INTERNAL MEDICINE

□ CASE REPORT □

Double Extramedullary Plasmacytoma of the Stomach with a Long-term Endoscopic Follow-up

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Abstract

A 56-year-old woman was referred to our hospital with a growing gastric submucosal tumor. An upper endoscopic examination revealed two gastric tumors, an original polypoid tumor and a newly diagnosed superficial tumor. Boring biopsied specimens of the submucosal tumor showed gastric plasmacytoma; however, the other specimens showed no malignancy. Blood diseases were ruled out using various examinations; therefore, we diagnosed the tumor as extramedullary gastric plasmacytoma. The patient underwent laparoscopic distal gastrectomy, and both tumors were thus revealed to be plasmacytomas. We experienced a rare case with two differently shaped extramedullary gastric plasmacytomas without significant morphologic change during the follow-up.

Key words: extramedullary plasmacytoma, gastric plasmacytoma

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Introduction

Plasmacytoma is divided into two classes according to the site of onset. The first is defined as solitary plasmacytoma, which develops in bones or the bone marrow. The second is extramedullary plasmacytoma, which develops everywhere else, for example the nasal cavity, nasal sinus, lungs, digestive tract, and other organs (1). Extramedullary plasmacytoma is a rare disease and accounts for approximately 2-4% of all plasmacytomas. Approximately 80% of tumors develop in the upper airway and oral cavity, and approximately 10% develops in the digestive tract (2). Primary gastric plasmacytoma is a rare disease, and approximately 100 cases have been reported since 1928.

We herein report a rare and informative case with separate plasmacytoma in the stomach. Furthermore, we present a relatively long-term natural history with endoscopic follow-up surveillance.

Case Report

A 56-year-old woman was diagnosed with a gastric submucosal tumor measuring 12 mm in size, which was found during a regular health check in 2005 at another hospital. After an upper endoscopic examination, the tumor grew slightly; however, there was no epithelial change from 2009 to 2010. She was referred to our hospital in 2011 for a growing gastric tumor work up because her tumor eventually grew to the size of 15 mm, and a depression clearly appeared at the top of tumor (Fig. 1).

The patient's past medical history included rheumatic fever and bilateral tonsillectomy during her 20s. She had Graves' disease without treatment since she was 54 years of age. A family history did not appear to contribute to the clinical picture.

Routine laboratory studies showed mild elevation of transaminase, and hematology, urology, and blood chemistry data

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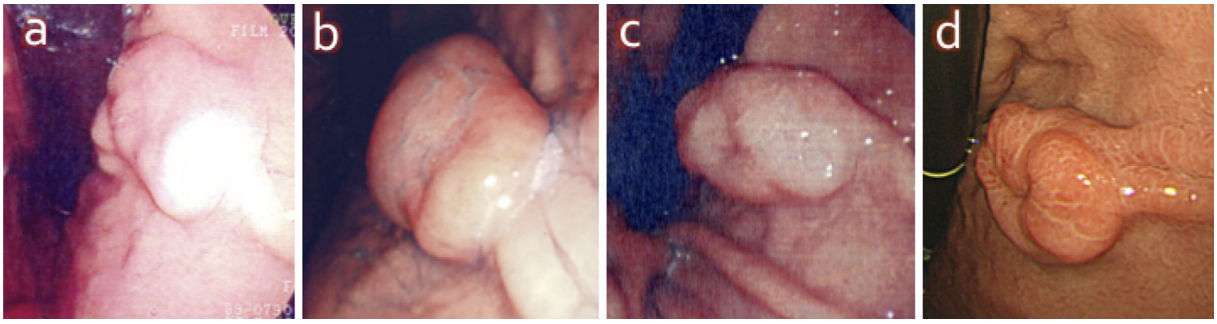

Figure 1. **a: Endoscopic findings in 2005 revealed an elevated lesion resembling a submucosal tumor with slight depression on the posterior wall of the middle body. b: Endoscopic findings in 2009 showed no change in the tumor size or shape. c: Endoscopic findings in 2010 showed a marked tumor growth and central depression. d: Endoscopic findings in 2011 showed tumor growth with a reddish appearance and a styloid form of the tumor root and deeper depression at the center.**

were within normal limits. Furthermore, the *Helicobacter pylori* antibody testing using an enzyme immunoassay kit (E-plate Eiken *H. pylori* antibody II; Eiken Kagaku, Tokyo, Japan) was negative (*H. pylori* antibody titer: 4 U/mL).

