Familial clusters of ANCA small-vessel vasculitis

Ana Marta Gomes¹, Filipe Nery², Ana Ventura¹, Clara Almeida¹ and Joaquim Seabra¹

¹Department of Nephrology, Centro Hospitalar Vila Nova Gaia/Espinho, Gaia and ²Department of Internal Medicine, Centro Hospitalar do Porto-Hospital Sto António, Porto, Portugal

Abstract
Small-vessel vasculiitides 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 vasculitides are described in the literature. We report two families with first-degree relatives affected with antineutrophil cytoplasmic antibodies’ small-vessel vasculitis.

Keywords: antineutrophil cytoplasmatic antibodies; familial vasculitis; systemic vasculitis

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 cyclofosfamide (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 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.

Correspondence and offprint requests to: Ana Marta Gomes, Department of Nephrology, Centro Hospitalar Vila Nova Gaia/Espinho, Rua Conceição Fernandes, 3343-502 Vila Nova de Gaia, Portugal. Tel: +351919859507; Fax: +351227538982; E-mail: ampgomes@gmail.com

© The Author (2008). Published by Oxford University Press on behalf of ERA-EDTA. All rights reserved. For Permissions, please e-mail: journals.permissions@oxfordjournals.org
**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**


Received for publication: 8.8.08
Accepted in revised form: 6.10.08