Esophageal Involvement in Microscopic Polyangiitis: A Case Report and Review of Literature

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Abstract

A 72-year-old man with cough and sputum showed esophageal wall thickening and pneumonia in chest computed tomography (CT) scan. Following endoscopy, we diagnosed reflux esophagitis and subscribed proton pump inhibitor. The esophageal lesion, however, was intractable. We diagnosed microscopic polyangiitis (MPA) because of vasculitis symptoms, cytoplasmic antineutrophil cytoplasmic antibodies (cANCA) in blood and no granulomatous change in the esophagus. We adopted pulse therapy of cyclophosphamide and oral prednisolone; the symptoms and esophageal lesion were markedly improved. We concluded that the esophageal lesion was an aspect of MPA. To our knowledge, this is the first report of esophageal involvement in MPA.

Key words: microscopic polyangiitis, Wegener's granulomatosis, esophagitis, vasculitis, ANCA

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Introduction

Microscopic polyangiitis (MPA) is a vasculitis syndrome similar to Wegener's granulomatosis (WG). MPA, as with WG, shows arteritis in the medium to small arteries and microangiitis especially in the lung and kidney (1). There has been no case report of MPA complicated with an esophageal lesion, though four cases of WG accompanied by esophageal lesion have been reported. Here, we report a case of MPA complicated with an esophageal lesion, which was remarkably improved by prednisolone (PSL) and cyclophosphamide (CPA).

Case Report

A 72-year-old man consulted the open clinic of the Department of Respiratory Medicine of Kitano Hospital in April 2002 complaining of cough, choking on food, bloody sputum and 3 kg body weight loss in one month. He had a

history of Type 2 diabetes mellitus (Type 2 DM) from 66 years old, and rheumatoid arthritis (RA) from 57 years old. He had chronically taken glibenclamide for Type 2 DM from the age of 60 years old. But before admission in August 2003, he had not taken non-steroidal anti-inflammatory drugs (NSAIDs) or bisphosphonates. He was a smoker of 70 cigarettes a day from 17 through 65 years old. He showed elevated C-reactive protein (CRP; 6.05 mg/dl) and blood sugar (148 mg/dl), but his peripheral blood leucocyte count was within normal range at 8,000/ μ l. Chest CT showed infiltrative areas in both lungs and also revealed distal esophageal wall thickening (Fig. 1).

At first, we began antitussive and some antibiotics on the diagnosis of pneumonia: Amoxicillin/Clavulanic acid (AMPC/CVA)+Clarithromycin (CAM) from April 3 to April 9, Tosufloxacin (TFLX) from April 10 to April 30, CAM from May 1 to May 21 and CAM+TFLX from May 22 to June 12. In June 2002, original pneumonia improved on chest X ray after a long time. However, chest CT in July 2002 revealed a new pneumonia lesion in other site. We

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Figure 1. Chest computed tomography in April 2002 showing infiltrative areas and distal esophageal wall thickening (arrow). (A) lung field window setting. (B) mediastinal window setting.

Figure 2. Endoscopic examination in 2002. (A) Endoscopic examination in May 2002 revealed a longitudinal erosion from the middle esophagus to EC junction. (B) Endoscopic examination in June 2002 revealed a worsened longitudinal erosion, which easily bled due to air inflation.

clinically thought that pneumonia was repeatedly caused by meal aspiration refluxed from the stomach, though no chest

CT showed typical aspiration pneumonia until admission in August 2003.

During treatment for pneumonia, we performed endoscopic examination in order to rule out esophageal tumor. Endoscopic examination in May 2002 and June 2002 revealed a longitudinal erosion from the middle esophagus to esophagogastric junction, we clinically diagnosed the lesion as reflux esophagitis (Grade C) (Fig. 2). The pathological finding was severe erosion with inflammation cells consistent with reflux esophagitis. We therefore subscribed proton pump inhibitor (PPI). Dose, duration, and type of PPIs used in this case were lansoprazole 30 mg per day from May 24, 2002 to July 2, 2002, sodium rabeprazole 20 mg per day from July 3, 2002 to October 24, 2002, sodium rabeprazole 10 mg per day from November 27, 2002 to December 17, 2002, lansoprazole 30 mg per day from December 18, 2002 to September 23, 2003, sodium rabeprazole 10 mg per day from September 24, 2003. Though we repeated endoscopy in October 2002 and in January 2003, the esophageal lesion did not show remarkable change.

