

[CASE REPORT]

IgA Vasculitis with Simultaneous Cardiopulmonary Involvement

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Abstract:

A 60-year-old man with a history of hypertension, type 2 diabetes, and reflux esophagitis was admitted to our hospital with hemoptysis, dyspnea, and leg edema. We diagnosed him with adult IgA vasculitis based on the presence of purpura, elevated serum IgA fibronectin complexes, pathophysiological findings, a skin biopsy showing leukocytoclastic vasculitis, and immunofluorescence studies demonstrating granular IgA and C3 deposits in the blood vessel wall. He showed concurrent cardiopulmonary involvement without involvement of the gastrointestinal system and kidneys, which are commonly affected in IgA vasculitis patients. Following treatment with prednisolone, the patient recovered with improvement in cardiopulmonary manifestations.

Key words: IgA vasculitis, cardiac involvement, pulmonary involvement

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Introduction

IgA vasculitis, a systemic vasculitis commonly observed during childhood, usually involves the skin, gut, joints, and kidneys (1, 2). Historically, exclusive involvement of the heart and lungs has been reported in IgA vasculitis patients (3-9). However, simultaneous involvement of the heart and lungs has not been reported. We present a case of an adult patient with IgA vasculitis who demonstrated simultaneous involvement of the heart and lungs and recovered following steroid administration.

Case Report

A 60-year-old man was admitted to our hospital in November 2014 with hemoptysis, dyspnea, and leg edema. He had a medical history of hypertension, type 2 diabetes, and reflux esophagitis. His vital signs were stable, showing a regular heart rate of 112 beats/min, and his arterial blood pressure was 111/97 mmHg. A physical examination showed distended neck veins but unremarkable heart and lung sounds.

His abdomen was soft without tenderness or rebound

pain. The liver and spleen under the rib cage were not palpable, and bowel sounds were normal, as was bilateral renal percussion. There was no lymphadenopathy. However, he showed severe bilateral lower leg edema and purpura (Fig. 1). His neurological examination revealed no abnormalities, and he showed clear consciousness on a mental status examination.

A 12-lead electrocardiogram showed a sinus rhythm with a few ventricular premature beats and low voltage in the limb leads. Chest X-ray revealed cardiomegaly with pleural effusion and a nodular shadow in the right lower lung field (Fig. 2). Pulmonary computed tomography revealed high-density shadows in the lower lobe of the right lung in addition to pleural effusion with pulmonary congestion (Fig. 3). Transthoracic echocardiography (TTE) showed near akinesis of the left ventricle (LV) in conjunction with severe hypokinesis of the anterolateral area of the LV with an ejection fraction (EF) of 20%, estimated using modified Simpson's method.

His complete blood count revealed a white blood cell count of 10,500/ μ L with 87% neutrophils, 0.1% bands, 7.5% lymphocytes, a hematocrit of 26.1% and platelet count of 263,000/ μ L. Serum creatinine was 1.2 mg/dL, and blood urea nitrogen (BUN) was 26 mg/dL. The serum anti-



Figure 1. Severe edema and purpura noted on the bilateral lower legs.

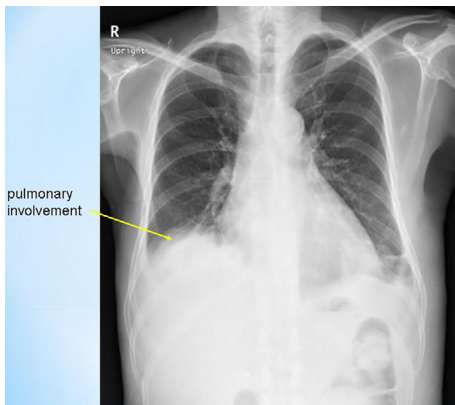


Figure 2. Cardiomegaly with pleural effusion and a nodular shadow in the right lower lung field observed on chest X-ray.

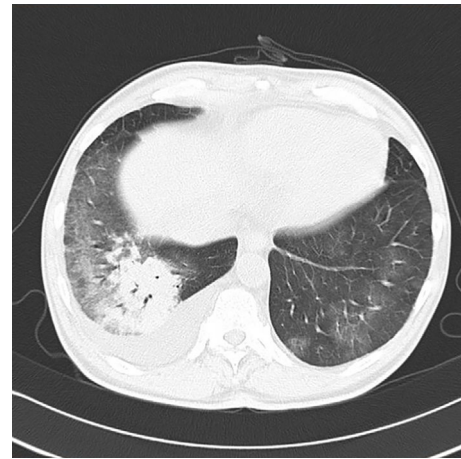


Figure 3. Pleural effusion with pulmonary congestion and high-density shadows observed in the lower lobe of the right lung using pulmonary computed tomography.

