[症例報告]Acase of overlap syndrome (rheumatoid arthritis and systemic lupus erythematosus) with ileal perforation in amyloidosis

A case of overlap syndrome (rheumatoid arthritis and systemic lupus erythematosus) with ileal perforation in amyloidosis

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ABSTRACT

A case of an ileal perforation in vasculitis and secondary amyloidosis due to rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) (overlap syndrome) in a 43-year-old female is reported. On February 14, 1994, the patient with associated symptoms of oliguria, fever, abdominal pain and vomiting, was admitted to the Okinawa Daiichi Hospital for hemodialysis. She had a history of RA (rheumatic factor was positive, ulnar deviation, morning stiffness, multiple and symmetrical arthritis) in 1977 and also SLE in 1986. Her disease was diagnosed as overlap syndrome, and she received 8 year continuous treatment with steroid. On the 11th day post admission, she developed acute peritonitis with free air on abdominal X-ray. An emergency laparotomy revealed a perforation of the ileum on the anti-mesenteric side 20 cm proximal to the ileocecal valve and multiple ileal ulcers over the entire ileal length (approximately 130 cm long). The affected ileum, 130 cm in length, was resected and two current type ileostomies were made. Pathologically, amyloid deposition was found mainly in the small to medium-sized vessel walls in the submucosal layers. Occlusive vascular amyloid deposition and non-occlusive perivasculitis were more evident in the severely affected portion. The patient developed intestinal perforation after surgery. She expired with clinical manifestations of disseminated intravascular coagulopathy 49 days after surgery. The pathological findings of the ileum suggested that the vasculitis had been caused by overlap syndrome while occlusion due to amyloid deposition had led to the perforation of the ileum. An autopsy was not performed. We therefore present evidence of an ileal perforation as a result of overlap syndrome and subsequent amyloidosis. *Ryukyu Med. J., 16(3)135~138, 1996*

Key words: ileal perforation, secondary amyloidosis, overlap syndrome

INTRODUCTION

Amyloid is classified on the basis of the predominant fibril type and the underlying process[1]. In primary amyloidosis no underlying disease is recognized. Secondary amyloidosis is associated with chronic infections and inflammation, as well as with several types of neoplasms[1~3]. Gastrointestinal involvement is frequent in secondary amyloidosis, accounting for about 50%[4]. Gastrointestinal amyloidosis may cause malabsorption, ischemia, hemorrhage[5~6] and perforation[7~14]. We recently encountered a case of small intestine perforation and multiple ileal ulcers in secondary amyloidosis due to RA and SLE (overlap syndrome)[15], in which the degree of intestinal vascular amyloid deposition was remarkable. To our knowledge, no case of overlap syndrome with intestinal perforation has been reported. We present a report of an ileal perforation which occurred as a direct result of overlap syndrome (vasculitis) and subsequent amyloidosis.

CASE REPORT

On February 14, 1994, a 43-year-old female with episode of oliguria, vomiting, fever and abdominal pain was referred to the Okinawa Daiichi Hospital to undergo hemodialysis. Her past history revealed that she had a 14 year duration of RA, an 8 year duration of SLE, and had also been on steroid treatment continuously for 8 years. Her disease was diagnosed as overlap syndrome.

On admission, she appeared critically ill. Physical examination revealed, malnourishment with general edema and moderate distress from abdominal pain and fever. Her lungs were moist vesicular on auscultation. The abdomen was distended, mildly tender but with no bowel sounds.

Table 1 Laboratory findings on admission

CBC		BUN	28.4 mg/dl
WBC	6800/mm³	CRE	2.1 mg/dl
RBC	322×10⁴ / mm³	Na	135 mEq/ℓ
Hb	7.5 g/dl	K	4.0 mEq/ℓ
Ht	22.7 %	Cl	101 mEq/ℓ
Plt	17.1×10⁴ / mm³	Ca	3.7 mEq/ℓ
CRP	10.4 mg/dl	Coagulation	
Chemistory		PT	13.6 S
TP	6.0 g/dl	APTT	40.7 S
ALB	2.0 g/dl	Fib	168 mg/dl
T-Bil	0.7 mg/dl	Urinalysis	
D-Bil	0.5 mg/dl	pH	5.0
TTT	11.3 U	occult blood	(±)
ZTT	32.5 U	protein	(+)
GOT	28 U/ℓ	glucose	(±)
GPT	11 U/ℓ	ABG	
ALP	584 U/ℓ	pH	7.408
LDH	450 U/ℓ	PCO_2	33.4 mmHg
ChE	985 U/ℓ	HCO_3	21.0 mEq/ℓ
γ-GPT	35 U/ℓ	PO_2	88.5 mmHg
LAP	67 U/ℓ	O_2 SAT	96.9%
T-Cho	63 mg/dl	BE	-2.1
Auto-immune Antibody			
ASO	×20	Anti-nuculer Ab	×2560
Anti-DNA Ab	5.1IU/ml		(homogeneous)
Anti-Sm Ab	4.0IU/ml		

