CASE REPORT

Polyangiitis overlap syndrome of granulomatosis with polyangiitis (Wegener's granulomatosis) and eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome)

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SUMMARY

Polyangiitis overlap syndrome is defined as systemic vasculitis that cannot be classified into one of the well-defined vasculitic syndromes. In this report, a female patient who presented with vasculitis-like and asthmatic symptoms was diagnosed as having polyangiitis overlap syndrome of granulomatosis with polyangiitis (GPA; formerly known as Wegener's granulomatosis) and eosinophilic granulomatosis with polyangiitis (EGPA; formerly known as Churg-Strauss syndrome). The patient fulfilled the American College of Rheumatology diagnostic criteria for GPA and EGPA. She was successfully treated with immunosuppressants and steroids and has been in remission for 20 months. It is important to establish a proper diagnosis and introduce an appropriate treatment modality in patients with this rare and serious pathology to prevent irreversible organ damage.

BACKGROUND

Polyangiitis overlap syndrome is defined as a type of systemic vasculitis that shows overlapping features of several distinct vasculitides and cannot be classified into one of the well-defined vasculitic syndromes.¹ Although several polyangiitis overlap syndromes have been identified, polyangiitis overlap syndrome of granulomatosis with polyangiitis (GPA) and eosinophilic granulomatosis with polyangiitis (EGPA) has been seldom reported before. It is important to recognise polyangiitis overlap syndrome because treatment modalities differ depending on the type of vasculitis. Polyangiitis overlap syndrome can result in irreversible organ damage if not treated promptly and appropriately.¹ We present the case of a patient with polyangiitis overlap syndrome of GPA and EGPA with positive proteinase-3 antineutrophil cytoplasmic antibodies (PR3-ANCA).

CASE PRESENTATION

A 78-year-old woman presented with a 4-month history of sinus congestion, epistaxis and cough and a 1-month history of dyspnoea. She had no significant travel or family history, and she denied a history of asthma or atopic disease. She had been previously diagnosed with sinusitis and treated by an otorhinologist in a private practice, but without success. A physical examination revealed mild anaemia, bibasilar lung wheeze sounds and knee

ache, as well as diffused itchy erythemas with ulceration on both lower legs. Laboratory tests revealed the following results: a white cell count of 8400 cells/ μ L (eosinophils, 23.3%); an elevated C reactive protein (CRP) level (136 mg/L); high levels of PR3-ANCA titres (930 U/mL) and a negative result for myeloperoxidase ANCA (MPO-ANCA; <1.3 U/mL). A urine dipstick test revealed urinary occult blood (2+). A pulmonary function test showed that the percentage of vital capacity was 82% and the forced expiratory volume in 1 s was 49.6% with no reversibility of airflow limitation. Possible causes of eosinophilia, such as drugs or parasites, were not detected. A chest radiography and CT revealed alveolar consolidation that had spread to all the right lung lobes and the left lung lingula, without any lymphadenopathy or pleural effusions. A sinus CT revealed bilaterally thickened nasal mucosae and soft shadows in the maxillary and ethmoidal sinuses, without any broken structures in the nasal cavity.

Fibre-optic bronchoscopy showed narrowing of the superior segmental bronchus of the right inferior lobe (figure 1). A transbronchial lung biopsy revealed fresh alveolar haemorrhage associated with a perivascular inflammatory infiltrate (figure 2) composed of numerous neutrophils and some eosinophils and a mild intra-alveolar accumulation

Figure 1 Bronchoscopy showing stenosis of the superior segmental bronchus for the right lower lobe.

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Figure 2 Light microscopy of H&E-stained transbronchial lung biopsy of the right lower lobe (×400 magnification).

of macrophages. Neither necrotising angitis nor granulomatous reaction was apparent. A skin biopsy obtained from an erythematous lesion of the lower leg (figure 3) revealed a focal accumulation of neutrophils and macrophages scattered in the dermis, particularly within and around many small-sized and a few medium-sized arteries with necrotising angitis that was characterised by fibrin deposition and necrotic nuclear debris, and small-sized veins and capillaries (figure 4). A partial reaction of activated histiocytes was observed around the affected arteries. Cyclophosphamide (oral, 50 mg daily) and methylprednisolone (intravenous, 1 g daily) were initiated for 3 days, followed by prednisolone (oral, 50 mg daily). Consequently, the symptoms of dyspnoea and fatigue rapidly diminished. Anaemia and eosinophilia resolved, and the serum levels of CRP and PR3-ANCA returned to the normal range. The alveolar infiltrates in the chest radiograph and wheezing sounds in the lungs promptly diminished. Thus, the oral cyclophosphamide and prednisolone therapy improved her condition, and she had been in remission for 20 months.

