

[ CASE REPORT ]

## Sclerosing Mesenteritis Mimicking IgG4-related Disease

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### Abstract:

A 72-year-old man was followed as an outpatient at our hospital for 6 years after surgery for small cell carcinoma of left adrenal gland origin. Follow-up abdominal computed tomography showed a 6-cm mass in the left lower mesentery. The patient underwent open laparotomy. The histological diagnosis was sclerosing mesenteritis. The previous specimens of the left adrenal mass were then re-examined with a microscope, and panniculitis was found around the small cell carcinoma. Both lesions were histologically similar to IgG4-related disease (RD), but they did not completely meet the diagnostic criteria of IgG4-RD clinically or histologically.

**Key words:** sclerosing mesenteritis, panniculitis, IgG4-related disease

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### Introduction

Sclerosing mesenteritis (SM) is a nonspecific inflammatory disease of unknown etiology that occurs locally in mesenteric adipose tissue (1). Nonspecific inflammation in the mesentery was first described as “retractile mesenteritis” by Sulla in 1924 (2). Later, another report showed panniculitis of the mesentery characterized as inflammation in adipose tissue (3). These are now considered to be the same as SM.

Although SM is a benign condition, computed tomography (CT) shows an inhomogeneous, hyperattenuated, fatty mass, which makes it difficult to distinguish SM from a malignant tumor or lymphoma (4). Histopathologically, SM is characterized by the small bowel mesentery showing some degree of fibrosis, chronic inflammation with lymphocyte infiltration, and fat necrosis (5). In addition, some cases of SM show histologically characteristic findings of IgG4-related disease (RD), such as an increased number of IgG4-positive plasma cells, storiform fibrosis, and obliterative

phlebitis. Therefore, these entities have been called “IgG4-related mesenteritis” or “mimic of IgG4-RD” (6-18). While patients with IgG4-RD often have lesions in several organs, either synchronously or metachronously, there has been only one case report of IgG4-related SM with multi-organ IgG4-RD involvement (10).

We herein report a case of SM with metachronous panniculitis histologically mimicking of IgG4-RD.

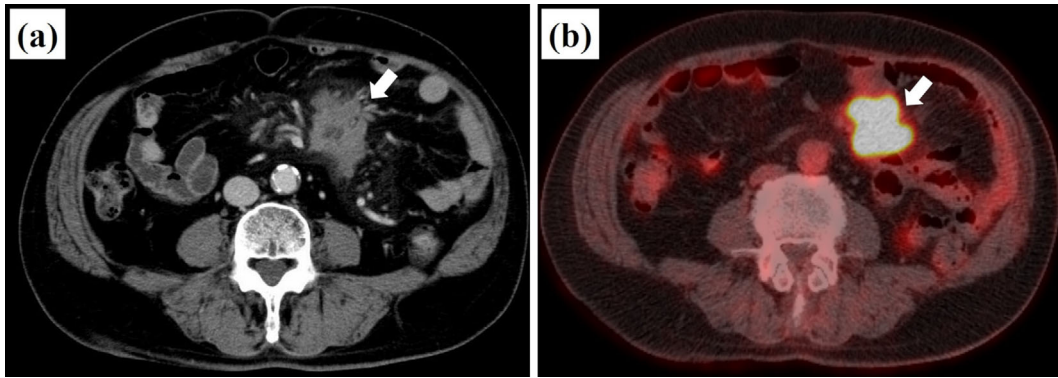
### Case Report

A 72-year-old man with a history of surgery for small cell carcinoma of left adrenal gland origin at 66 years of age was followed as an outpatient at our hospital for 6 years, and abdominal CT was performed once a year to check for tumor recurrence. Abdominal CT revealed a high-density area appearing in the peritoneal cavity near the area of the original tumor. The lesion gradually grew each year, and he was aware of discomfort in the left lower abdomen. He was admitted for a clinical examination and treatment at this

