CASE REPORT

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A case of eosinophilic polyangiitis with granulomatosis that evolved to cardiac arrest due to advanced atrioventricular block

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ABSTRACT

Cardiac manifestations are the major cause of mortality in patients with eosinophilic granulomatosis with polyangiitis (EGPA). Among these manifestations in EGPA patients, in the literature, there are fewer reports describing bradycardia in EGPA patients than those describing tachycardia. A 50-year-old woman with a history of childhood-onset asthma. At age 28, she was diagnosed with eosinophilic gastroenteritis without the diagnosis of EGPA and was started on a systemic steroid and had maintenance daily dose of 2.5 mg after gradually tapered. She had experiencing dizziness and palpitations 2 weeks after discontinuation of the steroid treatment. At emergency visit, electrocardiography revealed an advanced atrioventricular block of 3:1 or less. Forty-eight minutes after the start of electrocardiography, only a P wave was observed and cardiac arrest occurred for 9 s and temporary emergency pacing was performed immediately. She was diagnosed as EGPA presenting leukocyte count, 16,500/μL, 42.8% of which were eosinophils and sinusitis in computed-tomography. She could be survival by treatment of steroid, following the patient to withdraw from an external pacemaker. She received prednisolone of 60 mg, intravenous cyclophosphamide and intravenous immunoglobulin. She had relapsed presenting peripheral eosinophilia, abdominal and numbness in the toes of the left leg pain, but not arrythmia after tapered of prednisolone. Following additional steroid pulse, she had an increase of prednisolone and continued by intravenous cyclophosphamide, intravenous immunoglobulin and started mepolizumab. We presented a severe case of EGPA presenting an advanced atrioventricular block into cardiac arrest.

Keywords: advanced atrioventricular block, eosinophilic granulomatosis with polyangiitis, eosinophilic gastroenteritis, immunoglobulin, mepolizumab

Abbreviations:
EGPA: eosinophilic granulomatosis with polyangiitis
^{123}I-MIBG: iodine-123–labeled metaiodobenzylguanidine

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INTRODUCTION

Eosinophilic granulomatosis with polyangiitis (EGPA; also known as Churg–Strauss syndrome) is a rare disease characterized by the presence of allergic granulomatosis and necrotizing vasculitis with tissue and peripheral blood eosinophilia.[1]

In EGPA, mortality rate and prognosis are related to disease severity, which is assessed by using a five-factor score (currently the 2009 Revised Five-Factor Score) where each of five factors (ie, age ≥ 65 years, severe cardiac involvement, severe gastrointestinal tract involvement, renal insufficiency, and absence of sinusitis) are scored as 0 for absent or 1 for present.[2] Among these five factors, severe cardiac involvement is the major cause of mortality in EGPA patients. For example, survival rate at 6 years after diagnosis of myocardial involvement is reported to be only one-third that in the absence of myocardial involvement.[3] Also, EGPA patients with cardiac involvement have a lower 5-year survival rate[4] and poorer long-term prognosis than patients without cardiac involvement.[5]

The most commonly reported the percentage of patients showing each cardiac involvement among patients with EGPA are myocarditis (37.1%–89.5%), pericarditis (9.4%–50.4%), heart failure (36.8%–51.6%), and arrhythmia (12.5%–27.4%).[6-10] With respect to arrhythmia, there are fewer reports in the literature describing bradycardia in EGPA patients—for example as a result of bundle branch block,[8] advanced atrioventricular block,[9] or first-degree atrioventricular block[11]—than those describing tachycardia.[7-10,12-15]

Here, we report a rare case of EGPA in which the patient presented with bradycardia due to atrioventricular block that evolved into cardiac arrest; treatment by steroid pulse could be survival, following the patient to withdraw from an external pacemaker.

CASE PRESENTATION

A 50-year-old woman with a history of childhood-onset asthma. At the age of 8, she entered asthma remission, but at age 19 the asthma relapsed. Since age 30, she had used fluticasone plus salmeterol (250 + 50 mg; twice daily) or fluticasone propionate (200 mg; twice daily) when she had asthma symptoms. At age 28, she was diagnosed with eosinophilic gastroenteritis without the diagnosis of EGPA and was started on a systemic steroid (prednisolone, 30 mg per day). Over time, the prednisolone was gradually tapered to a maintenance daily dose of 2.5 mg; however, occasional self-interruption of the steroid treatment resulted in the gastroenteritis returning. At the time of presentation at our emergency visit, she had discontinued the steroid treatment 3 weeks previous and had experiencing dizziness and palpitations 2 weeks after discontinuation.