Abdominal computed tomography (CT) showed no metastatic lesion. Bone marrow aspiration and a biopsy did not show plasmacyte infiltration. A serum electrophoretic study revealed no abnormalities, and urine for Bence Jones protein was also negative. Therefore, we ruled out multiple myeloma and diagnosed the tumor as extramedullary gastric plasmacytoma.

An endoscopic examination revealed two isolated gastric tumors, one was the original tumor, and the other was a superficial tumor with a depressed area (Fig. 2). Boring biopsied specimens of the submucosal tumor showed gastric plasmacytoma, whereas the other showed no malignancy. However, this specimen showed an increased number of plasmacytes. Because gastric plasmacytomas occasional occur in multiple sites, we suspected this was also a plasmacytoma.

We suspected that the submucosal tumor invaded the submucosa or more deeply, therefore there were no indication for endoscopic treatment. The legion limited to the middle of the stomach had a sufficient margin, thus the patient underwent laparoscopic distal gastrectomy. A macroscopic examination revealed an elevated lesion resembling a submucosal tumor, 16×9 mm in size, in the posterior wall and a slightly elevated lesion with a depressed central area, 19×15 mm in size, in the lesser curvature of the middle of the stomach.

Histological findings of the resected specimen revealed diffuse proliferation of plasmacytes with Dutcher bodies. Immunoperoxidase staining showed monoclonal growth of Kappa chain-positive cells and IgA chain-positive cells (Fig. 3). After surgery, both tumors were diagnosed as plasmacytomas.

Thus, we diagnosed the patient as having extramedullary gastric plasmacytoma. Because the tumor was contained and could be completely resected, the patient was followed up closely without additional treatment. No recurrence has been observed 3 years after surgery.

Discussion

We herein reported a case of early extramedullary gastric plasmacytoma that was followed up over a long duration. This case was quite rare with regards to two characteristics: (1) we observed almost no morphologic change in the gastric plasmacytoma for 7 years, and (2) there were two different types of plasmacytoma in the affected stomach.

Because the patient was not diagnosed with gastric plasmacytoma until she was referred to our institution, we could not determine whether the plasmacytoma in this case grew and changed its appearance or a benign tumor had resulted in a malignant change into plasmacytoma. The finding of the presence of Dutcher bodies was required to accurately diagnose plasmacytoma because we could not diagnose the superficial tumor.

Plasma cell neoplasms can be divided into four pathology types: multiple myeloma, plasma cell leukemia, solitary plasmacytoma of the bone, and extramedullary plasmacytoma. Extramedullary plasmacytoma is rare and account for approximately 2-4% of all plasmacytomas. Extramedullary plasmacytoma is less frequently observed; approximately 10% of cases develop in the digestive tract. The most frequent digestive organ of extramedullary plasmacytoma is the small intestine.

Gastric plasmacytoma can be grossly classified into four tumor types: nodular, infiltrative, ulcerative, and polypoid (3). Alternatively, gastric plasmacytoma can also be classified as a fifth type, namely the superficial type.

