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CASE REPORT

A case of IgG4-related mesenteritis

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Abstract IgG4-related disease is a newly recognized fibroinflammatory condition characterized by tumefaction consisting of fibrosis with dense infiltration of IgG4-positive plasma cells; affecting various organs. A case of IgG4-related sclerosing mesenteritis is reported. A 64-year-old man was admitted to our hospital with a suspected tumor of the small intestine. Abdominal computed tomography demonstrated a 6-cm soft tissue mass in the right lower mesentery compressing the jejunum, which also showed accumulation of fluorodeoxyglucose uptake on fluorine-18 fluorodeoxyglucose positron emission tomography. With a preoperative diagnosis of suspected malignant lymphoma with lymphadenopathy in the mesentery, partial small bowel resection was performed. Macroscopically, a hard mass, including several swollen lymph nodes, was detected in the mesentery. Microscopically, marked fibrosis showing partially storiform pattern, obstructive phlebitis, follicular hyperplasia, and abundant infiltration of IgG4-positive plasma cells were detected. IgG4-related mesenteritis was diagnosed histopathologically, but the serum IgG4 level was 81 mg/dl postoperatively. Five months after the surgery, an 11-cm soft tissue mass involving the left ureter appeared. Histological examination of a biopsy specimen from the retroperitoneal mass showed fibrosis with inflammatory infiltration. Although IgG4-related retroperitoneal fibrosis could not be confirmed histologically, the tumor responded well to steroid therapy.

Keywords IgG4 · Sclerosing mesenteritis · Retroperitoneal fibrosis

Introduction

Sclerosing mesenteritis is a chronic, nonspecific, inflammatory and fibrotic process involving the adipose tissue of the small bowel mesentery. Sclerosing mesenteritis is usually of unknown etiology and can be mistaken for malignant lymphoma, fibromatosis, inflammatory myofibroblastic tumor, and panniculitis [1].

IgG4-related disease is a newly recognized fibroinflammatory condition characterized by tumefaction consisting of fibrosis with dense infiltration of IgG4-positive plasma cells and steroid responsiveness [2]. A resected case of histologically confirmed IgG4-related sclerosing mesenteritis, which was later associated with retroperitoneal fibrosis that was successfully treated with steroids, is reported.

Case report

A 64-year-old man visited his regular doctor complaining of abdominal pain in September 2013. He was admitted to our hospital with a suspected tumor of the small intestine on abdominal computed tomography (CT) in February 2014. He had a personal history of type 2 diabetes mellitus and an unremarkable family history. There were no abnormal findings on physical examination at admission, and he had

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Table 1 Laboratory findings

WBC	6900/μl	TP	7.5 g/dl	CRP	2.35 mg/dl
RBC	423 × 10^4/μl	Alb	4.1 g/dl	IgG	1192 mg/dl
Hb	11.8 g/dl	BUN	17 mg/dl	IgG4	81.3 mg/dl
Plt	32.9 × 10^4/μl	Cr	0.8 mg/dl	IgE	63.1 IU/ml
PT	11.5 s	Na	143 mEq/l	ANA	<40
APTT	28.0 s	K	4.3 mEq/l	RF	<5 IU/ml
		T-Bil	0.3 mg/dl	CEA	0.9 ng/ml
		AST	19 U/l	CA19-9	11.9 U/ml
		ALT	22 U/l	sIL-2R	603 U/ml
		LDH	231 U/l		
		ALP	350 U/l		
		Amy	84 U/l		
		Glucose	108 mg/dl		
		HbA1c	7.5 %		