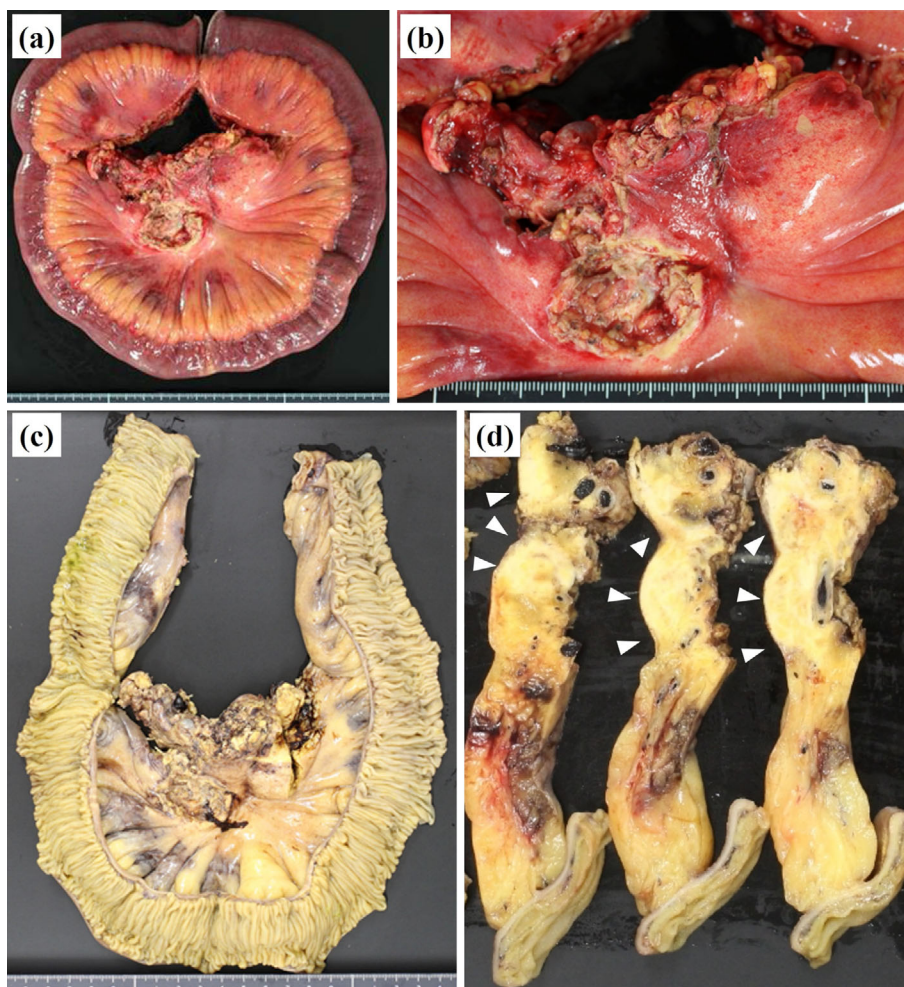
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**Figure 1.** CT and PET-CT of abdomen at 72 years of age. (a) Contrast-enhanced CT shows a 6-cm lobulated mass with contrast effect in the left lower mesentery. (b) PET-CT shows the accumulation of fluorodeoxyglucose in the mesentery.