neutrophil cytoplasmic antibody, anti-ribonucleoprotein antibody, anti-Smith antibody, anti-glomerular basement membrane antibody, anti-mitochondrial antibody, anti-Sjögren's syndrome-related antigen A (anti-SS-A/Ro antibody), anti-Sjögren's syndrome type B (anti-SS-B/Ro antibody), anti-scleroderma antibody, anti-double stranded DNA, IgG antibody, anti-Jo1 antibody, rheumatoid factor, and hepatitis B surface antigen were negative. However, IgA fibronectin complexes were positive on testing. Tumor markers, including cytokeratin 19 fragment (CYFRA), squamous cell carcinoma antigen (SCC), sialyl Lewis X-i antigen (SLX), and gastrin-releasing peptide (ProGRP), were within reference ranges, although neuron-specific enolase (NSE) showed mild elevation at 41.8 mg/mL. His sputum cytology was negative.

Tests to identify infection, including anti-*Legionella* antibody, *Streptococcus pneumoniae* urinary antigen, *Aspergillus* antigen, and serum *Cryptococcal* antigen, were negative. A bacteriological examination of the sputum did not show specific findings. Microscopic hematuria and proteinuria were absent. He did, however, show marked elevation in his N-terminal pro-brain natriuretic peptide levels (7,985 pg/dL, reference range <125 pg/mL).

We diagnosed the patient to have acute decompensated heart failure (ADHF) with a reduced ejection fraction and initiated conventional medical treatment for the management of ADHF, although we could not diagnose his purpura or the abnormal pulmonary shadow upon admission. Despite combined therapy with phosphodiesterase (PDE) III inhibitors, intravenous infusion of furosemide, and oral tolvaptan, there was no improvement in his symptoms. On the 16th day of hospitalization, we performed a skin biopsy, which revealed interstitial and perivascular infiltration of highly inflammatory cells, viz., neutrophils (Fig. 4A). We diagnosed him as having leukocytoclastic vasculitis with cell disruption of neutrophils and extravasation of red blood cells. Immunofluorescence showed granular IgA and C3 deposits in the blood vessel walls (Fig. 4B and C). Based on the clinical picture of purpura, elevated serum IgA fibronectin complexes, and the pathological findings described, we diagnosed him with adult IgA vasculitis.

He was administered prednisolone on the 23rd day of

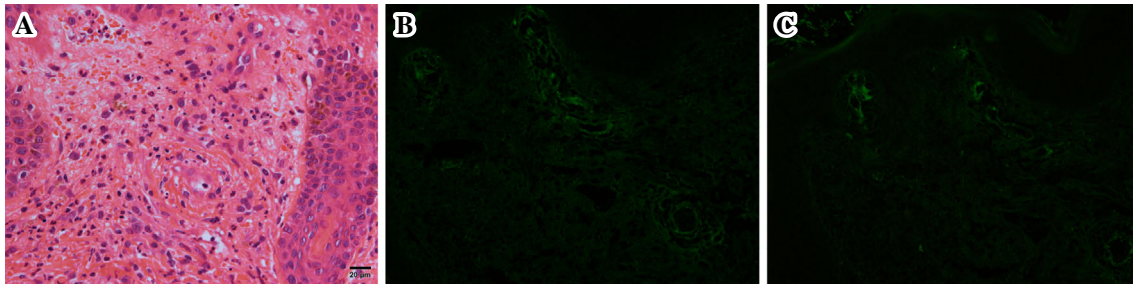


Figure 4. (A) Interstitial and perivascular infiltration with highly inflammatory cells (primarily neutrophils), indicating leukocytoclastic vasculitis. (B) Immunofluorescence study showing granular deposits of IgA in the blood vessel walls. (C) Immunofluorescence study showing C3 deposits in the blood vessel walls.