Laboratory data showed that hemoglobin level was 7.5 g/dl, albumin 2.0 g/dl, and C-reactive protein 10.4 mg/dl. The liver and renal functions were high above normal limits. A urinalysis showed mild positive evidence (Table 1). Diagnosis was made as an acute onset of renal failure due to SLE (lupus nephritis).

Consequently hemodialysis was started for renal insufficiency and gastrointestinal decompression through a naso-gastric tube for bowel obstruction. However, she remained ill and febrile. The bowel obstruction was considered to be dynamic on the gastrointestinal series, but the cause of renal insufficiency remained obscure. On the 11th day post admission, she developed severe abdominal pain and a general deterioration of symptoms. An abdominal X-ray revealed a dilated small bowel with air-fluid-levels (Fig.1, top). The patient underwent an emergency laparotomy, and the cause of peritonitis was found to be a perforation of the ileum on the anti-mesenteric side 20 cm from the ileocecal valve. In addition, an approximately 130 cm length of the ileum was found to have multiple ulcers scattered all over it. Consequently, the affected ileum, measuring 130 cm in length, was resected and a double current ileostomy was constructed.

Immediately after surgery, the patient was placed on hemodialysis for oliguria. Because of the absence of any bowel movements, a gastrografin study through the pro-

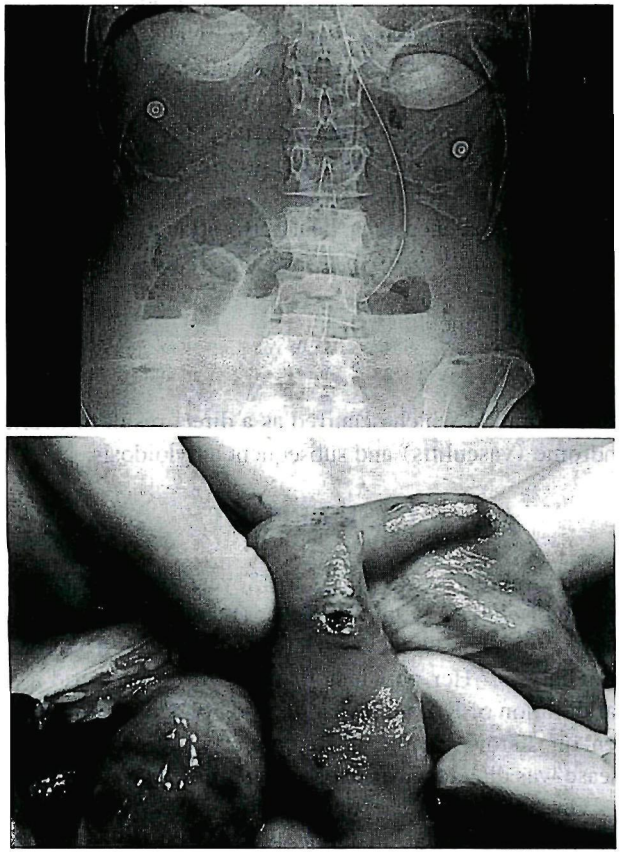

Fig.1 A radiophotograph of the abdomen showing a dilated small bowel with air-fluid levels (top), and a macrophotograph of the ileum at surgery showing a perforation (bottom).

