CASE REPORT

Familial eosinophilic granulomatosis with polyangiitis in a mother and daughter

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SUMMARY

A 17-year-old girl was admitted to our unit with weight loss, dyspnoea, arthralgia and sinusitis. Her medical history was noteworthy for bronchial asthma and she required systemic steroid therapy. Her mother had a history of eosinophilic granulomatosis with polyangiitis (EGPA). Laboratory tests revealed excessive eosinophilia and elevated erythrocyte sedimentation. The assay for peripheral antineutrophil cytoplasmic antibodies was negative. Histopathological examination of lung biopsy revealed EGPA. The patient was treated with methylprednisolone; her eosinophil count normalised and she began to improve clinically and radiographically. There is no genetic factor to influence susceptibility to this disease. To the best of our knowledge, this is the second report of familial EGPA disease in the literature, with a mother and daughter both being affected. EGPA disease should be kept in mind in a patient with uncontrolled asthma and eosinophilia with a positive family history for EGPA.

BACKGROUND

Eosinophilic granulomatosis with polyangiitis (EGPA, also known as Churg-Strauss syndrome) is a rare vasculitis that is defined by the presence of eosinophil-rich and necrotising granulomatous inflammation, and necrotising vasculitis primarily affecting the small to medium sized arteries and veins.¹ Asthma and eosinophilia are highly associated clinical features with EGPA.¹ There is no evidence that genetic factors influence the presence of the disease. Previously, two elderly sisters have been reported with EGPA and the heritability of the disease was not associated with HLA typing.² We present a second familial case of EGPA, of a mother and daughter.

CASE PRESENTATION

A 17-year-old girl presented to our paediatric allergy and immunology unit with weight loss, dyspnoea, arthralgia and symptoms related with upper respiratory tract infection. She had moderate bronchial asthma since the age of 5 years, which was not controlled with inhaled corticosteroids. She had positive skin prick test for house dust mite and grass pollen. Her medical history was negative for other systemic and metabolic disease. She had bilateral rales on physical examination of the lungs. Laboratory tests revealed leucocytosis of 19 800/mm³, 69.1% of which were eosinophils, and a negative perinuclear antineutrophil cytoplasmic antibody (p-ANCA) result. Serum electrolytes, renal and liver function tests were within normal

limits. Chest X-ray examination revealed infiltration at the right lobe (figure 1), high-resolution CT of the chest revealed a 'budded tree view' in the right lower lobe and extensive peribronchial wall accompanied by thickening of the acinar infiltrates. As her mother was diagnosed with EGPA 1 year, open lung biopsy was performed. Histopathological examination of biopsy specimens revealed infiltration of eosinophils, histiocytes and erythrocytes in the alveoli and interstitium.

The 45-year-old mother of the index case had bronchial asthma at the age of 32 years, and has persistent symptoms related with asthma and sinusitis. She had a positive IgE radioallergosorbent test result for house dust mite. At the age of 44 years, she had persistent symptoms of asthma, she often required systemic corticosteroids. In May 2011 (at the age of 45 years) she was admitted to hospital with slightly elevated fever, weight loss (approximately 12 kg within 6 months), paresthesia/paralysis of the lower legs and both hands, palpitations, dyspnoea and skin eruption. Laboratory tests revealed leucocytosis of 18.500/mm³, 29.1% of which were eosinophils, and a negative peripheral antineutrophil cytoplasmic antibodies (p-ANCA) result. High-resolution CT of the chest revealed localised parenchymal opacities and patchy peripheral areas of parenchymal consolidation with ground-glass attenuation. Eosinophils in bronchoalveolar lavage fluid were found to be 20%. She was diagnosed as EGPA in accordance with the criteria

Figure 1 Chest radiograph of the patient at the time of diagnosis.

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of the American College of Rheumatology. With the treatment with corticosteroid and cyclophosphamide, the pulmonary infiltration and skin eruption improved.

TREATMENT

The patient was diagnosed as EGPA, has been treated with 0.5 mg/kg/day of prednisolone for 6 months.

