mm semipedunculated polypoid tumor with a superficial wide erosion had newly developed on the inferior transverse fold of the rectal anterior wall. **c, d** Narrow band imaging revealed a regular surface pattern and no abnormal vessels on the erosive area of the tumor

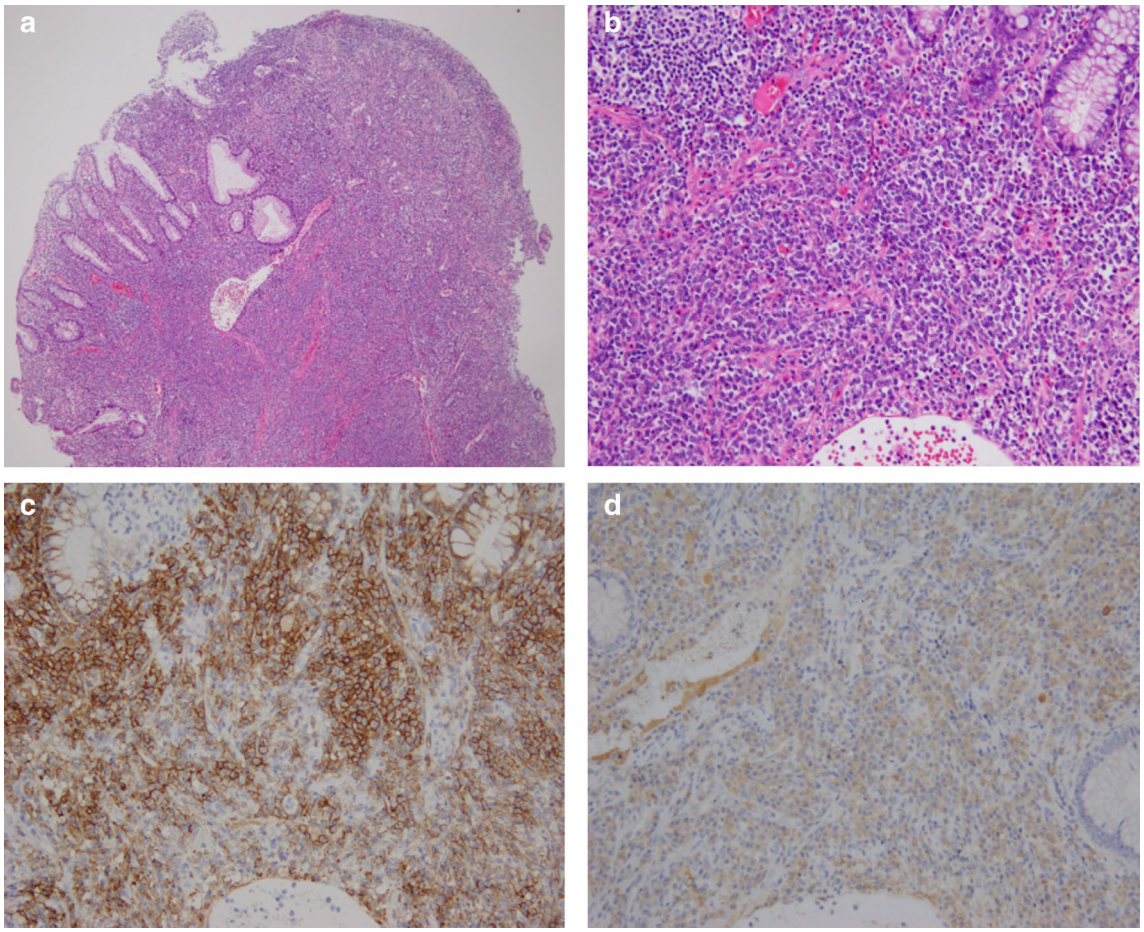

Fig. 2 Histological findings of the specimen obtained by endoscopic mucosal resection. Massive infiltration of atypical plasmacytoid cells nearly occupied the whole polyp from submucosa to mucosa as shown by hematoxylin and eosin staining. **a** ×40, **b** ×200. Immunohistochemical staining revealed that the tumor cells were positive for CD138 and IgG. **c** CD138, ×200. **d** IgG, ×200

with kappa light chain restriction by the proliferating plasma cells, indicating monoclonality. The tumor cells were negative for CD3, CD5, and CD20, and neither centrocyte-like cells nor lymphoepithelial lesions were present in the tumor.