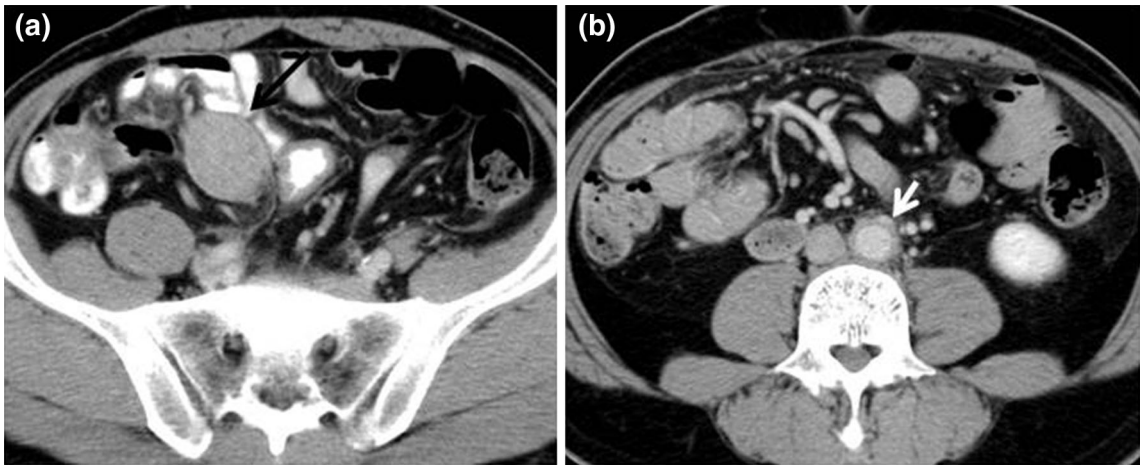

Fig. 1 Abdominal CT shows a 6-cm soft tissue mass (*long arrow*) in the right lower mesentery (**a**), and multiple enlarged lymph nodes and mild soft tissue mass encasing the aorta (*short arrow*) (**b**)

no past history of symptoms suggestive of IgG4-related disease or allergic diseases. On laboratory examination, mild anemia (Hb, 11.8 g/dl) and increases of HbA1c (7.5 %), CRP (2.35 mg/dl), and soluble IL-2 receptor (609 U/ml) were detected. Other serological parameters and tumor markers were within normal limits (Table 1).

Abdominal CT showed a 6-cm soft tissue mass enhanced at late phase in the right lower mesentery that compressed the jejunum (Fig. 1a). A mild soft tissue mass encasing the aorta, and multiple enlarged lymph nodes, up to 1-cm diameter, were also observed in the abdominal cavity (Fig. 1b). There were no abnormal findings in the pancreas, biliary tree, or salivary glands. Fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET)/CT showed significant 4-cm accumulation of FDG uptake in the mesentery [early maximum standardized uptake value (SUV) max: 4.7 and delayed SUV max: 6.3] (Fig. 2). Significant FDG uptake was not seen in any other lesions. Gastroduodenoscopy and colonoscopy showed no particular findings. Percutaneous biopsy or endoscopic ultrasound guided fine needle aspiration biopsy was impossible due to surrounding intestine. With a

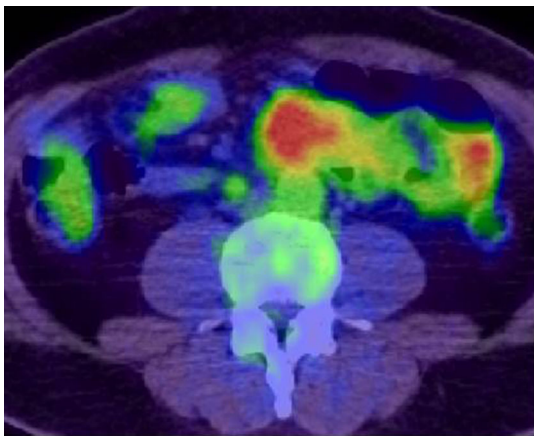

Fig. 2 FDG-PET/CT shows significant 4-cm accumulation of FDG uptake in the mesentery

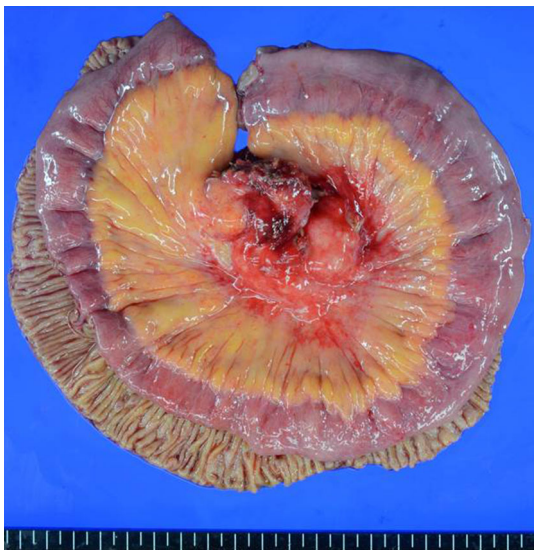

Fig. 3 Macroscopically, the resected specimen can be seen as a hard mass with several swollen lymph nodes in the mesentery