OUTCOME AND FOLLOW-UP

The patient was followed up and remained asymptomatic and in remission for 20 months after the treatment.

DISCUSSION

There are several reports about polyangiitis overlap syndrome.^{1 2} To the best of our knowledge, however, only a few cases which

Figure 3 Cutaneous findings of the left lower limb.

Figure 4 Light microscopy of the H&E-stained skin biopsy of the left leg (×400 magnification).

were considered as polyangiitis overlap syndrome of GPA and EGPA have been reported until now.^{3 4} For small-sized vessel vasculitis, peripheral blood eosinophil counts in excess of $1.5 \times 10^9/L$ and asthma should prompt suspicion of EGPA rather than GPA.⁵ Although our patient presented with peripheral eosinophilia and asthmatic symptoms, she was diagnosed with polyangiitis overlap syndrome of GPA and EGPA rather than mere EGPA, for the following reasons: first, the serum PR3-ANCA level, which has a much higher specificity for GPA than for EGPA, was elevated, and the MPO-ANCA titres were negative.⁶ Second, the skin biopsy revealed focal panarteritis with necrotising vasculitis and histiocytic proliferation, and leucocytoclastic vasculitis. Eosinophilic infiltration, frequently observed in EGPA,⁷ was not accentuated. Third, the patient developed nasal obstruction, epistaxis and microhaematuria, which are rare in patients with EGPA.⁸ Fourth, she had no history of asthma or atopy, both of which are common in EGPA.³

A skin biopsy was useful not only for differentiating cutaneous lesions due to non-vasculitic disorders, but also for distinguishing the different types of vasculitides. It helped confirm that there was no eosinophilic infiltration and fibrinoid necrosis around the inflamed small-sized or medium-sized blood vessel wall, which most likely indicated GPA. Our skin biopsy was not specific for GPA in that, it showed no granuloma which is a hallmark of GPA. However, those findings were considered as an early stage of vasculitis before granuloma formation, because the histology characterised by exudative change with histiocytic proliferation was usually encountered in the early lesion as well as in the progressing phase of GPA.⁹ We could not obtain histopathological findings supporting the diagnosis of GPA or EGPA through transbronchial lung biopsy. Moreover, the sensitivity of a transbronchial lung biopsy is reported to be low,¹⁰ and the sensitivity of a skin biopsy for diagnosing GPA or EGPA is considered superior.^{11 12} Therefore, we considered it appropriate to look for skin lesions and perform a skin biopsy in order to diagnose this case more accurately.

It is important to identify patients with polyangiitis overlap syndrome of GPA and EGPA because the treatment modalities are different for GPA and EGPA. Although the majority of patients with EGPA achieve remission with corticosteroids alone,¹³ patients with GPA or polyangiitis overlap syndrome are usually treated with immunosuppressants such as cyclophosphamide combined with corticosteroids.^{1 4 14} Considering the

possibility of severe side effects associated with immunosuppressant use,¹⁵ it is crucial to accurately diagnose patients with EGPA, GPA or overlapping syndromes, in order to deliver accurate and appropriate treatment. Besides, more studies will be required to confirm the appropriate treatment options of overlap syndrome between GPA and EGPA, because, at present, there is little evidence to support the treatment.

The existing criteria for the classification of ANCA-associated vasculitides, such as those developed by the American College of Rheumatology, Chapel Hill Consensus Conference and Lanham *et al*, remain confusing. Although Watts *et al*¹⁶ have recently suggested that vasculitis with peripheral eosinophilia and asthma should be classified as EGPA, their diagnostic algorithm could not be applied in our case of GPA with peripheral eosinophilia and asthmatic symptoms. Therefore, the algorithm would need to be modified in order to classify our case as polyangiitis overlap syndrome of GPA and EGPA.