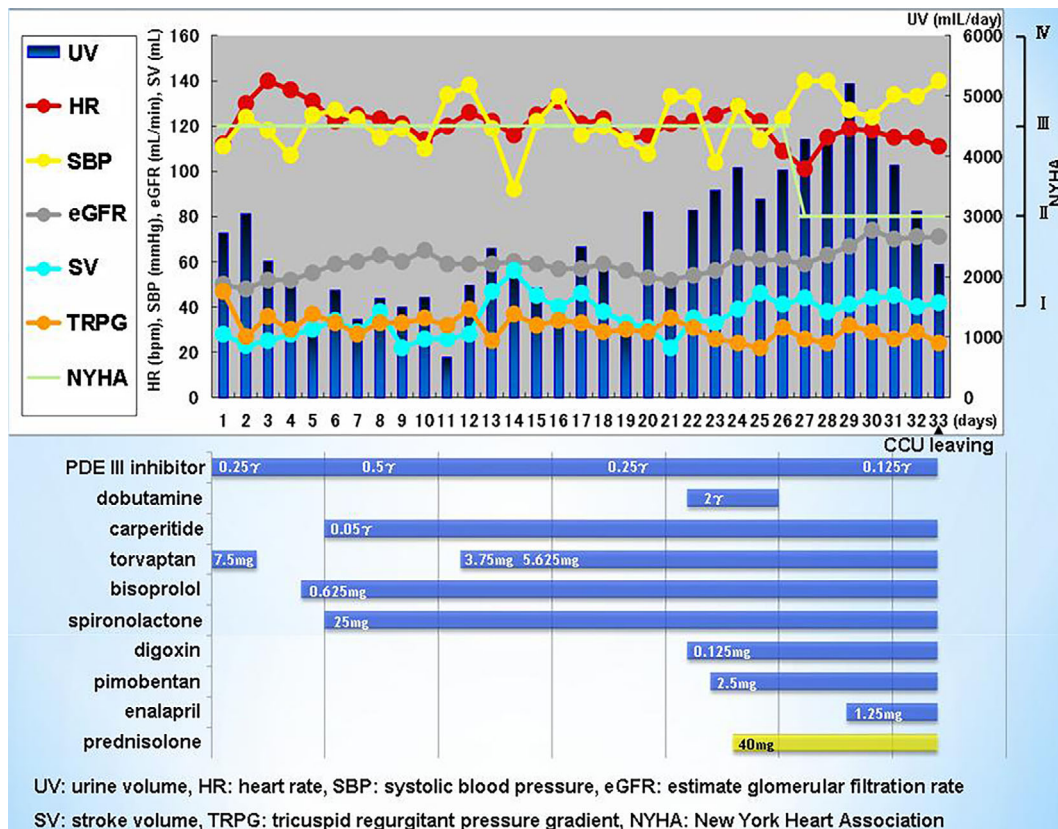


Figure 5. The patient's clinical course during coronary care unit (CCU) stay, showing improvement in acute decompensated heart failure with prednisolone administration.

hospitalization based on the diagnosis of IgA vasculitis, after which his cardiothoracic ratio observed on X-ray continued to decrease with improved LV wall motion noted on TTE. His urine output improved, as did his LV systolic function and symptoms of ADHF (Fig. 5). On the 47th day of hospitalization, we performed adenosine stress-rest ^{99m}Tc -tetrofosmin single-photon emission computed tomography (SPECT), which showed only a small fixed defect in the LV mid septal and apical areas without any stress-induced ischemia. On the 49th day of hospitalization, we performed coronary angiography (CAG) and a cardiac biopsy. CAG showed a moderate-to-severe stenotic lesion with a reduced fractional flow reserve (FFR) estimated at 0.51 in the left anterior descending artery (LAD) (Fig. 6). The biopsy revealed

no infiltration of inflammatory cells, such as neutrophils or eosinophils, indicating vasculitis or eosinophilic myocarditis.

He was discharged on the 53rd day of hospitalization on a regimen of prednisolone at 25 mg per day. One month after discharge, we performed percutaneous coronary intervention (PCI) based on a reduced FFR. Prednisolone was prescribed for almost a year. TTE obtained four months later, after the discontinuation of prednisolone, revealed improvement in the LV wall motion to almost normal kinesis aside from septal basal mid-severe hypokinesis and apical akinesis. TTE showed improvement in the LVEF from 20% on admission to 30% after the administration of prednisolone, and 41% four months later, after the discontinuation of prednisolone. TTE also showed improvement in the stroke

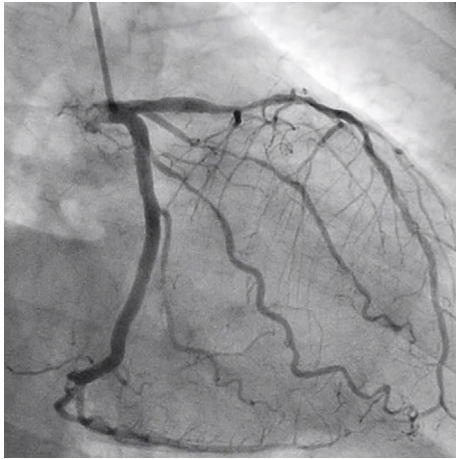


Figure 6. Coronary angiography (CAG) showing a moderate-to-severe stenotic lesion in the left anterior descending artery.

volume from 28 mL on admission to 73 mL four months later, after the discontinuation of prednisolone.