A biopsy of rectal mucosa adjacent to the polyp showed irregularly distributed and distorted glands with increased infiltration of lymphocytes (mainly plasma cells), leading to the formation of lymphoid follicles. These findings were consistent with the development of a plasmacytoma in the rectal mucosa with chronic active UC.

The tumor cells were negative for Epstein–Barr virus (EBV)-encoded RNA by in situ hybridization. No evidence of complicating MM was demonstrated through serum electrophoresis, bone marrow aspiration, urinary test for Bence Jones protein, and fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT). Therefore, the diagnosis of an EMP arising in the rectal mucosa was made.

The vertical cut margin of the EMP was not free of tumor cells by histology, suggesting residual tumors in the rectum. After 3 months of administration of rectal mesalazine, which promptly achieved both clinical and endoscopic remission of UC, local excision of the rectal EMR scar was performed transanally to examine the residual plasmacytoma. We found no plasmacytoma remaining in the excised rectal specimen, including the EMR scar, which was probably due to the burning effect of EMR on the cut margin of the rectum.

CT, magnetic resonance imaging (MRI), and FDG PET/CT revealed no involvement of local lymph nodes or other organs; therefore, we performed no additional treatment such as radiotherapy for the plasmacytoma. No relapse of the plasmacytoma or progression to MM was observed during a 3-year follow-up period.

Discussion

EMP arising in the rectum is extremely rare; to our knowledge, only ten reports exist in the English-language literature (Table 1) [4–12].

Table 1 Reported cases of rectal extramedullary plasmacytoma

Author	Year	Age	Sex	Symptom	Gross appearance	Lymph node	Treatment	Outcome	Comorbid diseases
Brown	1939	57	M	Rectal bloody discharge	Numerous polypoid mass	+	None	Death	Ileal EMP
Hampton	1956	41	F	Rectal bleeding	4.5 × 4 cm soft mass	–	Ope	No rec in 12 months f/u	n.d.
Sharma	1960	50	M	Difficulty in defecation for a year	3 cm circumferential stenosis and ulcer	–	Ope	Lost to f/u studies	n.d.
Price	1987	55	M	Tenesmus	8 cm mass	n.d.	RT	No rec in 36 months f/u	n.d.
Price	1987	90	F	Anemia and rectal bleeding	Polypoid tumor on the posterior wall	n.d.	RT	Regressed in 3 months	Hemorrhoids
Pais	1992	87	F	None	2 cm pedunculated polyp	–	Polypec + RT	No rec in 12 months f/u	Diabetis UTI
Hashiguchi	2004	47	M	Bloody diarrhea	2 cm reddish protruded lesion	–	EMR + RT	No rec in 6 months	UC (proctitis)
Nakagawa	2011	84	F	None	2 mm sessile polyp	–	EMR	n.d.	Cecal EMP (4 mm polyp)
Hoton	2015	60	M	Hematechezia and diarrhea	4 × 3 × 2.5 cm polyp	–	EMR	No rec in 8 months f/u	Ischemic heart disease
Gohil	2015	55	M	Perianal pain	13 × 8 cm mass	–	Ope + RT	No rec in 3 months f/u	n.d.
Our case	2018	55	M	Bloody diarrhea	8 mm semipedunculated polyp	–	EMR + local excision	No rec in 3 years f/u	UC (proctitis)

n.d. Not described, *ope* operation, *RT* radiation therapy, *polypec* polypectomy, *rec* recurrence, *f/u* follow-up, *UTI* urinary tract infection

Including our 11th case, the patients' ages ranged from 41 to 90 years (mean 61.9 years), and a male prevalence was observed (seven men vs. four women); these features are similar to those of EMP at other sites [13]. In general, the clinical presentation of EMP is variable depending on the site of the tumor, and bleeding is the most common symptom among rectal EMPs as observed in four cases (even when two cases with concomitant UC were excluded). Endoscopic and CT/MRI findings of GI EMP are thought to be nonspecific; therefore, GI EMP is sometimes misdiagnosed as a carcinoma or inflammatory bowel disease [13–15]. In our review of the literature, rectal EMP most commonly presented as a mass or polypoid lesion.