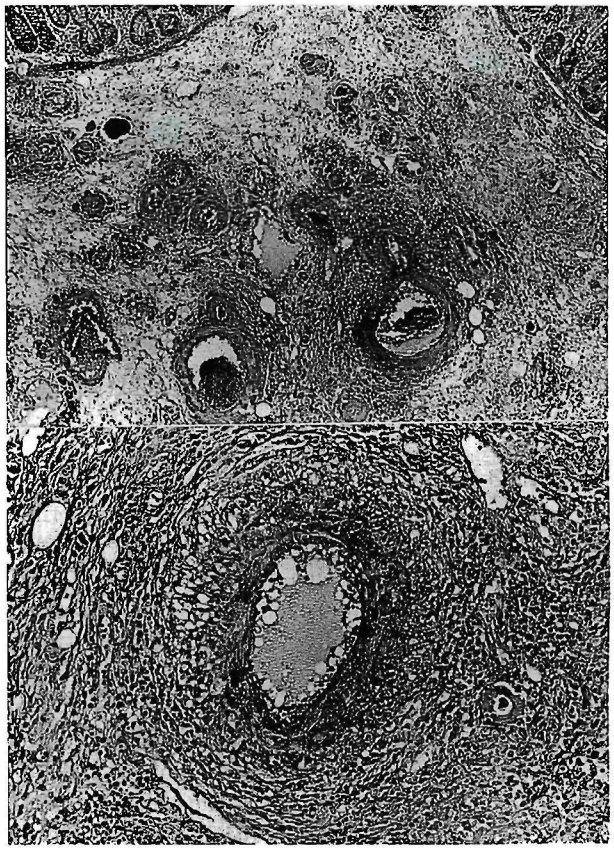

Fig.2 Microphotographs of the resected ileum revealing a thickening of the vascular walls and perivasculitis in the submucosal layer (top; HE, ×10) (bottom; HE, ×50).

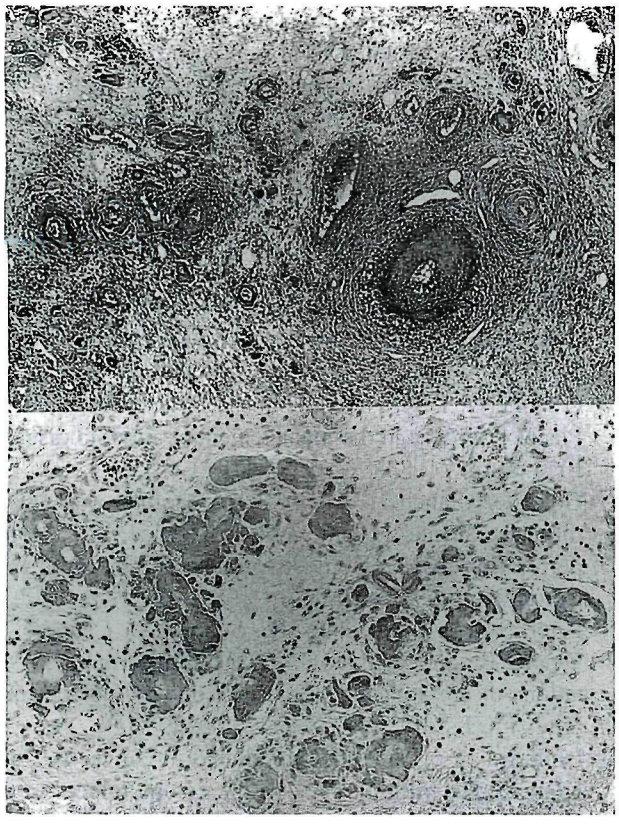

Fig.3 Microphotographs of the resected ileum showing vascular wall thickening with amorphous material (top; E, ×20) and material positive for Congo red staining (bottom; Congo red, ×20).

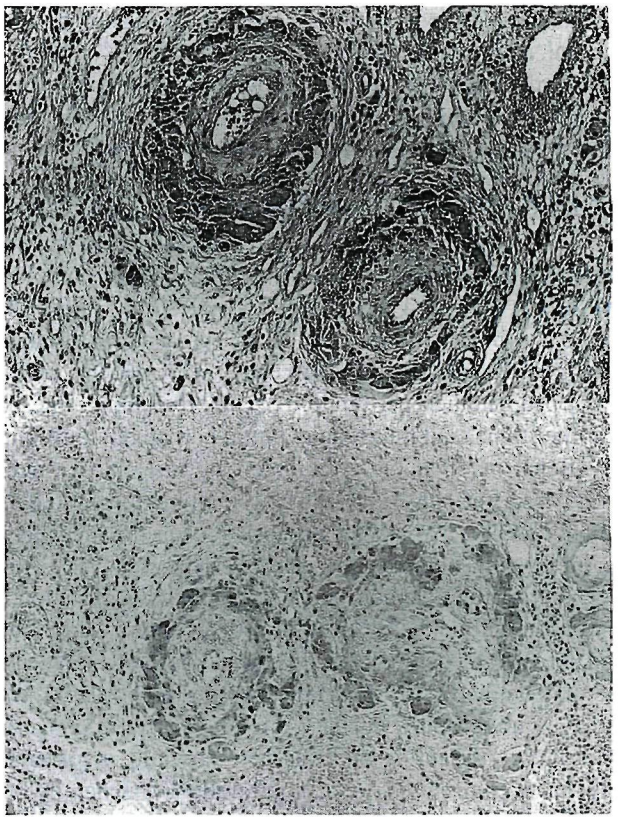

Fig.4 Microphotographs of the ileum showing wall thickening and an occlusive lumen with amyloid deposition in the medium-sized vessels (top; HE, ×50) (bottom; Congo red, ×50).