At presentation, her blood pressure was 136/82 mmHg and heart rate was 61 beats per min. Electrocardiography revealed an advanced atrioventricular block of 3:1 or less (Figure 1A). Chest X-ray revealed mild cardiac enlargement and pulmonary congestion (Figure 2). Echocardiography revealed an ejection fraction of 52%, mild mitral regurgitation, mild tricuspid regurgitation, and inferior vena cava enlargement; a small amount of pericardial fluid was observed, but left ventricular contractile function was good. Forty-eight minutes after the start of electrocardiography, only a P wave was observed and cardiac arrest occurred for 9 s (Figure 1B). Temporary emergency pacing was performed immediately.

Fig. 1 (A)

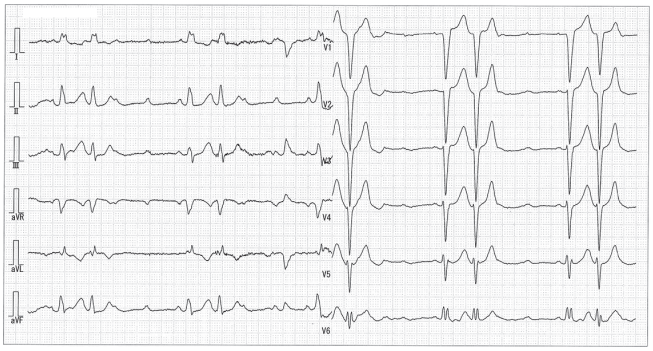

Fig. 1 (B)

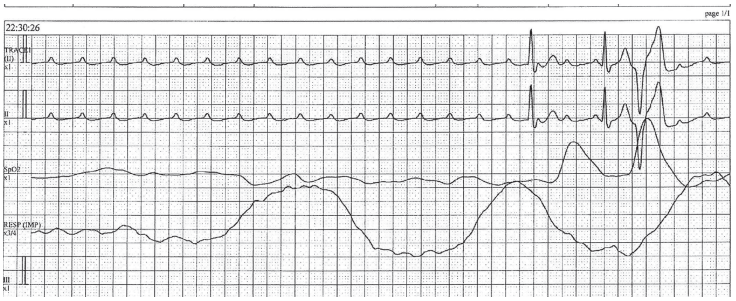

Fig. 1 Electrocardiography at presentation at our emergency outpatient clinic

Fig. 1A: Electrocardiogram showing advanced atrioventricular block of 3: 1 or less.

Fig. 1B: At 48 min after the start of electrocardiography, a P wave only was observed and cardiac arrest occurred for 9 s.

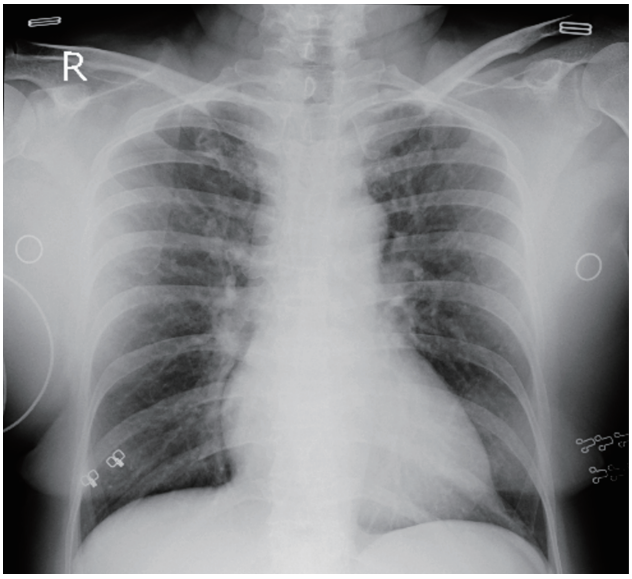

Fig. 2 Chest X-ray at presentation at our emergency outpatient clinic

Chest X-ray revealed mild cardiac enlargement and pulmonary congestion.

At the diagnosis of EGPA, laboratory tests revealed leukocytosis (leukocyte count, 16,500/μL, 42.8% of which were eosinophils); serum total IgE, 280 IU/mL; elevated brain natriuretic peptide, 123.8 pg/mL; elevated C-reactive protein, 0.44 mg/mL; and a negative myeloperoxidase-antineutrophil cytoplasmic antibodies. Antigen-specific serum IgE was positive at class 4 for house dust-mite, class 3 for cedar pollen, and class 2 for cat.

