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Case Report

A Case of Polyarteritis Nodosa Diagnosed at Cholecystectomy

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ABSTRACT

A 63-year-old woman was admitted with pyrexia and right upper quadrant pain. Although cholecystitis had previously been diagnosed, the cause was unknown, and symptoms persisted and were accompanied by anemia and leukocytosis. To relieve the symptoms and to correct the anemia and leukocytosis attributed to chronic cholecystitis, laparoscopic cholecystectomy was performed. Histopathological examination revealed infiltration into the muscular layer of the gallbladder by eosinophils, lymphocytes, and plasma cells in association with necrotizing vasculitis, a feature characteristic of polyarteritis nodosa. Polyarteritis nodosa was localized to the gallbladder ; hence, the cholecystitis appeared to represent the primary presentation of polyarteritis nodosa, rather than a complication of systemic vascular disease. Polyarteritis nodosa was diagnosed at cholecystectomy at an early stage, with the resulting early treatment yielding a favorable clinical outcome. (Jikeikai Med J 2005 ; 52 : 87-91)

Key words : cholecystitis, polyarteritis nodosa, necrotizing angitis

INTRODUCTION

Polyarteritis nodosa is a systemic collagen disease involving the gallbladder in 10% of 40% of cases at autopsy[1,2], with acalculous cholecystitis observed in 2% to 9% of cases[3-5]. Although we have frequently diagnosed polyarteritis nodosa when evaluating cases of cholecystitis of unknown origin[1], only a single case in which symptoms of mononeuritis multiplex appeared after surgery has been reported[2]. Under the classification system of Chen[1], gallbladder vasculitis most frequently presents as a manifestation of systemic polyarteritis nodosa and present less frequently in such diseases as systemic lupus erythematosus, Wegner's granuloma, and other collagen-associated diseases. In addition, isolated gallbladder vasculitis can occur with localized polyarteritis nodosa. In this latter case, although the cause of the pyrexia and inflammation in localized cholecystitis is unknown, surgical resection can be performed for both treatment and diagnosis.

CASE REPORT

A 63-year-old woman with a history of repeated episodes of abdominal pain and pyrexia during the previous several months was admitted to our hospital's department of surgery for a detailed evaluation. Physical examination revealed a height of 155 cm, a body weight of 43 kg, a blood pressure of 122/60 mm Hg, low-grade pyrexia (37.5°C), and pale palpebral conjunctivae. Physical examination of the chest, abdomen, nervous system, and skin yielded no abnormal findings. Results of laboratory studies were

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Table 1. Laboratory Data on admission

Hematology		Coagulation		Blood Chemistry		Urinalysis	
WBC	10,700/mm³	PT	80%	TP	6.3 g/dl	pH	7.0
RBC	300×10⁴/mm³	APTT	36.5 sec	Alb	2.0 g/dl	SG	1.046
Hb	8.2 g/dl	TT	54%	T-Bil	0.3 mg/dl	Protein	(−)
Ht	24.8%	HPT	75%	D-Bil	0.0 mg/dl	Sugar	(−)
Plt	46.8×10⁴/mm³			AST	12 IU/1	Urobilinogen	(−)
Gran	78.2%			ALT	6 IU/1	Aceton	(−)
Lymph	9.6%			ALP	324 IU/1	Bilirubin	(−)
Eosino	6.8%			LDH	140 IU/1	Occult	(−)
Mono	5.0%			UN	9 mg/dl		
Baso	0.4%			Cr	0.4 mg/dl		
				Na	138 mmol/1		
				K	3.6 mmol/1		
				Cl	100 mmol/1		
				CRP	10.4 mg/dl		

WBC; White Blood Cell, RBC; Red Blood Cell, Hb; Hemoglobin, Ht; Hematocrit, Plt; Platelets, Gran; Granulocyte, Lymph; Lymphocyte Eosino; Eosinocyte, Mono; Monocyte, Baso; Basocyte, PT; Prothrombin time, APTT; Activated partial thromboplastin time, TT; thrombin time, HPT; Hepaplastin test, TP; Total protein, Alb; Albumin, T-Bil; Total Bilirubin, D-Bil; Direct Bilirubin, AST; Alanine Aminotransferase, ALT; Asparate Aminotransferase, ALP; Alkline Phosphatase, LDH; Lactate Dehydrogenase, UN; Urea nitrogen, Cr; Creatinin, Na; Natrium, K; Potassium, Cl; Chloride, CRP; C-reactive protein