preoperative diagnosis of suspected malignant lymphoma with lymphadenopathy in the mesentery, partial small bowel resection was performed. Macroscopically, a hard mass, including several swollen lymph nodes, was detected in the mesentery (Fig. 3). On histopathological examination, marked fibrosis showing partially storiform pattern (Fig. 4a), obstructive phlebitis (Fig. 4b), follicular hyperplasia, and abundant infiltration of lymphocytes and IgG4-positive plasma cells [IgG4-positive plasma cells: 38/high power field (hpf); and IgG4-positive plasma cells/IgG-positive plasma cells: 80 %] without monoclonality (Fig. 4c) were seen. IgG4-related mesenteritis was diagnosed histopathologically. Postoperative serum IgG and IgG4 levels were 1192 and 81 mg/dl, respectively. Antinuclear antigen and rheumatoid factor were negative.

On follow-up CT (Fig. 5a) and MRI (Fig. 5b, c) performed 5 months after the surgery, an 11-cm soft tissue mass involving the left ureter in the left pelvis and left hydronephrosis were detected, although he had no

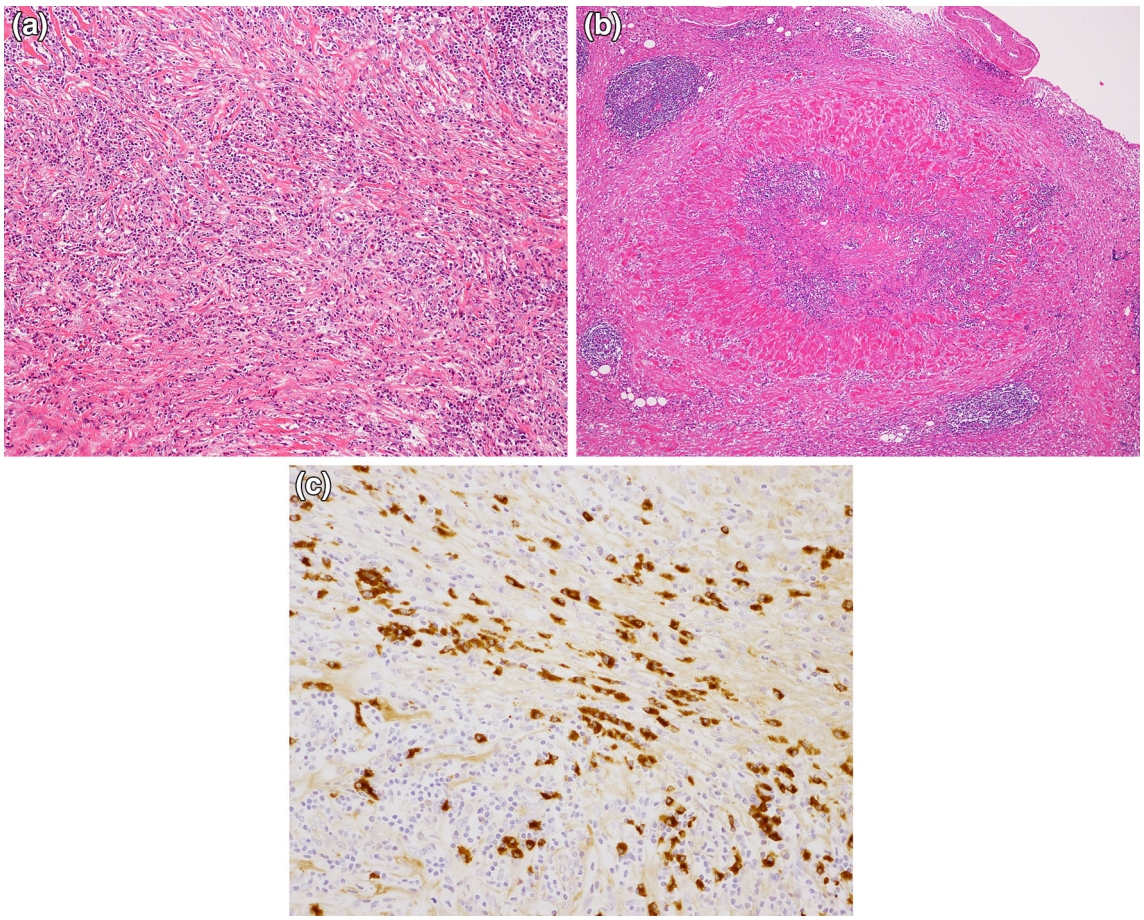

Fig. 4 Histological features showing fibrosis with storiform pattern (**a**), obstructive phlebitis (**b**), and abundant infiltration of IgG4-positive plasma cells (**c**)

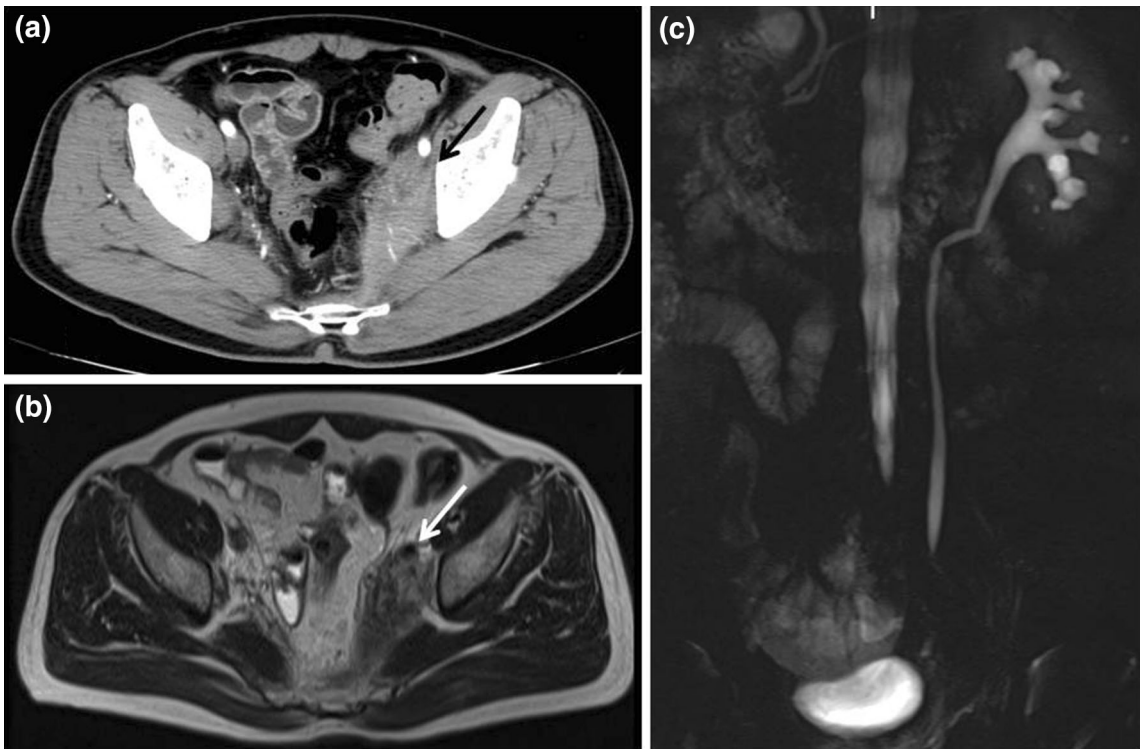

Fig. 5 Follow-up CT (**a**) and MRI (**b**, **c**) performed 5 months after surgery show an 11-cm soft tissue mass (*arrows*) involving the left ureter in the left pelvis and left hydronephrosis

