

Case Report

Familial clusters of ANCA small-vessel vasculitis

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Abstract

Small-vessel vasculitides associated with the presence of antineutrophil cytoplasmic antibodies in the serum are characterized by inflammation and necrosis of small vessels. A pauci-immune necrotizing crescentic glomerulonephritis typically occurs when there is renal damage. Pathogenesis of these diseases remains unclear although infectious, genetic and environmental factors have been involved. Few familial clusters of antineutrophil cytoplasmic antibodies' small-vessel vasculitis are described in the literature. We report two families with first-degree relatives affected with antineutrophil cytoplasmic antibodies' small-vessel vasculitis.

Keywords: antineutrophil cytoplasmic antibodies; familial vasculitis; systemic vasculitis

Background

Wegener granulomatosis, microscopic polyangiitis and Churg–Strauss syndrome are small-vessel vasculitides that are associated with the presence of antineutrophil cytoplasmic antibodies (ANCA) in the serum. Pathologically, there is a necrotizing vasculitis that affects predominantly capillaries, venules and arterioles with the absence or paucity of immune-complex deposits in vessel walls. Renal pathology is typically characterized by a pauci-immune crescentic necrotizing glomerulonephritis. Generally, there is multi-organ involvement, but sometimes the pauci-immune crescentic glomerulonephritis occurs in the apparent absence of systemic vasculitis and is referred as a renal-limited vasculitis [1]. Infectious, genetic and environmental factors have been implicated in the pathogenesis of ANCA-associated vasculitis [2–5]. Few familial clusters of this disease have been described and those could support either a genetic susceptibility or a common environmental trigger [6].

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Case report

Family 1

In 1997, a 59-year-old woman presented to our hospital with haemoptysis. Chest CT scan showed diffuse pulmonary infiltrates. She had rapidly progressive renal failure with an active sediment and proteinuria. Myeloperoxidase (MPO)-ANCA was positive. A renal biopsy showed a pauci-immune crescentic glomerulonephritis with crescents in 70% of the glomeruli. Immunosuppressive treatment with corticosteroids (CC) and cyclofosamide (CFF) was started with partial improvement of renal function and resolution of pulmonary infiltrates. Over the following years she developed progressive renal failure, and 3 years later haemodialysis (HD) was started. She died in 2005 due to sepsis. Her 72-year-old sister presented to our hospital in 2006 with general malaise. She was found to have acute renal failure with an active sediment and proteinuria. Chest CT scan revealed diffuse ground-glass opacities. MPO-ANCA was positive. A renal biopsy showed a pauci-immune crescentic glomerulonephritis with crescents in 60% of the glomeruli. She started haemodialysis, CC, CFF and plasmapheresis. There was no improvement in renal function, and she remains on HD.

Family 2

A 40-year-old woman presented to another hospital, in 2001, with fever, arthralgias, bilateral uveitis and purpura. She was found to have acute renal failure with an active sediment and proteinuria. Chest CT scan showed bilateral ground-glass opacities. Proteinase 3 (PR3)-ANCA was positive. A skin biopsy showed a leucocytoclastic vasculitis, and a renal biopsy showed a pauci-immune crescentic glomerulonephritis. CFF and CC were started with renal function improvement.

Her 77-year-old father presented in 2005 with severe renal failure. Urinalysis showed an active urine sediment and proteinuria. He was found to be MPO-ANCA positive. A renal ultrasound revealed small, hyperecogenic kidneys. A renal biopsy was not performed nor immunosuppressive treatment started, and he was started on HD.

Discussion

In most of the family clusters of ANCA-associated small-vessel vasculitis previously described, the presenting features of the different members affected were separated in time, as occurred in our cases. However, in other reported cases they presented almost simultaneously [4,6–8]. In general, first-degree relatives were affected, as in our families [4,6,7,9]. Different organs can be involved in different relatives, but in some families the presenting clinical picture was the same [6,7,9]. In our first family, both sisters had kidney and lung involvement, whereas in the second family, the daughter had joint, eye, skin, lung and kidney involvement but the father had only renal-limited disease. Serological findings can also be different in different relatives, as occurred in our second family. Most of the families previously reported share the same type of ANCA [4,6,8].

The occurrence of familial clusters of ANCA vasculitis suggests that genetic factors might be involved in its pathogenesis. However, a Swedish study found that the occurrence of Wegener's granulomatosis among close biologic and non-biologic relatives of patients with the disease was low, providing evidence against an increase in familiar risk, such as that noted for other auto-immune diseases [2]. Few studies also suggested an increased susceptibility associated with some HLA classes, such as HLA-B8, DR2 and DR4 [6,10]. A more detailed investigation, especially with

HLA typing, is necessary to find if there are any alleles associated with these diseases.

Conflict of interest statement. None declared.

References

1. Falk R, Jennette C. ANCA small-vessel vasculitis. *J Am Soc Nephrol* 1997; 8: 314–322
2. Knight A, Sandin S, Askling J. Risks and relative risks of Wegener's granulomatosis among close relatives of patients with the disease. *Arthritis Rheum* 2008; 58: 302–307
3. Albert D, Albert A, Vernace M *et al.* Analysis of a cluster of cases of Wegener granulomatosis. *J Clin Rheumatol* 2005; 11: 188–193
4. Manganelli P, Giacosa R, Fietta P *et al.* Familial vasculitidis: Churg-Strauss syndrome and Wegener's granulomatosis in 2 first-degree-relatives. *J Rheumatol* 2003; 30: 618–621
5. Falk C, Jennette C. ANCA are pathogenic—Oh yes they are!. *J Am Soc Nephrol* 2002; 13: 1977–1979
6. Hay EM, Beaman M, Ralston AJ *et al.* Wegener's granulomatosis occurring in siblings. *Br J Rheumatol* 1991; 30: 144–145
7. Muniain M, Moreno J, Cámpora R. Wegener's granulomatosis in two sisters. *Ann Rheum Dis* 1986; 45: 417–421
8. Heras M, Fernandez-Reyes MJ, Sánchez R *et al.* Pauci-immune necrotising glomerulonephritis associated with ANCA in two siblings. *Port J Nephrol Hypert* 2008; 22: 197–200
9. Sewell R, Hamilton D. Time associated Wegener's granulomatosis in two members of a family. *Nephrol Dial Transplant* 1992; 7: 882
10. Nowack R *et al.* Familial occurrence of systemic vasculitis and rapidly progressive glomerulonephritis. *Am J Kidney Dis* 1999; 34: 364–373

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