In April 2003, endoscopy showed irregular ulcer, protrusion and multiple non-dyed areas with Lugol's iodine solution. Histologically we did not find malignant tissue, but did inflammation cell infiltration. The protrusion was histologically diagnosed as granulation (Figs. 3, 4).

In August 2003, he was admitted to the hospital for the third time because of repeated fever for two days, bilateral wrist joint pain and swelling from May 2003 and five kilograms decrease of body weight in a year. He had not taken drugs for joint pain and swelling before the third admission. He was suspected of repeated pneumonia and recurrence of RA. Laboratory data on admission is shown in Table 1. He also showed symptoms of urine protein, occult blood with red blood cell columns, and positive cytoplasmic antineutrophil cytoplasmic antibody (cANCA).

The head CT showed a tumor in the right maxillary sinus (Fig. 5). Though we performed biopsy twice from the maxillary sinus in September 2003 and October 2003, the pathological findings were not consistent with vasculitis or granu-

Figure 3. Esophagus before treatment. (A) The endoscope demonstrates erosion, ulcer and protrusion in the middle-distal esophagus. (B) The lesion shows multiple non-dyed areas by Lugol's iodine solution.

Figure 4. The histological specimen from the esophagus before treatment demonstrates aggregated inflammation cells. HE stain, (A) $\times 100$, (B) $\times 400$

loma. Based on these signs and symptoms, we diagnosed him as suffering from microscopic polyangiitis (MPA).

To treat him, we used 5 g of immunoglobulin intravenously for three days. After informed consent, we started

Figure 5. Head CT shows a mass in the right maxillary sinus (arrow), ethmoid bone transformation and mucus membrane thickening in the nasal cavity.

plasma exchange, and gave him 700 mg of cyclophosphamide (CPA) intravenously. His malaise, joint pain and CRP improved markedly. We added 10 mg of oral Prednisolone (PSL) per day, and adopted CPA of 1000-1200 mg per body once a month (Fig. 6). We also used 2 to 3 g of trimethoprim-sulfamethoxazole (ST) per day. In February 2004, five months after the beginning of medication (PSL, CPA and ST), fever, joint pain, urine findings, cANCA and pneumonia improved remarkably. There was no erosion, ulceration, or protrusion in the lower esophagus on endoscope (Figs. 7, 8). We repeated esophageal endoscopy nine times and took twenty-seven biopsy specimens from May 17, 2002 to August 24, 2004. No biopsy specimens showed vas-

Table 1. Laboratory Data on Admission in August 2003

Hematology		Cl	107 mEq/l
WBC	4800 / μ l	Ca	8.2 mg/dl
Neut	49.5 %	CRP	4.09 mg/dl
Lym	33.4 %	HbA1c	8.3 %
Mo	7.1 %	Fe	25 $\bullet$ g/dl
Eo	9.4 %	UIBC	194 $\bullet$ g/dl
Ba	0.6 %	Ferritin	122 ng/ml
Hb	6.5 g/dl	Anti-nuclear Ab	(-)
Ht	21.2 %	C-ANCA	46 EU
Ret	38 %	P-ANCA	(-)
Plt	35.9 $\times$ 10 ⁴ / μ l	Anti-GBM Ab	(-)
Blood chemistry		RF	730 IU/ml
AST	12 IU/l	IgG	1452 mg/dl
ALT	10 IU/l	IgA	407 mg/dl
LDH	386 IU/l	IgM	151 mg/dl
ALP	179 IU/l	IgE	162.7 IU/ml
γ -GTP	28 IU/l	C3	73 mg/dl
T.Bil	0.5 mg/dl	C4	9 mg/dl
T.pro	5.5 g/dl	CH50	34 U/ml
Alb	2.6 g/dl	IC (C1q)	6.7 $\bullet$ g/ml
BS	92 mg/dl	IC (antiC3d)	8.1 $\bullet$ g/ml
T.chol	123 mg/dl	ESR	86 mm/hr
TG	54 mg/dl	Urinalysis	
BUN	13.7 mg/dl	Occult blood	(++)
UA	8.8 mg/dl	Protein	($\pm$)
Cr	0.71 mg/dl	Sugar	(-)
Na	142 mEq/l	Ketone	(-)
K	2.9 mEq/l	Creatinine clearance	67 ml/min