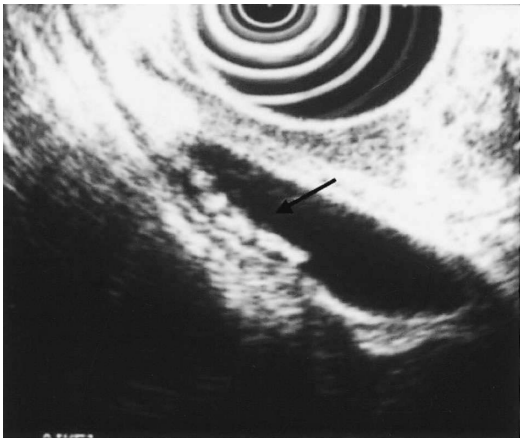

Fig. 1. Endoscopic ultrasonograpy. The gallbladder was enlarged, and debris was identified. A strongly echoic lesion consistent with a gallstone was identified. The arrowhead indicates debris.

normal except for a high titer of C-reactive protein (10.4 mg/dL), hypoalbuminemia (2.0 g/dL), and leukocytosis (10,700/mm³) with eosinophilia (6.8%; Table 1). Ultrasonography and abdominal computed tomography revealed a distended gallbladder (Fig. 1). Endoscopic retrograde cholangiopancreatography revealed isolated distension of the gallbladder (Fig. 2) with no evidence of common bile duct dilatation. Because of the possibility of an associated leukemia or other malignancy, gallium scintigraphy and bone marrow aspiration biopsy were performed. Gallium scintigraphy revealed diffuse accumulation throughout the skeletal system, but the results of bone marrow aspiration biopsy were inconclusive. Although the causes of the pyrexia and upper quadrant pain were unclear, we suspected these symptoms might be due to chronic inflammatory cholecystitis and, therefore, performed laparoscopic cholecystectomy. Histopathological examination of the resected specimen revealed the presence of vascular angitis (Fig. 3). After surgical resection, the abdominal pain resolved, but the pyrexia and associated elevated levels of inflammatory proteins in the serum remained.

Therefore, to establish a definitive diagnosis, the patient was transferred to the department of rheumatology for a more comprehensive evaluation. Serological analyses yielded the following values: perinuclear antineutrophilic cytoplasmic antibody (P-

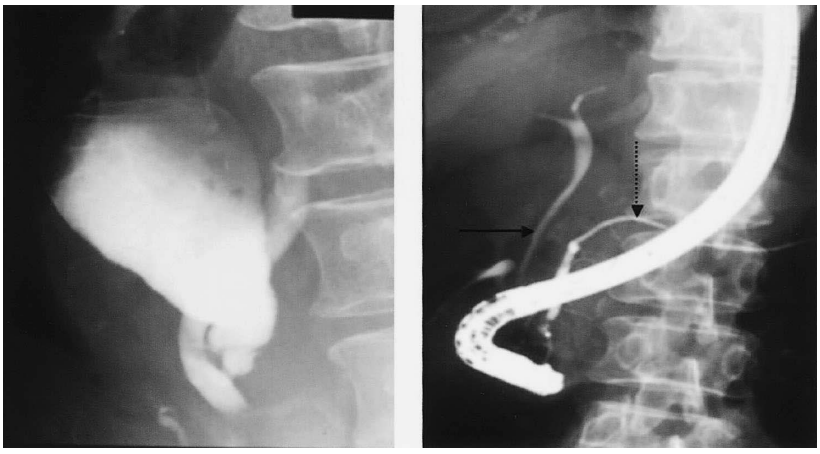

Fig. 2. Cholangiopancreatography revealed isolated distension of the gallbladder. No pancreatic or bile duct involvement was noted. The solid arrowhead indicates the cystic duct and the dotted arrowhead shows pancreatic duct.

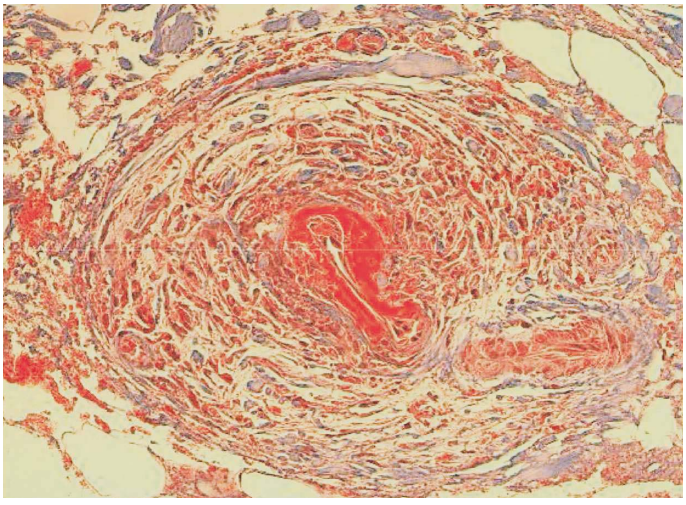

Fig. 3. Microscopic evaluation of the resected gallbladder revealed pronounced infiltration by lymphocytes and eosinophils. Necrotizing angitis and fibrin infiltration were also noted in blood vessels.