Our case was diagnosed to have a plasmacytoma using a boring biopsy. There were two tumors; one was a polypoid type with tumor cells invading the submucosa and the other was a superficial type with tumor cells invading the lamina propria. We found that the tumor cells differentiated into plasma cells that produced monoclonal IgA, with a limited immunoglobulin light chain. Extramedullary plasmacytomas are predominantly found in women in their 50s in Japan and are likely to occur at multiple sites. Our case is therefore

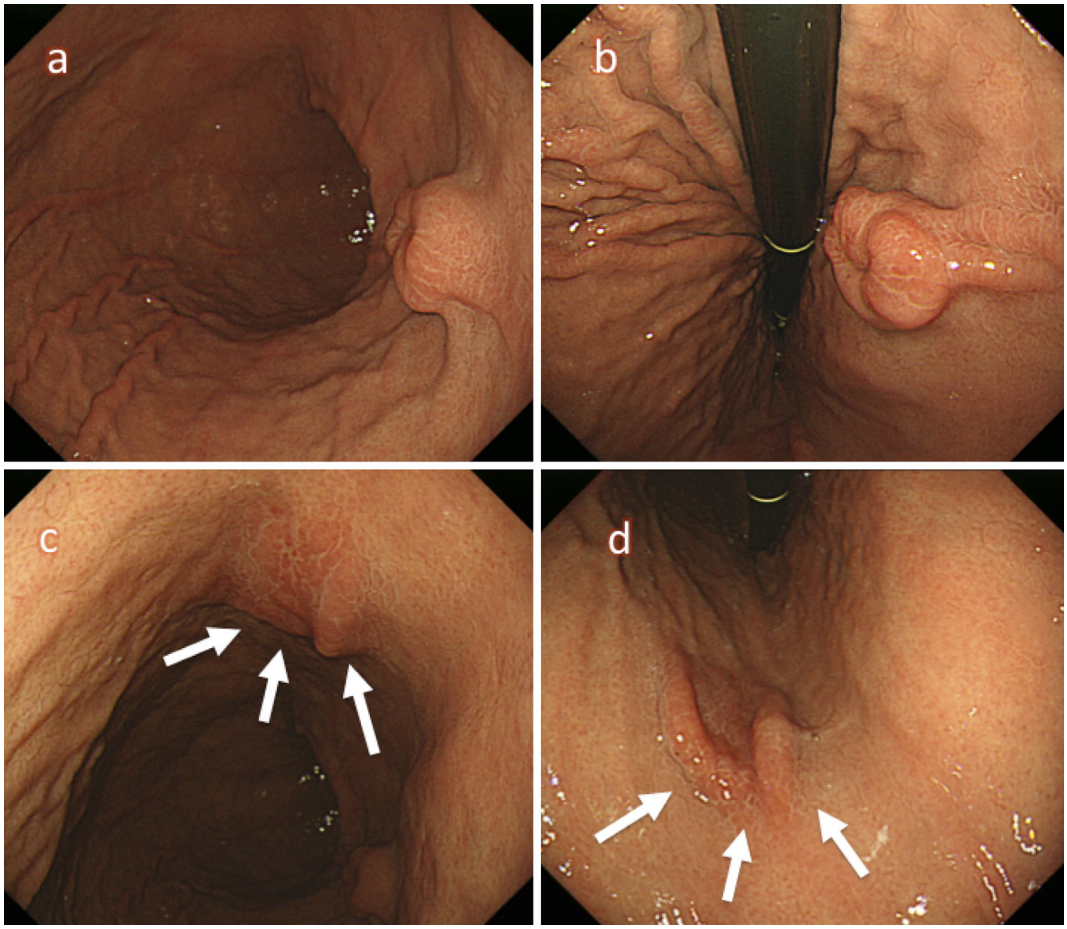

Figure 2. **a: An endoscopic examination revealed an elevated lesion, similar to a submucosal tumor, with erosion on the posterior wall of the middle body. b: A retroflexion picture of a showed a styloid form of the tumor root. c: An endoscopic examination revealed a distinct elevated lesion with a depressed area on the lesser curvature of the middle body (arrows). d: A retroflecion image of c showed an erythrogenic tumor without ulcerative change (arrows).**

consistent with these previous reports.