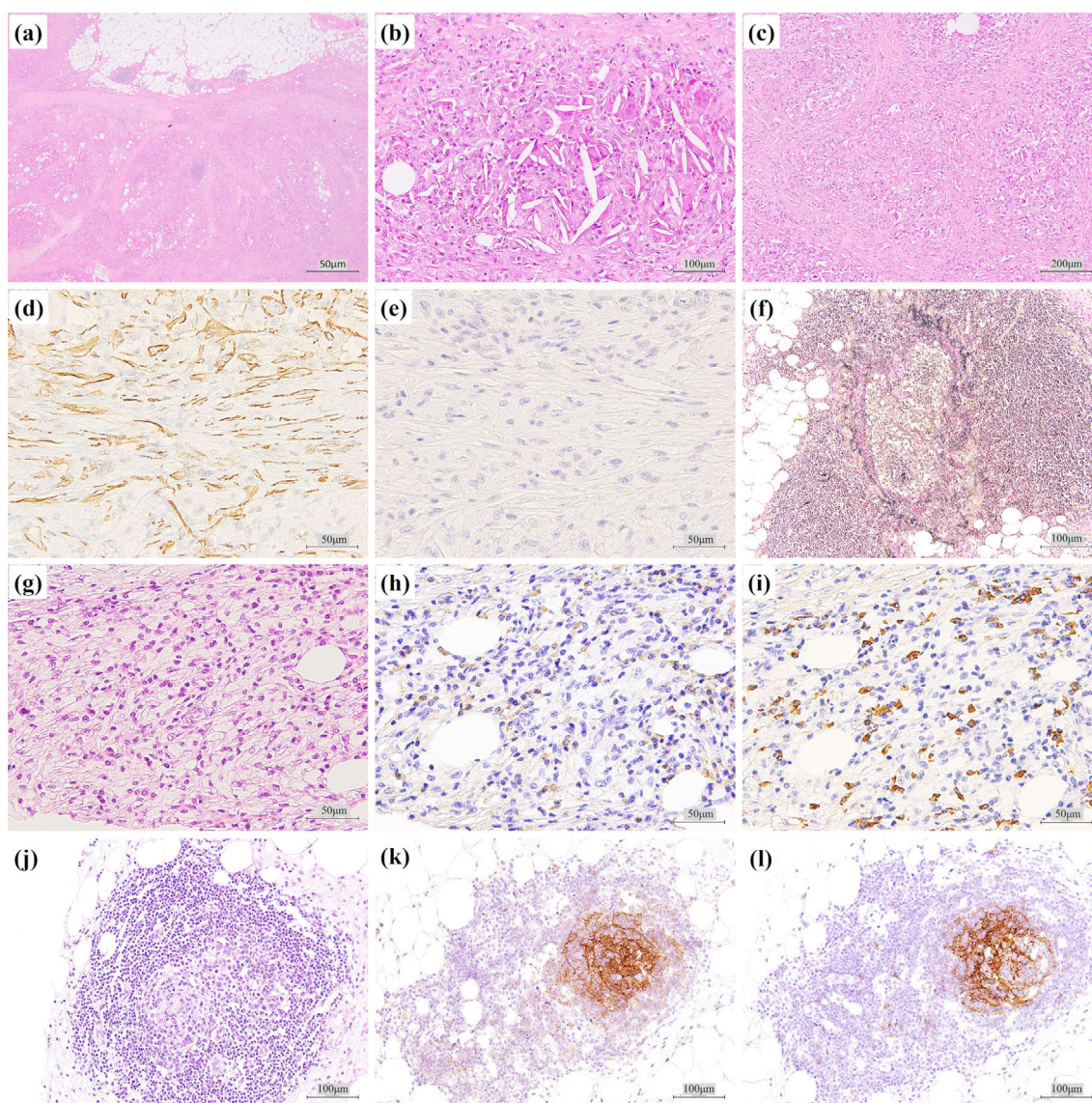
**Figure 2.** Macroscopic image of a partially resected specimen of the small intestine and mesentery at 72 years of age. (a) The surgically removed mesentery and small intestine are shown. (b) A 55×35-mm<sup>2</sup> large mass is located at the root of the mesentery. (c) The resected small bowel segment is 40 cm long, and no inflammation or hemorrhaging can be seen in the lumen. (d) The sagittal section shows white mass lesions with an unclear border with adipose tissue of the mesentery (arrowhead).

time.