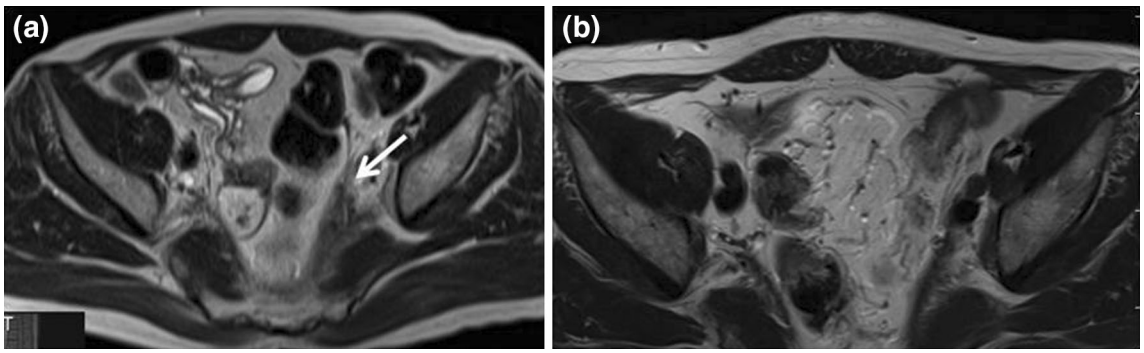

Fig. 6 MRI performed 1 month after starting steroids shows reduction in size of the retroperitoneal mass (*arrow*) (**a**). The mass almost disappeared on MRI performed 10 months later (**b**)

symptom. CT-guided biopsy of the retroperitoneal tumor was performed, and fibrosis with inflammatory infiltration was seen histologically. As the number of IgG4-positive plasma cells was 8/hpf, and the IgG4/IgG ratio was 30 %, the lesion was not diagnosed histopathologically as IgG4-related retroperitoneal fibrosis. The serum IgG and IgG4 level were 1517 and 88.2 mg/dl, respectively. Steroid therapy was started at a dose of 30 mg/day of prednisolone to treat the retroperitoneal fibrosis. One month later, the retroperitoneal mass was reduced on MRI (Fig. 6a). The dose of steroid was gradually tapered, and the patient underwent maintenance therapy with a dose of 5 mg/day of prednisolone to prevent recurrence of IgG4-related disease. The mass almost disappeared on MRI performed 10 months later (Fig. 6b).

Discussion

Sclerosing mesenteritis is a rare disease characterized by chronic nonspecific mesenteric inflammation of unknown origin [1]. IgG4-related disease is a novel clinical entity characterized by tumefaction with infiltration of IgG4-positive plasma cells and often, but not always, elevated serum IgG4 concentrations [2]. IgG4-related disease is a systemic disease that affects various organs of the body,

and mesentery may be a site of IgG4-related disease. The histological criteria of IgG4-related disease consist of histological features of dense lymphoplasmacytic infiltration, storiform fibrosis, obliterative phlebitis, and abundant infiltration of IgG4-positive plasma cells (IgG4 counts >10 cells/hpf and IgG4-positive cells/IgG-positive cells >40 %) of the targeted swollen organ or site [3, 4]. The diagnosis becomes more definitive with elevation of serum IgG4 concentrations, other organ involvement that is consistent with IgG4-related disease, and effective response to steroid therapy [3–5]. In the present case, the diagnosis of IgG4-related mesenteritis was histologically confirmed by the findings of storiform fibrosis, obliterative phlebitis, and abundant infiltration of lymphocytes and IgG4-positive plasma cells. Clinically, the serum IgG4 levels were not elevated, and retroperitoneal fibrosis appeared 5 months after the operation. The lesion could not be histologically confirmed from the biopsy specimen as an IgG4-related retroperitoneal fibrosis. However, the retroperitoneal fibrosis decreased after steroid therapy, and this might be part of the spectrum of IgG4-related disease.

IgG4-related sclerosing mesenteritis is not a definitely recognized clinicopathological entity of IgG4-related disease. To consider a previously unrecognized organ or site as being involved by IgG4-related disease, Deshpande et al. [3] recommended appropriate histological findings with one additional criterion (high serum IgG4 concentrations, other organ involvement and steroid responsiveness). According to their proposed terminology, this case is placed as histologically highly suggestive of IgG4-related disease.