WBC; white blood cell, Neut; neutrophile, Lym; lymphocyte, Mo; monocyte, Eo; eosinophile, Ba; basophile, Hb; hemoglobin, Ht; hematocrit, Ret; reticulocyte, Plt; platelet, AST; aspartate aminotransferase, ALT; alanine aminotransferase, LDH; lactate dehydrogenase, ALP; alkaline phosphatase, γ -GTP; gamma-glutamyltranspeptidase, T.Bil; total bilirubin, T.pro; total protein, Alb; albumin, BS; blood sugar, T.chol; total cholesterol, TG; triglycerides, BUN; blood urea nitrogen, UA; uric acid, Cr; creatinine, Na; sodium, K; potassium, Cl; chloride, Ca; calcium, CRP; C-reactive protein, Fe; iron, UIBC; unsaturated iron binding capacity, C-ANCA; cytoplasmic antineutrophil cytoplasmic antibodies, P-ANCA; perinuclear antineutrophil cytoplasmic antibodies, Anti-GBM Ab; anti-glomerular basement membrane antibody, RF; rheumatoid factor, IgG; immunoglobulin G, C3; complement 3, CH50; complement titer, IC; immune complex, ESR; erythrocyte sedimentation rate

culitis or granuloma.

Discussion

Wegener's granulomatosis (WG) and MPA are vasculitis syndromes commonly affecting the kidney, and upper and lower respiratory tracts (1). The clinical features of these vasculitis syndromes are very similar and the differential diagnosis is somewhat difficult. At the Chapel Hill Consensus Conference in 1994, WG was defined as necrotizing vasculitis affecting small to medium-sized vessels (e.g., capillaries, venules, arterioles, and arteries) accompanied with granulomatous inflammation involving the respiratory tract. MPA was defined as necrotizing vasculitis with few or no immune deposits, affecting small vessels (i.e., capillaries, venules, arterioles). The name "Wegener's granulomatosis" is restricted to patients with granulomatous inflammation. Patients with

Figure 6. Clinical course after admission. Abbreviations: PE, plasma exchange; CPA, cyclophosphamide; PSL, prednisolone; IVIG, intravenous immunoglobulin; CRP, C-reactive protein; cANCA, cytoplasmic antineutrophil cytoplasmic antibody.

exclusively nongranulomatous small vessel vasculitis involving the upper or lower respiratory tract (e.g., alveolar capillaritis) fall into the category of microscopic polyangiitis (microscopic polyarteritis) (2). In the present case, we did not obtain granuloma histologically, though we sampled biopsy specimens repeatedly both from the esophagus and maxillary sinus. Therefore, in conformity with Chapel Hill Consensus Conference, we diagnosed the patient as MPA.

WG and MPA are commonly referred to as the ANCA-associated vasculitis. The ANCA is antibody to neutrophil cytoplasmic antigen and may constitutively activate primed neutrophils and promote binding of the primed neutrophils to the vascular endothelium, degranulation, and the release of neutrophil chemoattractants, hence creating an auto-amplifying loop (1). ANCA is determined by the state of neutrophil activation. cANCA (cytoplasmic ANCA) has been reported to be positive in 70 to 90% of WG and in approximately 10% (5/51) of MPA, while pANCA (perinuclear ANCA) has been reported to be positive in 50 to 80% of MPA and in approximately 10% of WG (1, 3-5). In the present case with MPA, cANCA was positive. There is substantial overlap in many of the cases of ANCA-associated vasculitis (1, 6).

As the initial treatment of MPA or WG, PSL and CPA are generally used. More than 90% of patients with WG improve substantially by using PSL and CPA, and there is no apparent difference between MPA and WG in the initial response to treatment (1, 7). In the present case, we used PSL and CPA to control MPA (1, 8). As a result, symptoms as pneumonia, sinusitis, and esophageal change also, remarkably improved with medical treatment. We, therefore, concluded that the intractable change in the esophagus was one clinical aspect of MPA. In patients with MPA or WG, it is

Figure 7. Esophagus after treatment. (A) The endoscope does not show ulcer, erosion or protrusion. (B) The lesion does not show any non-dyed areas by Lugol's iodine solution.

Figure 8. The histological specimen from the esophagus after treatment does not show inflammation cells. HE stain, $\times 400$

rare to observe lesions in the alimentary tract, compared with those with polyarteritis nodosa or Churg-Strauss syn-

drome. In patients with WG, only 4 cases complicated with symptomatic esophageal lesion have been reported (9-12). However, there is no case report of MPA complicated with an esophageal lesion. This is, therefore, the first case report of esophageal involvement in a patient with MPA. In autopsy cases, one out of 29 with WG presented arteritis in the esophagus (13). The lesion in the alimentary tract in patients with WG and MPA may be not rare but uncommon. It may be important to consider vasculitis syndrome when observing intractable esophageal lesions.

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