Blood tests showed a mild elevation of C-reactive protein (CRP) to 0.44 mg/dL (normal: <0.30 mg/dL). Because of diabetes, his HbA1c level was increased to 7.2% (normal:

<6.2%). A high level of soluble IL-2 receptor (sIL2-R), 619 U/mL, was observed (normal: <483.0 U/mL). There was no increase in the levels of the tumor markers CEA, CA 19-9, NSE, or ProGRP. The serum IgG4 and IgG levels were





**Figure 3.** Histological findings of a partially resected specimen of the small intestine and mesentery at 72 years of age. (a) Findings of inflammation, fibrosis, and bleeding are observed in the adipose tissue. (b) Multinucleated giant cells and foamy histiocytes are admixed with a cholesterol cleft and chronic inflammatory cells. (c) Spindle cells are located in an irregular fashion. (d) The spindle cells are positive on immunohistochemical staining for  $\alpha$ -SMA. (e) The spindle cells are negative on immunohistochemical staining for ALK. (f) Elastica van Gieson staining shows that the vessel is completely obliterated by the dense inflammation. (g) Numerous lymphocytes, including plasma cells are mixed in with foamy cells. Immunohistochemical staining for plasma cells with IgG (h) and IgG4 (i) shows an IgG4/IgG-positive cell ratio of approximately 87%. (j) Lymphoid follicles consisting of lymphocytes without atypia are seen. (k, l) Immunohistochemical staining with CD21 (k) and CD23 (l) is positive only in the follicle center.

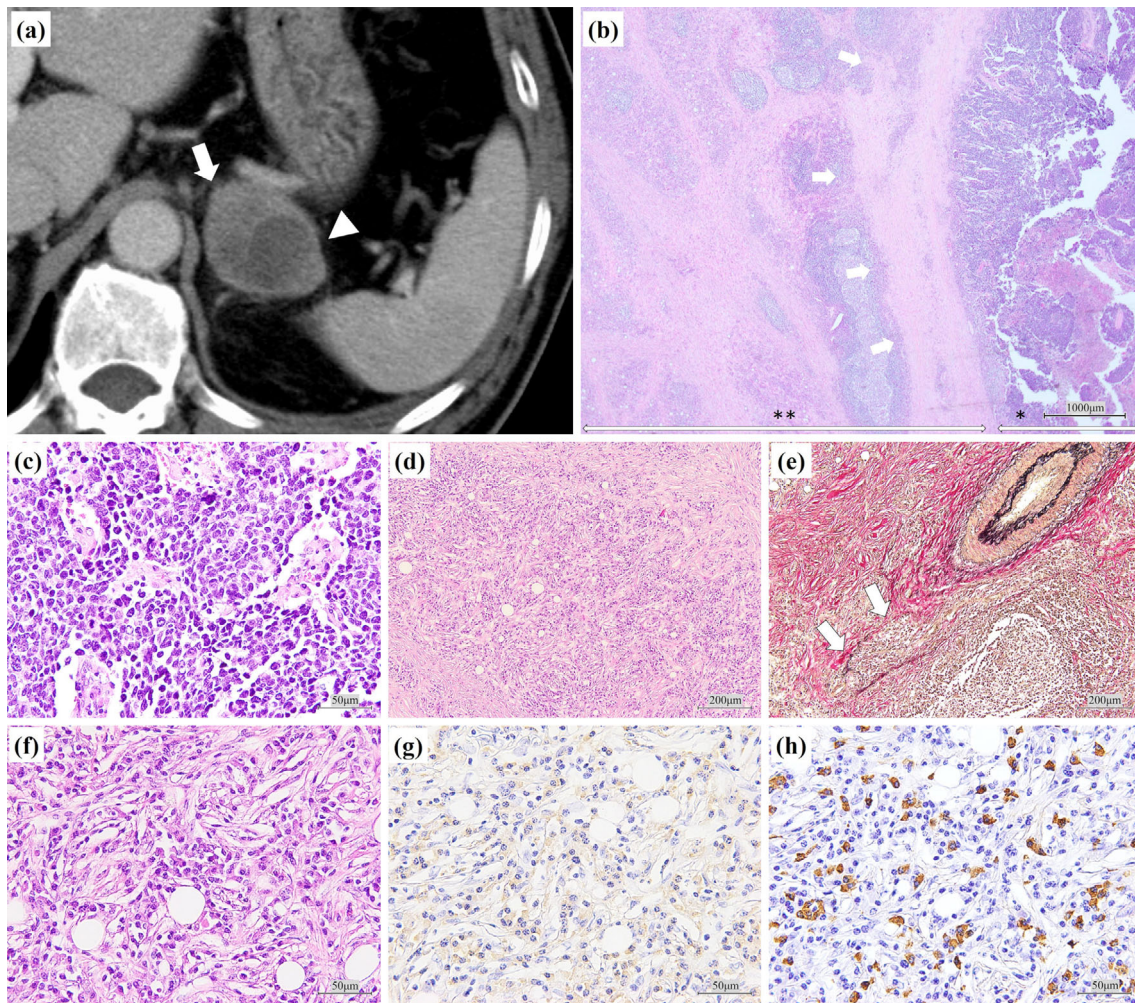
measured from preoperative preserved blood samples after the surgery, and IgG4 was within the normal range, 50.8 mg/dL (reference range, 4.8 to 105.0 mg/dL), while IgG was mildly increased to 2,056 mg/dL (reference range, 870 to 1,700 mg/dL).