ANCA)/myeloperoxidase (MPO), 79 EU; IgE, 290 U/mL; IgG, 2,717 mg/dl; IgA, 391 mg/dl; IgM, 119 mg/dl; C_{1q}, 6.0 mg/dl; C_{3d-Ab}, <40 mg/dl; C_{3b}, >4.0 mg/dl; C_3, 90 mg/dl; C_4, 20.5 mg/dl; CH_{50}, 48.6; antinuclear antibody, 40; rheumatoid factor, 232.8 IU/ml; RAPA 1280; negative, RNP; negative, Sm; negative, SS-A; negative, AMA; negative, AMA-M_2Ab; <5.0, SMA; negative, cytoplasmic antineutrophilic cytoplasmic antibody, >10; and antiphospholipid antibody, negative.

During the evaluation, symptoms of lateral paresthesia developed in the upper extremities. Electromyography suggested mononeuritis multiplex. A kidney biopsy was also performed at this time but showed no evidence of vasculitis. Because of the presence of both a high-grade fever and mononeuritits multiplex, as well as histological findings of necrotizing angitis and serological findings of P-ANCA/MPO and high titers of C-reactive protein, IgG, and IgE, and eosinophilia, the diagnosis of classic polyarteritis nodosa was made. The pyrexia, mononeuritis multiplex, and histological evidence of fibrinoid necrotizing angitis of small muscular arteries were consistent with the diagnostic criteria for polyarteritis

nodosa established by the Ministry of Health, Labor and Welfare of Japan[6]. On the basis of this diagnosis, prednisolone (60 mg/day) and cyclophosphamide (50 mg/day) were administered, producing marked improvements in the patient's symptoms (pyrexia and serological inflammatory reaction) and general condition over the next several days. However, dysesthesia and weakness of the lower extremities were not alleviated by this treatment.

DISCUSSION

Cholecystitis has many possible causes, including adenocarcinoma of the gallbladder, diabetes mellitus, torsion of the gallbladder, unusual bacterial infections of the gallbladder, parasitic infestation of the gallbladder, sarcoidosis, cardiovascular disease, tuberculosis, syphilis, and actinomycosis[8]. All these causes had to be ruled out in our patient before rarer conditions, such as vasculitis, were considered. When no obvious organic findings are apparent and isolated cholecystitis is present, the differential diagnosis should include polyarteritis nodosa and other allergic vasculidities, such as polyarteritis nodosa, allergic granulomatous vasculitis, Wegner's granulomatosis, and giant cell arthritis[1,9,10].

Although the present patient had isolated gallbladder vasculitis, because cholecystitis was complicated by mononeuritis multiplex, we consider this case to represent "gallbladder vasculitis as a manifestation of polyarteritis nodosa." The symptom of mononeuritis multiplex was not present until after surgery. Also a single case with such a clinical course has been reported previously, by Livolsi et al.[2]. According to the report of Chen et al.[1], when cholecystitis occurs as a primary manifestation (i.e., isolated polyarteritis nodosa), the prognosis after surgery is generally favorable. In contrast, polyarteritis nodosa classified as "gallbladder vasculitis as a manifestation of polyarteritis nodosa" generally has a poor prognosis with many complications. However, the clinical outcome in the present case, which we have categorized as "gallbladder vasculitis as a manifestation," was extremely favorable, despite sensory disturbances, as previously reported[1].

Polyarteritis nodosa progresses rapidly and has a 6-month mortality rate of 50% if left untreated. Early and aggressive treatment is therefore required to improve the prognosis. With corticosteroid therapy alone, the 3-year survival rate ranges from 52% to 60%. However, with the advent of combination therapy with corticosteroids and immunosuppressants, remission can be induced and maintained, and the 5-year survival has been improved to 80%[7]. Our patient has survived for 6 years after the diagnosis of polyarteritis nodosa, during which time the disease has been in remission. This favorable outcome is attributable in part to early diagnosis and appropriate therapy. According to the classification of Chen et al.[1] this case does not represent "isolated gallbladder vasculitis" but rather a "gallbladder vasculitis as a manifestation." However, despite the poor prognosis associated with "gallbladder vasculitis as a manifestation" in the past[1], our patient had an extremely good clinical course after early surgical resection and drug treatment.

In conclusion, we report a patient with polyarteritis nodosa presenting as acute cholecystitis, which we consider to be "gallbladder vasculitis as a manifestation" of polyarteritis nodosa[1]. Because early treatment resulted in a favorable clinical outcome, atypical types of cholecystitis, such as acalculous cholecystitis, should suggest the possibility of systemic vasculitis, as in the present case.

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