OUTCOME AND FOLLOW-UP

The patient's leucocytosis was $10\,400/\text{mm}^3$, 16% of which were eosinophils; she improved clinically and radiographically (figure 2).

DISCUSSION

Eosinophilic granulomatosis with polyangiitis, also known as Churg-Strauss syndrome, is a rare disease typically characterised by the triad of late onset asthma, eosinophilia and vasculitis.¹ This disease was first described in 1951 by Dr Jacob Churg and Dr Lotte Strauss.³ EGPA is described as having three progressive phases: (1) a prodromal *allergic/atopic phase* of asthma and rhinosinusitis, (2) an *eosinophilic phase* in which eosinophil-rich inflammatory tissue infiltrates develop and (3) a *vasculitic phase* the manifestations of which are similar to other ANCA-associated vasculitis.^{1 4} Our patient and her mother have been diagnosed as having asthma, and medical history of both showed severe, uncontrolled asthma requiring steroids. Asthma in EGPA occurs in almost all cases, often of a severe nature requiring steroids, as in our patients.^{1 5} Asthma in EGPA occurs for several years until the onset of the vasculitic phase.⁵ In our report, the patient was evaluated at a younger age than those cases in the previously published reports, because of the EGPA history of her mother. Upper airway involvement occurs in the majority of cases in the form of rhinosinusitis, which our patient and her mother both had.¹ Pulmonary involvement consists of irregular, migratory and bilateral infiltrates with areas of ground-glass appearance, as in our case. Extrapulmonary findings have been commonly reported among patients with EGPA, such as constitutional symptoms, musculoskeletal symptoms, cutaneous, peripheral nervous system, cardiac and gastrointestinal

involvement, mainly related to the vasculitic phase.^{1 6} The patient had weight loss and arthralgia; her mother had weight loss, paralysis and cutaneous involvement. p-ANCA is positive in approximately 40% of patients with EGPA, and our patient and her mother are both negative.⁷ Mild disease forms (without a severe life-threatening manifestation such as cardiac involvement) can usually be controlled with corticosteroids alone, as in our adolescent patient. Severe cases require prompt aggressive treatment based on combined corticosteroids and immunosuppressants (mainly cyclophosphamide).⁸

EGPA is a rare disease; a cross-sectional nationwide survey in Japan estimated the prevalence of EGPA at 17.8 per million patient.⁸ The mean age at onset was 55 ± 14 years.⁸ We diagnosed our patient as EGPA earlier than expected because of the positive history in her mother. EGPA does not exhibit gender predominance and the exact pathogenesis of EGPA is unknown.^{1 8} Genetic factors such as HLA-DRB4 may play a role in EGPA pathogenesis, however, there are no clear links between the genetic background and the disease.⁹ While familial cases of systemic vasculitis associated with p-ANCA-positive vasculitis and Wegener granulomatosis have been reported, as have cases of patients with EGPA with positive history for other vasculitides, there has been only one report of familial EGPA apart from our case report.^{2 10–12} In 2007 Tsurikisawa *et al*² first reported familial EGPA in two elderly sisters. They investigated the human leucocyte antigen typing of the sisters and their six living siblings but did not find any evidence of heritability of EGPA and could not explain the heritability of the disease from HLA typing.² To the best of our knowledge, ours is the second familial case of EGPA to be written up. We also present an adolescent patient with EGPA with histopathological examination supported by family history, her mother's diagnosed EGPA.

Learning points

- ▶ Eosinophilic granulomatosis with polyangiitis, also known as Churg-Strauss syndrome, is a rare disease typically characterised by the triad of late onset/uncontrolled asthma, eosinophilia and vasculitis.
- ▶ More than half of eosinophilic granulomatosis with polyangiitis (EGPA) patients have negative results for peripheral antineutrophil cytoplasmic antibodies.
- ▶ The exact pathogenesis of EGPA is unknown. We present the second known familial case of EGPA in a mother and daughter. EGPA disease should be kept in mind in a patient with uncontrolled asthma and eosinophilia with a positive family history of EGPA.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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Figure 2 Chest radiograph of the patient after steroid treatment.

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