Primary gastric plasmacytoma is rare; approximately 100 cases have been reported since 1928 in both Europe and the US. The number of gastric plasmacytoma cases reported in Japanese journals is increasing, and to date, we identified 95 patients presented in Japanese case reports. Early extramedullary gastric plasmacytomas with the depth to the submucosa or mucosa level have become more frequent in Japan, 51 cases to date that have been reported mostly in Japanese manuscripts (4-19). Table shows the determined characteristics. The improvement in the early diagnosis is likely due to the improved quality of endoscopic resolution and diagnosis procedures. Thus, the successful identification of such cases is likely to improve over time.

Among the 51 reported cases of early gastric plasmacytomas, 30 patients were women and 21 men, and the median age was 56 years. The superficial type was the most common (38 cases), whereas the polypoid type was least common (4 cases), which is consistent with our case reports from Japan. Moreover, the accurate diagnosis rate increased by approximately 73%. We suspect that we could not confirm plasmacytoma using biopsied specimens due to the small amount of sampling tissue and/or we may have overlooked the possibility of plasmacytoma in making a differential diagnosis. According to our preliminary pathological evaluation, biopsied specimens suggested poorly differentiated adenocarcinoma and/or gastritis with plasmacyte accumulation. Hence, we recommend that adequate sample volumes are obtained to improve the diagnosis.

Regarding treatment, it is recommended that plasmacytoma of the head and neck is treated using radiation therapy, while other plasmacytomas should be treated with complete surgical resection, if possible. Additional radiation therapy postsurgical treatment should be performed if complete resection is not achieved (20). Chemotherapy is not the standard treatment because few reports have described its efficacy. The present case included tumors that could be treated by complete surgical resection. Table shows that almost all early gastric plasmacytoma patients survived and generally demonstrated a good prognosis. Our patient was alive at 42 months post-surgery. It has been reported that the 3-year overall survival of early gastric plasmacytoma patients is 100%. It is likely that most early gastric plasmacytomas do not metastasize to the lymph node, hence the high survival