A search of PubMed using "IgG4" and "mesenteritis" as key words resulted in five cases that seemed to be IgG4-related sclerosing mesenteritis [6–10]. These five cases and the present case are summarized in Table 2. The mean age of the patients was 49.0 (range 7–82) years, and the male-to-female ratio was 3:1. These findings are compatible with previous reports that IgG4-related disease is more common in elderly men. The initial symptom was abdominal pain in four patients, and the average size of the lesion was 7.1 cm. Elevation of serum CRP was observed in four of five patients. Serum IgG4 levels were elevated in only two of five patients, and the levels were not markedly elevated. On CT, a hypoattenuating mass with or without encasement of mesenteric vessels was observed in the mesentery. Preoperative diagnosis was difficult, and five cases underwent resection. Histologically, the presence of storiform fibrosis and obliterative phlebitis was mentioned in two and three cases, respectively. Abundant infiltration of IgG4-positive plasma cells (>10/hpf) was detected in all five patients, and an elevated ratio of IgG4-positive plasma cells/IgG-positive plasma cells (>40 %) was detected in four of six patients. Case 2, as diagnosed by biopsy, was successfully treated with steroids. Other organ involvement was not seen except in the present case.

Chen et al. reported marked (>30/hpf) and moderate (11–30/hpf) infiltration of IgG4-positive plasma cells in two and four of nine cases of sclerosing mesenteritis, respectively, but only one case fulfilled the histological criteria of IgG4-related sclerosing disease [6]. In a large case series of 92 patients with sclerosing mesenteritis, two had autoimmune pancreatitis, and IgG4-immunostaining was positive in four of the 12 other patients without autoimmune pancreatitis [11]. Since abundant infiltration of IgG4-positive plasma cells is detected in various lesions, including pericancerous lesions [12], additional findings such as obliterative phlebitis and storiform fibrosis are needed for the histological diagnosis of IgG4-related disease. However, it seems likely that a subset of patients with sclerosing mesenteritis have a disorder that falls along the spectrum of IgG4-related disease. Although preoperative diagnosis of IgG4-related sclerosing mesenteritis is quite difficult, histological examination of biopsy specimens may lead to correct diagnosis and steroid therapy.

Table 2 Summary of the clinicopathological findings of IgG4-related sclerosing mesenteritis

Case	Age (years)	Sex	Symptom	Sample	CRP	IgG4 (mg/dl)	Size (cm)	Fibrosis	Obliterative phlebitis	IgG4+ cells/ HPF	IgG4+/ IgG+ (%)	Steroid therapy
1 [6]	46	M	NA	Resection	NA	NA	7	+	NA	>100	<1/3	ND
2 [7]	7	F	Abdominal pain	Biopsy	236 mg/dl	149	NA	+	NA	NA	52	Effective
3 [8]	42	M	Incidental	Resection	Normal	119	4	+	NA	60	40	ND
4 [9]	53	M	Abdominal pain	Resection	4.5 mg/dl	127[a]	7	+[b]	+	74.8	64	ND
5 [10]	82	F	Abdominal pain	Resection	11.2 μg/dl	171[a]	11.7	+	+	130	75.9	ND
Present	64	M	Abdominal pain	Resection	2.35 mg/dl	81[a]	6	+[b]	+		80	ND

NA not available, *ND* not done, *HPF* high power field

[a] The data after resection

[b] Storiform fibrosis

In conclusion, a case of IgG4-related sclerosing mesenteritis was presented. It is important to keep in mind that IgG4-related disease could involve the mesentery and that suitable treatment is needed.

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Compliance with ethical standards

Conflict of Interest: Erika Mori, Terumi Kamisawa, Taku Tabata, Satomi Shibata, Kazuro Chiba, Sawako Kuruma, Go Kuwata, Tomoko Onishi, Takashi Fujiwara, Junko Fujiwara, Takeo Arakawa, Kumiko Momma, Koichi Koizumi, Hiroshi Matsumoto and Shinichiro Horiguchi declare that they have no conflict of interest.

Human 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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