ximal ostomy showed two perforations of the intestine 7 cm proximal to the ostomy. Her general condition gradually deteriorated and she finally expired with clinical manifestations of DIC (DIC score 9 point) 49 days after surgery. An autopsy was not performed.

Pathological findings

The resected ileum showed a 5 mm-perforation on the anti-mesenteric side and multiple small ulcers measuring 2-3 mm in size scattered over its entire length. The small to medium-sized vascular walls in the submucosal layers generally showed remarkable thickening and occasional occlusion with amorphous homogeneous eosinophilic material. The eosinophilic material was positive for Congo red staining (Fig.2, 3, 4). Some vessels also showed perivasculitis which was particularly noted at the site of ulceration. The submucosal layer was often fibrotic with lymphocytic and neutrophilic infiltrate adjacent to the ulcer. Amyloid deposition was confined to only the vascular wall and was not evident in any other tissue. The pathological findings of the ileum suggested that the vasculitis caused by the overlap syndrome and occlusion due to amyloid deposition had thus led to the perforation of the ileum.

DISCUSSION

The fibrils in primary amyloidosis are made up of amyloid light chain type proteins (AL protein) which are thought to be derived from immunoglobulin light chains and also originate from plasma cells. On the other hand, in secondary amyloidosis the fibrils consist of a protein unrelated to immunoglobulins which is known as *amyloid A* protein (AA type). This protein is thought to be a cleavage product of the serum amyloid A protein. The levels of this protein rise with age and also increase in such chronic inflammatory disorders as tuberculosis and rheumatoid arthritis[1~3].

The pathogenesis of amyloid deposition is unclear. Amyloid may cause damage in the gastrointestinal tract[4]. Localized amyloidosis is essentially a benign condition, and recurrence is rarely observed after a surgical excision. Systemic amyloidosis, however, is almost invariably fatal and treatment is mainly supportive ; death usually follows cardiac or renal failure[1,16]. In our case small bowel amyloidosis was thought to be associated with generalized secondary amyloidosis because of a diffuse amyloid deposition of the resected small intestine over its entire length.

The organic infiltration by amyloid substances is generally localized in the wall of the vessels in the gastrointestinal tract[4]. The clinical manifestations of gastrointestinal amyloidosis are directly related to the location and extent of amyloid deposition, and range from asymptomatic to death[5,6]. Vascular amyloid deposits may cause intestinal ischemia which may thus contribute to the

development of perforation. An intestinal perforation is unusual, and in the literature, only a few cases[7~14] have been described. Such a perforation generally occurs in the small bowel. In our case, it was mandatory to perform emergency surgery for acute peritonitis secondary to the perforation of the intestine. Surgical intervention should be done with extreme caution since hemorrhagic diathesis can occur. The resection margins should be well cleared of any amyloid deposits or anastomotic dehiscence may follow poor local healing[7]. We opted to construct an ileostomy rather than perform primary anastomosis since primary anastomosis may lead to anastomotic dehiscence. Our patient, in fact, developed another perforation of the remaining intestine near the stoma, and thus required total parenteral nutrition.

Renal involvement is common in amyloidosis and is also a frequent cause of death, accounting for 43-65% of patients with secondary amyloidosis[16]. On the other hand, treatment with hemodialysis improves the survival. However, our patient demonstrated a gradual deterioration of general condition because of intestinal complications and died in spite of hemodialysis therapy. To our knowledge, this may be the first case of intestinal perforation associated with vasculitis and secondary amyloidosis due to overlap syndrome. Vasculitis and vascular amyloid involvement may have contributed to the perforation. Generally, the available treatment of systemic forms remains unsatisfactory. In secondary amyloidosis, treatment of the primary disease is important[3]. Although considerable progress has recently been made in understanding the pathogenesis of amyloidosis, medical treatment remains unsatisfactory. Surgery plays an important role in the treatment of this condition since the disease is systemic. When surgical complications arise, operative intervention should be considered and if successfully the results may be rewarding despite the limited and uncertain long term prognosis.

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