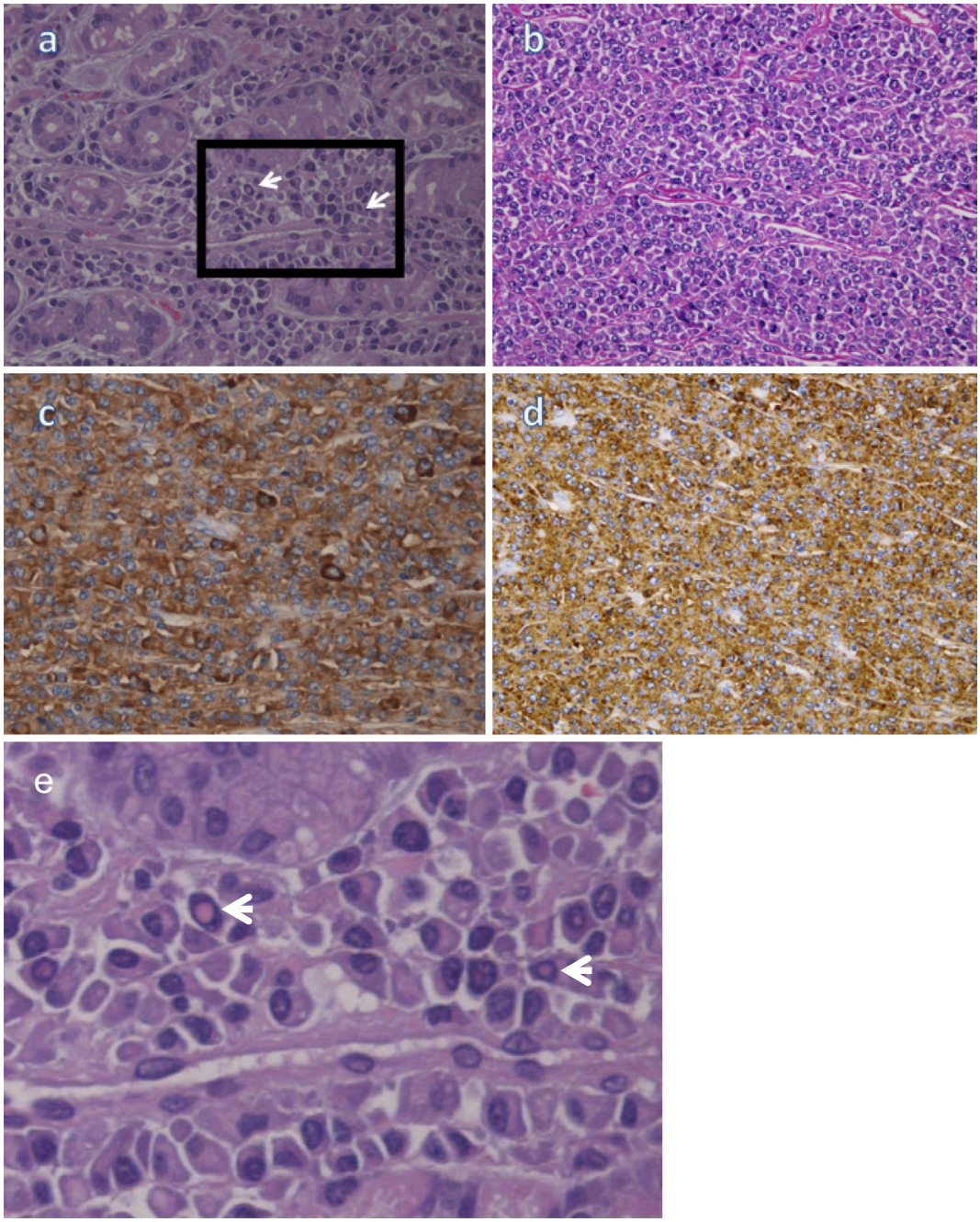

Figure 3. **Histological findings of the resected specimen revealed diffuse proliferation of the plasmacytoid cells with Dutcher bodies. a: A histological examination of the biopsied samples taken from superficial type plasmacytoma [Hematoxylin and Eosin (H&E) staining, 400×]. b: A histological examination of biopsied samples taken from nodular/SMT type plasmacytoma (H&E staining, 400×). c: Immunohistochemistry of b showing positivity for Kappa chains in tumor cells (immunoperoxidase stain, 400×). d: Immunohistochemistry of b showing positivity for IgA chains in tumor cells (immunoperoxidase stain, 400×). e: A high-power field of a represents Dutcher bodies (arrow) (H&E staining, 400×).**

rate.

Although controversial, some reports have described the efficacy of *H. pylori* eradication as a treatment for early gastric plasmacytoma (18, 21-23). Additionally, endoscopic submucosal dissection has been reported as a treatment option for early gastric plasmacytoma, where the mucosa has been infiltrated, and its prognosis is much better than advanced plasmacytoma (24, 25). The number of reports of extramedullary gastric plasmacytoma has recently increased; therefore, it is very important to diagnose early gastric plasmacytoma at an early stage to improve the prognosis.

Our case demonstrated a natural history of slow-growing gastric plasmacytoma over a period of >7 years, and there was almost no obvious change in its size and appearance.

Table. Reported Cases of Gastric Plasmacytoma in Japan (depth ≤ sm).