No guidelines for the treatment of GI EMP have been established because of its extreme rarity. Although EMP is a highly radiosensitive tumor, surgical resection has been proposed as the first choice for GI EMP [2, 3]. Additional radiotherapy is recommended if complete resection is not achieved or lymph node areas are affected [2]. Price et al. [7] reported two patients with rectal EMP treated only by radiotherapy, suggesting that primary radiotherapy should be considered for rectal EMP demanding major surgery or colostomy. Quite recently, endoscopic treatments such as EMR and endoscopic submucosal dissection have been shown to be alternatives to surgery in select patients with GI EMPs [16, 17]. In the present case, no residual plasmacytoma was found in the rectum after EMR; therefore, additional radiotherapy was not performed, and no relapse occurred during a 3-year follow-up.

EMP generally has an indolent course, and its prognosis is better than other LPDs with a 10-year overall survival rate of 70% [2, 3], as observed with rectal EMPs. However, long-term follow-up is recommended because EMP may relapse or progress to MM in a minority of cases [2].

The etiology of EMP is still unknown, although viruses, overdose of irradiation, chronic stimulation, and gene mutations in the reticuloendothelial system have been suggested as etiologic factors [18, 19]. Wiltshaw [18] suggested that EMP arises from plasma cells within the mucosal surface, while MM originates from bone marrow plasma cells. The present report describes the second known case of GI EMP arising from the chronically inflamed rectal mucosa of a patient with proctitis-type UC among only 11 cases of rectal EMP. This prompted us to investigate a possible causal relationship between UC and rectal EMP.

EMP is a primary intestinal LPD of B-cell lineage. Although an increased risk of colorectal cancer has been well established in patients with UC [20], the risk of intestinal and extraintestinal LPDs has remained controversial since the first report of malignant lymphoma in a patient with UC in 1928 [21]. However, many well-designed, population-based studies have failed to show that UC itself is

a risk factor for LPDs [22–24]. Nevertheless, patients with UC receiving thiopurines have been shown to be at significantly higher risk of LPDs [25–27]. Use of thiopurines is an accepted risk factor for EBV-associated LPDs in post-organ transplant patients, in whom thiopurine impairs T-cell activity of immunosurveillance, leading to reactivation of the oncogenic virus [28]. Similarly, LPDs observed in patients with inflammatory bowel disease treated with thiopurines are predominantly EBV-associated and histologically comparable with those in the post-transplant setting, suggesting a causal role of immunosuppression.

However, both patients with UC who developed rectal EMP are thought to have been immunocompetent; they had only been treated with mesalazine therapy and had taken no immunosuppressive agents including thiopurines, corticosteroids, or biologics. In our patient, no EBV-positive plasmacytoma was demonstrated using in situ hybridization for EBV-encoded RNA. Therefore, immunosuppressive treatments for UC and reactivated EBV were not considered to play a role in the genesis of the two herein-described rectal EMPs with UC.

The clinical course of both patients was surprisingly similar. Both patients had a relatively long 8-year history of proctitis-type UC. Most importantly, both rectal EMPs were detected when the remittent UC flared up only 8–10 months after mucosal healing was confirmed by colonoscopy. This suggests the possibility that both rectal EMPs developed in association with the disease activity of chronic UC and that the development of the UC-associated EMP may have been more than coincidental in these patients.

Why both patients were from Japan remains unclear. A previous study revealed a significantly lower incidence of plasmacytoma and MM in Asians than in whites and blacks [30], suggesting no racial predilection, especially for Japanese individuals. Doi et al. [31] proposed that improvements in the quality of endoscopic resolution and diagnostic techniques may be a reason for the high detection rate of gastric EMPs in Japan, especially those reaching the mucosal or submucosal level.

In summary, we have herein presented the second case of a rectal EMP with UC after the first similar report by Hashiguchi et al. [9] among only 11 cases of rectal EMP. Both patients with UC were totally free of immunosuppressive agents that could induce EBV-associated plasmacytoma, such as thiopurines. Additionally, the activity of proctitis-type UC corresponded well with the development of rectal EMP. These findings suggest a possible association between rectal EMP and UC itself.

Compliance with ethical standards

Conflict of interest Wataru Miwa, Takashi Hiratsuka, Shutetsu Tei, Ken Sato, Yo Kato declare that they have no conflict of interest.

Human/animal rights All procedures followed have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Informed consent Informed consent was obtained from all patients for being included in the study.

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