His right lower lobe pulmonary nodule continued to improve on chest X-ray after steroid administration, and eventually, the abnormal pulmonary shadow became a small pulmonary nodule, indicating healed inflammation (Fig. 7). His purpura and leg edema continued to improve and disappeared completely at the time of discharge following steroid administration.

He continued to take prednisolone for a year and showed no recurrence of purpura, no signs of worsening LV systolic dysfunction, and no signs attributable to an increase in the abnormal pulmonary shadow after discontinuation of prednisolone intake for 15 months.

Discussion

In the present case, we diagnosed adult IgA vasculitis based on purpura noted on the patient's bilateral lower legs, elevated serum IgA fibronectin complexes, and typical pathophysiological findings without involvement of the gastrointestinal and renal system, which are commonly affected in patients with IgA vasculitis.

Erol et al. reported that the event percentages of purpura, arthritis, gastrointestinal system involvement, and renal involvement were 100%, 42.9%, 67.9%, and 39.3%, respectively (2). Purpura is reportedly a pathognomonic sign to confirm the diagnosis of IgA vasculitis, and arthritis and gastrointestinal and renal involvement are not absolutely necessary to diagnose this condition. Cardiac or pulmonary involvement is rare in IgA vasculitis, and only a few reports have described exclusive cardiac or pulmonary involvement in IgA vasculitis. To our knowledge, reports of simultaneous cardiopulmonary involvement in patients with IgA vasculitis are extremely rare.

Although a myocardial biopsy revealed no infiltration of inflammatory cells, such as neutrophils and eosinophils, the

timing of the myocardial biopsy might have affected the results (negative findings) because the myocardial biopsy was performed after improvement of ADHF following prednisolone administration.

Although CAG showed a moderate-to-severe stenotic lesion in the LAD, the reduced ejection fraction was likely not due to ischemic cardiomyopathy for the following reasons: 1) Coronary artery disease with the LAD being affected could not explain the wall motion abnormalities, such as near akinesis of the LV and the severe hypokinesis in the anterolateral area of the LV upon admission; 2) the adenosine stress-rest ^{99m}Tc -tetrofosmin SPECT scan showed only a small fixed defect in the LV mid septal and apical areas that could not explain the diffuse severe LV wall motion abnormality, and we could not accurately determine why the results of SPECT imaging did not correspond to the results of FFR; and 3) we consider the improvement in his ADHF and his cardiothoracic ratio noted on chest X-ray to be due to prednisolone administration because PCI was performed after improvement in the LV wall motion abnormality. It has been reported that conduction abnormalities, congestive cardiac failure, and extensive necrosis may occur when the heart is involved, and the severity of cardiac involvement may determine the prognosis in IgA vasculitis (5, 6). In the present case, the patient showed a favorable clinical course likely because he showed no conduction abnormalities and/or extensive necrosis.

Furthermore, the patient had a nodule in the right lower lung, leading us to the conclusion that the abnormal pulmonary shadow was indicative of pulmonary involvement of IgA vasculitis, although a confirmatory pulmonary biopsy was not performed. We drew this conclusion because the patient showed no significant elevation of pulmonary tumor markers, no abnormalities on sputum cytology, and no signs of bacterial infection. In addition, the most convincing evidence is the fact that steroid administration resulted in improvement in the abnormal pulmonary shadow in addition to improvement in his purpura and LV systolic function.

However, we did not clarify if renal involvement could be associated with IgA vasculitis without microscopic hematuria and proteinuria, although the kidneys are known to be affected in most cases of IgA vasculitis (10). Our patient showed improvement in his renal function throughout his clinical course, which we attributed to an improvement in the left ventricular systolic function and subsequent amelioration of heart failure and renal congestion instead of the direct effect noted with steroid administration for renal involvement in IgA vasculitis.