At diagnosis, enhanced computer tomography did not show cervical artery stenosis, aneurysms or thrombosis in artery. We performed cardiac scintigraphy with iodine-123–labeled metaiodo-

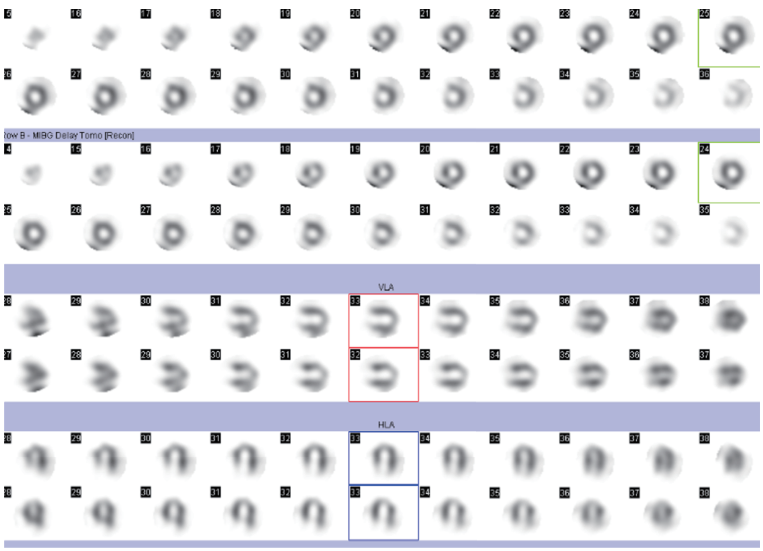

Fig. 3 Cardiac scintigraphy at diagnosis
Iodine-123–labeled metaiodobenzylguanidine scintigraphy did not show decreased myocardial uptake.

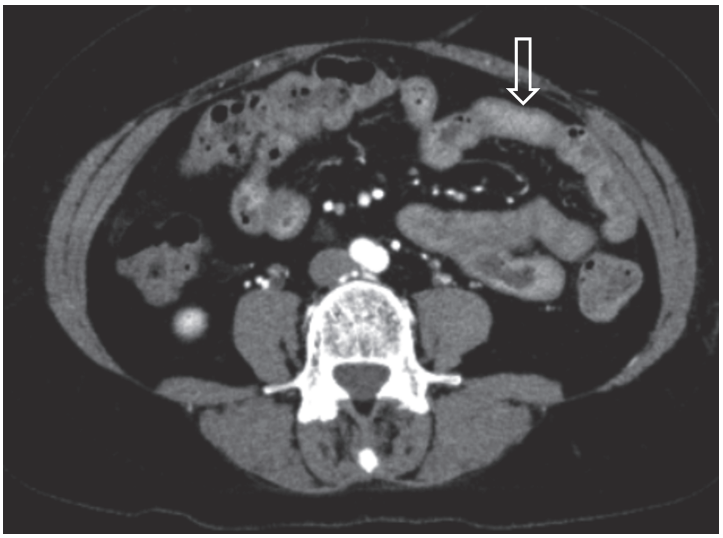

Fig. 4 Abdominal contrast-enhanced computed tomography at diagnosis
Arrow indicates the location of intestinal edema.

benzylguanidine (^{123}I-MIBG) and the heart-to-mediastinum (H/M) ratio was determined from the images. Also, the washout rate of MIBG within the myocardium was measured as the percent change in left ventricular activity from the early to the delayed images. Cardiac scintigraphy did not show any decreased uptake of ^{123}I-MIBG in the myocardium. H/M ratio was within the normal range at 2.27 in the early phase and 2.84 in the delayed phase, but the washout rate was high at 27.5% (Figure 3). Abdominal contrast-enhanced computed tomography (Figure 4) reveled intestinal edema and nasal polyps in the upper-right maxillary sinus in computed-tomography.

In line with the diagnostic criteria of Ministry of Health, Labour and Welfare for EGPA, the patient was diagnosed with EGPA on the basis of the presence of vasculitis with asthma and elevated levels of peripheral blood eosinophils.[16] Sinus rhythm returned 20 hours and 2 minutes after cardiac arrest on the next day of starting methylprednisolone pulse therapy (1000 mg intravenously daily for 3 consecutive days) from next day after emergency pacing.

At the end of methylprednisolone therapy, the patient was started on oral prednisolone (60 mg/day); the external pacemaker was removed 6 days later. She was treated with intravenous cyclophosphamide (600 mg/m^2) every 3–4 weeks and at 2 months after the start of steroid pulse treatment she also received intravenous immunoglobulin (400 mg/kg for 5 consecutive days). After that, the dose of prednisolone was gradually tapered because sinus rhythm was maintained at a mean heart rate of 70–80 beats per min. The patient reported intermittent numbness in the sole of the right foot, and one month after reduction of the dose of prednisolone to 12.5 mg, numbness appeared in the toes of the left leg but muscle weakness did not occur. After the prednisolone was tapered to 7.5 mg, her systolic blood pressure rose above 160 mmHg, so she was started on 20 mg of telmisartan. She also reported gastrointestinal symptoms (diarrhea and abdominal pain) and an increased heart rate (95 beats per min) and increased leukocyte count (14,400/μL; 29.0% of which were eosinophils); in response, the prednisolone dose was increased to 15 mg once daily, but her peripheral blood eosinophil count remained increased (leukocyte count, 16,100/μL; 29.0% of which were eosinophils) and she had abdominal pain and diarrhea although she did not have arrythmia. Following additional two courses of methylprednisolone pulse therapy, the dose of prednisolone was increased to 30 mg once daily. The intravenous cyclophosphamide was continued every 3–4 weeks, intravenous immunoglobulin was added three weeks after another two courses of steroid pulse therapy, and the patient received mepolizumab 300 mg monthly. The vasculitis symptoms gradually improved and the prednisolone was eventually tapered to 10 mg once daily.