CT of the abdomen and pelvis showed a 6-cm mesenteric mass in the left lower abdominal cavity. CT with intravenous contrast showed the tumor with a mild contrast effect (Fig. 1a). Positron emission tomography-CT showed a significant fluorodeoxyglucose uptake ( $SUV_{max}$ : 6.5) (Fig. 1b).

Clinically, SM or recurrence of small cell carcinoma was considered. Laparoscopic surgery was first performed, but the intraoperative rapid diagnosis revealed only necrotic tissue. Because it was difficult to diagnose the mass as a non-malignant tumor in small pieces, the mass was resected along with the mesentery and part of the small intestine via open laparotomy.

On a macroscopic examination when the patient was 72 years of age, the resected small bowel segment was 40 cm long (Fig. 2a), and the stiff mass at the root of the mesen-





**Figure 4.** CT of the abdomen and histopathological findings of the left adrenal mass and surrounding sclerosing lesion at 66 years of age. (a) Contrast-enhanced CT shows a circular, low-density area (arrow) in an oval iso-density area (arrowhead). (b) The low-magnification view of the specimen of the resected left adrenal mass shows a solid tumor (\*) surrounded by sclerosing fibrosis (arrow) (\*\*). (c) The high-magnification view of the tumor shows that the tumor consists of small atypical cells with a high nucleus to cytoplasm ratio with hyperchromatic nucleoli. (d-h) High-magnification view of the sclerosing fibrosis area. (d) The spindle cells are proliferated in an irregular fashion. (e) Elastic van Gieson staining shows the vessel with obstructive phlebitis. (f) Many plasma cells are mixed in with foamy cells. (g, h) Immunohistochemical staining for plasma cells with IgG (g) and IgG4 (h) shows an IgG4/IgG-positive cell ratio of approximately 60%.

tery was 5.5 cm×3.5 cm in size (Fig. 2b). There were no neoplastic lesions or ischemic changes in the lumen of the small intestine (Fig. 2c). Multiple cross sections of the mass and mesentery showed a solid fibrotic mass with an unclear border and surrounding adipose tissue (Fig. 2d). On a histopathological examination, the mass was mainly composed of fat necrosis and a sclerosing fibrotic lesion with lymphoplasmacytic infiltration and lymphoid follicles (Fig. 3a). Some giant cells and cholesterol clefts were observed in the fat necrosis (Fig. 3b). Sclerosing fibrosis was arranged in an irregular manner (Fig. 3c). Spindle cells in the area of fibrosis were positive for  $\alpha$ -SMA (Fig. 3d) and negative for ALK (Fig. 3e). Elastic van Gieson (EVG) staining showed the findings of obliterative phlebitis (Fig. 3f). The area of fat necrosis showed infiltration by lymphocytes and plasma