The gastrointestinal system is frequently affected in patients with IgA vasculitis (2). However, our patient had no abdominal pain, vomiting, hematemesis, or melena indicating gastrointestinal system involvement. Accordingly, we considered other types of small vessel vasculitis, such as double anti-neutrophil cytoplasmic antibody (ANCA)-negative microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), and eosinophilic granulomatosis

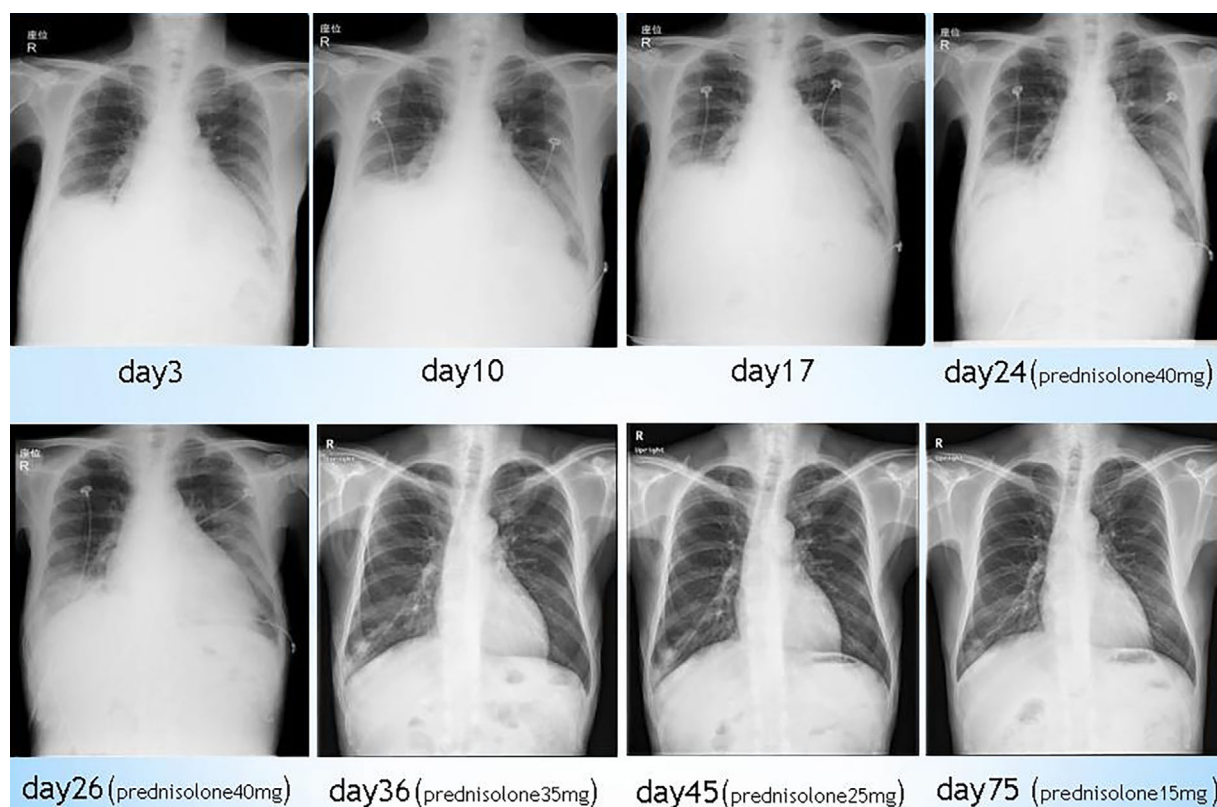


Figure 7. Chest X-ray showing improvement in the cardiothoracic ratio and right lower pulmonary nodule after prednisolone administration.

(EGPA), which are associated with cardiopulmonary manifestations and purpura. MPA shows necrotizing vasculitis with few or no immune deposits and very commonly presents with necrotizing glomerulonephritis. We therefore believe that the clinical features of our patient did not meet the criteria for MPA. GPA is usually associated with ANCA, and the clinical criteria for GPA include nasal or oral inflammation and abnormal urinary sediment. Our patient had no features indicating GPA. EGPA was ruled out due to the patient's lack of a history of asthma, hypereosinophilia, or mono- or polyneuropathy and the fact that his biopsy contained a blood vessel showing the accumulation of eosinophils in extravascular areas.

Although there is no consensus regarding their use, the administration of steroids is recommended for patients with IgA vasculitis complicated by renal invasion or severe abdominal symptoms (10). The indications for steroid use in IgA vasculitis complicated by myocardial or pulmonary invasion are also unclear, although our patients improved after the administration of prednisolone. We would have used other immunosuppressant drugs or combined therapy with steroid and immunosuppressants if a single course of prednisolone had not been effective in the present case (11).

In conclusion, we diagnosed adult IgA vasculitis in a patient, based on evidence of purpura, elevated serum IgA fibronectin complexes, and pathophysiological findings. This was a rare case of adult IgA vasculitis complicated with simultaneous cardiopulmonary involvement without involve-

ment of the gastrointestinal and renal system, which are commonly affected in IgA vasculitis. Our conclusions are based on the fact that that, during his clinical course, prednisolone administration improved his cardiopulmonary manifestations.

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

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