DISCUSSION

Increased adoption of the American College of Rheumatology criteria for the classification of EGPA has reduced the mortality rate of patients with EGPA diagnosed after 1996 is lower than that of those diagnosed before 1996.[4,17] More recently, the 5-, 10-, and 20-year survival rates reported in 2011 by Guillevin et al were about 90%, 75%, and 45%, respectively,[3] whereas those reported in 2013 by Moosig et al were 97%, 89%, and 72%, respectively.[5] Our group reported in 2017 survival rates of 91.1%, 83.7%, and 68.6%, respectively[18] However, the 30-year survival rate is reported to still be only about 55%,[19] which suggests that although the 5-year survival rate for patients with EGPA has improved, the 20- and 30-year survival rates remain poor. Patients with EGPA with cardiac involvement show a particularly poor prognosis.[3,5]

FDG-PET has reportedly detected active myocardial inflammation in patients with EGPA both before treatment and after remission.[20,21] Cardiac sympathetic nerve function was damaged in EGPA patients with cardiac involvement. We showed ^{123}I-MIBG scintigraphy was useful in

detecting cardiac involvement and in predicting cardiac events.[22] ^{123}I-MIBG scintigraphy can evaluate the viability of the myocardium by the value of H/M and the function of the myocardium by the value of WR. In one case we reported, ^{123}I-MIBG scintigraphy showed a mild decrease in accumulation and FDG-PET of EGPA with a mild increase in WR of 22.14% did not show significant accumulation in the heart.[23] We considered that EGPA has less accumulation of FDP-PET in the heart as reported in cardiac sarcoidosis.[24] Therefore, in EGPA, ^{123}I-MIBG scintigraphy is considered to be more suitable for screening including mild cardiac involvement.

Compared to EGPA with cardiac involvement, AVB is more frequent in cardiac sarcoidosis, and there are cases of permanent pacemaker insertion and heart transplantation even after treatment with steroids and immunosuppressants, and there are many reports of sudden death[25] or fibrosis to the myocardium.[26] There are few reports of EGPA presenting with arrhythmia, and among them, there are even fewer reports of bradyarrhythmia or AVB, but there are reports that steroids and immunosuppressive agents have been successful.[13,15]

The conventional treatment for EGPA is combined corticosteroid–cyclophosphamide therapy; however, this approach sometimes has little effect in EGPA patients with mononeuritis multiplex or heart failure.[27] Previously, we reported that intravenous immunoglobulin therapy was effective for the treatment of EGPA in patients with severe mononeuritis multiplex or heart failure who did not respond to combined corticosteroid–cyclophosphamide treatment.[28] In addition, we have reported that the long-term efficacy of intravenous immunoglobulin in EGPA patients with severe mononeuritis multiplex or heart failure is a result of an increased regulatory T-cell population (as $FOXP3^{+}CD4^{+}$ T cells) in the peripheral blood,[29] suggesting that intravenous immunoglobulin may improve prognosis in these patients.[18] Patients with EGPA in remission often relapse when prednisolone is tapered to below 10 mg.[30] Our group has also reported that EGPA patients with myocardial or gastrointestinal tract involvement show frequent relapses.[18]

In addition to conventional combined corticosteroid (prednisolone)–cyclophosphamide therapy, our patient received intravenous immunoglobulin but still showed relapse of vasculitis symptoms and an increased peripheral eosinophil count after reduction of the prednisolone dose. However, after the addition of mepolizumab her peripheral eosinophil count did not increase, suggesting that she might have entered remission. In EGPA patients, there are reports of sudden death due to coronary artery dissection,[31] coronary artery stenosis,[32] or arrhythmia.[33]

We presented a survival case of EGPA presenting an advanced atrioventricular block into cardiac arrest. A case with severe cardiac involvement may be need treatment not only corticosteroids, intravenous cyclophosphamide, intravenous immunoglobulin, but mepolizumab.

We obtained the patient's written informed consent to publish details of her case.

CONFLICTS OF INTEREST

No author has any conflict of interest to disclose.

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