Reference	Age	Sex	Pre. Dx	Type	Depth	Ig	Prognosis
4	41	F	Ca	n	sm		36 m alive
4	33	M	RLH	s	sm		alive
5	28	M	Ca	s	sm		19 m alive
4	78	F	Ca	u	sm		18 m alive
4	38	M	PL	s	m	IgA	alive
4	46	M	PL	s	sm	κ	alive
4	16	F	ML	u	sm	IgM-λ	alive
4	50	M	PL	s	m	IgA-λ	8 m alive
4	81	F	PL	s	m	IgM-λ	alive
4	40	F	ML	s	sm	IgM-κ	20 m alive
4	35	M	ML	u	m	IgM-λ	
4	60	F	ML	s	sm	IgM-κ	24 m alive
4	63	F	PL	s	sm	IgA-λ	
4	73	F	PL	s	sm	IgA-κ	
4	61	F	PL	u	sm	IgM-λ	12 m alive
4	81	F	PL	s	m	IgA-κ	13 m alive
4	61	F	PL	p	m	IgM-κ	26 m alive
4	61	F	PL	s	sm	IgM-κ	
4	53	F	PL	s	sm	IgM-λ	
4	60	M	PL	s	m	IgM-λ	25 m alive
4	39	M	SMT	n	sm	IgG-κ	16 m alive
4	51	F	PL	s	m	IgM-κ	6 m alive
4	67	F	PL	s	sm	IgM-λ	
4	42	M	Ca	n	sm	IgM-λ	
4	67	F	PL	s	sm	IgM-λ	
4	59	M	PL	s	m	IgM-λ	18 m alive
4	48	M	PL	s	sm	IgG-κ	
4	73	F	PL	n	sm	IgG,A-κ	24 m alive
4	40	F	Ca	s	sm	IgG-λ	10 m alive
4	56	M	PL	s	m	IgM-κ	
4	61	F	PL	s	m	IgM-κ	
4	39	M	PL	u	sm	IgM-λ	alive
4	65	F	PL	s	sm	IgA-λ	alive
4	49	M	PL	s	sm	IgA-κ	
6	54	F	SMT	n	sm	IgM-κ	20 m alive
7	34	F	PL	s	sm	IgM-κ	alive
8	66	F	PL	s	sm	IgM-λ	alive
5	51	F	PL	s	m	IgA-κ	
5	55	M	PL	s	sm	IgA-κ	alive
9	51	F	PL	s	m	IgM-κ	6 m alive
10	77	M	PL	s	sm	IgA-κ	12 m alive
11	78	F	PL	s	m	IgM-λ	10 m alive
12	77	M	PL	u	sm	IgA-κ	17 m alive
13	57	M	PL	p	m	IgA-λ	
14	55	F	Amy	s	m	IgM-λ	67 m alive
15	71	M	PL	s	sm	IgA-λ	13 Y alive
16	62	M	PL	s	m	IgA-κ	6 m alive
17	44	M	PL	s	m	κ	
18	49	F	PL	s	sm	λ	72 m alive
19	66	F	PL	s	m	λ	38 m alive
Our case	56	F	PL	p, s	sm, m	IgA-κ	42 m alive

M: male, F: female, Pre Dx: prediagnosis, Ca: cancer, RLH: reactive lymphoreticular hyperplasia, SMT: submucosal tumor, ML: malignant lymphoma, PL: plasmacytoma, Amy: amyloidosis, n: nodular, u: ulcer, p: polypoid, s: superficial, m: mucosa, sm: submucosa

For the first 5 years, the plasmacytoma did not show any morphological changes or malignant histological findings. For the last 2 years, the plasmacytoma changed slightly in size and appearance, and the patient's previous physician referred her to our hospital for further examination which thus resulted in the appropriate treatment. As a result we obtained long-term follow-up endoscopic examination data; however, surgical treatment would have been performed if the patient had been diagnosed earlier.

This is the first report of multiple extramedullary gastric plasmacytoma in Japan without any prominent disease progression with a long-term follow-up, and our findings indicate that early gastric plasmacytoma may have a good prognosis. However, if it progresses with metastases, it could have a poor prognosis similar to general gastric adenocarcinoma.

In conclusion, we reported a case of extramedullary gastric plasmacytoma. It was a unique case because we could follow the natural course of disease by regular long-term endoscopic examinations for 7 years, and two early plasmacy-

tomas with different morphologies and depths were observed. A greater accumulation of stomach cases will increase the understanding of the diagnosis and treatment of extramedullary gastric plasmacytoma.

The authors state that they have no Conflict of Interest (COI).

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