cells (Fig. 3g). In the sclerosing fibrotic lesion, increased number of plasma cells were observed (Fig. 3g). IgG and IgG4 immunohistochemical staining showed focally increased numbers of IgG- and IgG4-positive plasma cells (Fig. 3h and i, respectively). When 5 different high-power fields (hpf) were counted, the average number of IgG4-positive cells was 81 (range, 53-104), whereas the IgG4/IgG-positive cell ratio was 80.4% (range, 60.9-92.4%). Lymphocytes without atypia that formed lymphoid follicles were observed (Fig. 3j), and immunohistochemical staining for CD21 (Fig. 3k) and CD23 (Fig. 3l) was positive only in the follicle center. Given the above results, the histological diagnosis of the mass lesion was SM. However, there were insufficient typical findings to diagnose the lesion as IgG4-related SM clinically or histologically. In the differential di-

**Table. Summary of Past Reports with IgG4-related SM or Mimicking of IgG4-related SM.**

case (Reference)	Age (y)	Sex	Serum IgG4 (mg/dL)	Sample	Immunohistochemistry		Fibrosis	Obliterative phlebitis	IgG4-related disease at other sites
					IgG4 (/hpf)	IgG4/ IgG (%)			
1 [1]	48	female	NA	biopsy	12	20	yes	yes	none
2 [1]	52	male	NA	resection	13	NA	yes	yes	none
3 [1]	63	female	NA	biopsy	16	NA	yes	yes	none
4 [1]	65	male	NA	biopsy	16	NA	yes	yes	none
5 [1]	74	male	NA	biopsy	>100	>33	yes	no	none
6 [1]	46	male	NA	resection	>100	>33	yes	yes	none
7 [2]	42	male	119	resection	60	40	yes	NA	none
8 [3]	82	female	171	resection	130	75.9	yes	yes	none
9 [4]	53	male	127	resection	74.8	64	yes*	yes	none
10 [5]	64	male	81	biopsy	38	80	yes*	yes	retroperitoneal fibrosis
11 [6]	76	male	63.5	biopsy	56	33	yes*	yes	none
12 [6]	77	male	43.2	biopsy	46	28	yes*	yes	none
13 [6]	54	male	105	resection	85	35	yes*	yes	none
14 [7]	70	female	213	resection	NA	>90	yes*	yes	none
15 [8]	54	male	“normal”	biopsy	“rich”	NA	yes	yes	none
16 [9]	62	male	179	biopsy	NA	NA	NA	NA	none
17 [10]	56	female	134	resection	“increase”	NA	yes	no	none
18 [11]	7	female	149	biopsy	“predominant”	NA	yes	NA	none
19 [12]	56	male	416	biopsy	“dense infiltration”	NA	yes*	NA	none
20 [13]	60	male	47	resection	>40	NA	yes*	yes	none
Present case	72	male	50.8	resection	81	80.4	yes	yes	none

\*Storiform fibrosis.

hpf: high-power field, NA: not available

agnosis, inflammatory myofibroblastic tumor and follicular dendritic sarcoma were considered, but they were excluded based on the results of immunohistochemistry (ALK-negative and both CD21- and CD23-negative, respectively).

Previous medical records and specimens were then re-examined considering the possibility that IgG4-RD may have existed metachronously in multiple organs. The contrast-enhanced CT image of the left adrenal small cell carcinoma at 66 years old showed a round, low-density area with a surrounding oval iso-density area (Fig. 4a). Histologically, the round area matched the location of the small cell carcinoma, and the surrounding oval area was sclerosing fibrosis (Fig. 4b, c). In the sclerosing fibrotic lesion, the findings of irregularly arranged fibrosis, obliterative phlebitis, and increased number of plasma cells were observed (Fig. 4d-f). IgG and IgG4 immunohistochemical staining showed focally increased numbers of IgG- and IgG4-positive plasma cells (Fig. 4g, h). When 5 different hpf were examined, the average number of IgG4-positive cells was 78.6 (range, 57-113), and the IgG4/IgG-positive cell ratio was 48.4% (range, 36-60%). The lesion was therefore diagnosed as panniculitis. However, there were insufficient typical findings to diagnose the lesion as retroperitoneal fibrosis clinically or histologically.