Learning points

- Polyangiitis overlap syndrome of granulomatosis with polyangiitis (GPA) and eosinophilic granulomatosis with polyangiitis (EGPA) is rare.
- It is important to accurately identify the type of vasculitis because treatment modalities differ depending on the vasculitis type.
- A skin biopsy demonstrating vasculitis and histiocytic proliferation without eosinophilic infiltration is useful for diagnosing polyangiitis overlap syndrome of GPA and EGPA rather than EGPA alone.

Contributors All the authors reviewed the analysis of case clinical course and the discussion of the article. Diagnosis and treatment was mainly performed by HU and ST. Pathological assessments were performed by KS.

Competing interests None.

Patient consent Obtained.

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REFERENCES

- 1 Leavitt RY, Fauci AS. Polyangiitis overlap syndrome. Classification and prospective clinical experience. *Am J Med* 1986;81:79–85.
- 2 Madridano Cobo O, Sendino Revuelta A, Martínez Hernández PL, *et al*. [The polyangiitis overlap-Schonlein-Henoch purpura-PAN syndrome: a case of more than a rare association]. *An Med Interna* 1995;12:195–6. Spanish.
- 3 Potter MB, Fincher RK, Finger DR. Eosinophilia in Wegener's granulomatosis. *Chest* 1999;116:1480–3.
- 4 Shoda H, Kanda H, Tanaka R, *et al*. Wegener's granulomatosis with eosinophilia. *Intern Med* 2005;44:750–3.
- 5 Masi AT, Hunder GG, Lie JT, *et al*. The American College of Rheumatology 1990 criteria for the classification of Churg-Strauss syndrome (allergic granulomatosis and angiitis). *Arthritis Rheum* 1990;33:1094–100.
- 6 Rao JK, Weinberger M, Oddone EZ, *et al*. The role of antineutrophil cytoplasmic antibody (c-ANCA) testing in the diagnosis of Wegener granulomatosis. A literature review and meta-analysis. *Ann Intern Med* 1995;123:925–32.
- 7 Jennette JC, Falk RJ, Andrassy K, *et al*. Nomenclature of systemic vasculitides. Proposal of an international consensus conference. *Arthritis Rheum* 1994;37:187–92.
- 8 Gaffo AL. Diagnostic approach to ANCA-associated vasculitides. *Rheum Dis Clin North Am* 2010;36:491–506.
- 9 Jennette JC. "Nomenclature and classification of vasculitis: lessons learned from granulomatosis with polyangiitis (Wegener's granulomatosis)." *Clin Exp Immunol* 2011;164(Suppl 1):7–10.
- 10 Ensinger SA, Parkash UB. Is bronchoscopic lung biopsy helpful in the management of patients with diffuse lung disease? *Eur Respir J* 2006;28:1081–4.
- 11 Zycinska K, Wardyn K, Zielonka TM, *et al*. Cutaneous changes: an initial manifestation of pulmonary Wegener's granulomatosis. *Adv Exp Med Biol* 2013;755:307–10.
- 12 Kawakami T, Soma Y, Kawasaki K, *et al*. Initial cutaneous manifestations consistent with mononeuropathy multiplex in Churg-Strauss syndrome. *Arch Dermatol* 2005;141:873–8.
- 13 Ribi C, Cohen P, Pagnoux C, *et al*. Treatment of Churg-Strauss syndrome without poor-prognosis factors: a multicenter, prospective, randomized, open-label study of seventy-two patients. *Arthritis Rheum* 2008;58:586–94.
- 14 Hoffman GS, Kerr GS, Leavitt RY, *et al*. Wegener granulomatosis: an analysis of 158 patients. *Ann Intern Med* 1992;116:488–98.
- 15 Langford CA. Complications of cyclophosphamide therapy. *Eur Arch Otorhinolaryngol* 1997;254:65–72.
- 16 Watts R, Lane S, Hanslik T, *et al*. Development and validation of a consensus methodology for the classification of the ANCA-associated vasculitides and polyarteritis nodosa for epidemiological studies. *Ann Rheum Dis* 2007;66:222–7.

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