The patient has been free from recurrence for 20 months since the surgery for SM.

## Discussion

The present case was diagnosed as SM, and panniculitis had emerged six years before the operation for SM. SM is a rare idiopathic disease characterized by chronic inflammation and fibrosis in the adipose tissue of the bowel mesentery. Recently, some case reports and case series have shown the relationship between SM and IgG4-RD (6-18). IgG4-RD has been newly recognized as a systemic disease and a protean condition that mimics many malignant, infectious, and inflammatory disorders (19).

The diagnosis of IgG4-RD relies on the combined presence of the characteristic histopathological appearance and increased numbers of IgG4-positive plasma cells. The critical histopathological features are a dense lymphoplasmacytic infiltrate, a storiform pattern of fibrosis, and obliterative phlebitis (20). A consensus has been reached concerning 2 diagnostic criteria for IgG4-RD: 1) serum IgG4 concentration >135 mg/dL, and 2) >40% of IgG-positive plasma cells being IgG4-positive and >10 cells/hpf on a biopsy sample (21). According to the resected specimens of IgG4-RD, IgG4-positive plasma cells are usually present at numbers exceeding 50/hpf and typically exceeding 100/hpf (22).

Some case reports of IgG4-related SM or possible IgG4-RD, including the present case, are summarized in Table (6-18). These IgG4-related SM cases occurred predominantly in older men, as is observed with IgG4-RD (23). The



mean age of 21 patients with IgG-related SM was 58.4 (range, 7-82) years, and the sex ratio was 2.5:1 (men: women). Furthermore, most SM cases have been histologically similar to IgG4-RD, since findings of increased numbers of IgG4-positive plasma cells, lymphoplasmacytic infiltrate, storiform fibrosis, and obliterative phlebitis are observed. However, as Avincsal et al. reported, conclusive cases with the four characteristic features (high serum IgG4 level, tissue IgG4 elevation, multi-organ involvement, and steroid responsiveness) have never been reported (11). Although the present patient had an SM lesion that was histologically similar to IgG4-RD, irregularly arranged fibrosis was not typical storiform pattern fibrosis and increased IgG4 positive cells were located focally. And clinically, the patient's serum IgG4 levels were within the normal range. Therefore, we were not able to diagnose the SM lesion as IgG4-RD.

It is known that many patients with IgG4-RD have lesions in several organs, either synchronously or metachronously (21). In the present case, panniculitis around the small adenocarcinoma in the left adrenal gland was found six years before the operation for SM. The panniculitis was histologically similar to retroperitoneal fibrosis because not only abundant IgG4-positive cells but also findings of irregularly arranged fibrosis and obliterative phlebitis were observed. However, IgG4-positive cells have also been observed in carcinoma-associated inflammatory response lesions (24). Furthermore, in the present case, the irregularly arranged fibrosis differed from the typical finding of a storiform pattern, as in IgG4-RD, and IgG4-positive cells were increased focally. Therefore, we were unable to diagnose the panniculitis as retroperitoneal fibrosis.

According to previous reports, only one case has shown multi-organ involvement. In that case, retroperitoneal fibrosis appeared five months after the operation for IgG4-related SM (10). Another two idiopathic SM cases with retroperitoneal fibrosis have also been reported (25, 26). These case reports suggest a potential association between SM and IgG4-RD. Of note, in our present case, not only the SM lesion but also the metachronous panniculitis were histologically similar to IgG4-RD.

In conclusion, we encountered a case of SM mimicking IgG4-RD. A comprehensive examination, including a review of the patient's clinical and histological information, may be important for the accurate diagnosis of SM.

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

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