Rheumatology 2002;41:588–589

Wegener’s granulomatosis and rheumatoid arthritis overlap

Sir, Wegener’s granulomatosis and rheumatoid arthritis (RA) are clinically and immunologically independent diseases. In both cases, treatment with immunosuppression is required for active disease. Associations have been described. Schwarz-Eywill et al. [1] report a case of RA that manifested generalized Wegener’s granulomatosis despite treatment with methotrexate. A study by Mustila et al. [2] showed that in early RA, pANCA (antineutrophilic cytoplasmic antibodies, perinuclear pattern) was associated with serological markers of RA and predicted rapid radiographic destruction. Other reports have been published of patients with RA developing Wegener’s granulomatosis [3–6]. We report two patients with overlap, one of whom had Wegener’s granulomatosis, later developing RA.

Case 1 was a 32-yr-old man who was diagnosed with RA according to the American College of Rheumatology criteria in January 1990. He presented with symmetrical synovitis of the metacarpophalangeal (MCP) joints, proximal interphalangeal joints and nodule of the left elbow. Morning stiffness lasted 2 h. RA latex was positive and the C-reactive protein concentration was raised. Hand X-rays showed erosions in several MCPs. At the time he had an episodic productive cough of brown sputum. Serial chest X-rays had shown right apical and then left hilar shadowing. In January 1990, bronchoscopy revealed a mucous plug and histology showed non-specific type chronic inflammation. Repeat bronchoscopy a month later showed granulation tissue, and during the procedure it was noted that anaesthetic trickled out of the left nostril. He was empirically started on antituberculous therapy.

In March 1990, a positive ANCA was noted (1 : 1000). He was complaining of a blocked nose and his pharynx was inflamed. Nasal biopsy showed no granulomas. Open lung biopsy confirmed Wegener’s granulomatosis with focal necrotizing granuloma. The patient was commenced on prednisolone, and given a total of six pulses of intravenous cyclophosphamide. The antituberculous therapy was stopped. He improved significantly thereafter, and continued on azathioprine and prednisolone for 18 months. Oral cyclophosphamide and prednisolone were started in 1992, when further perihilar shadowing was noted. Subsequent investigations found positivity for pANCA with a titre of 1 : 512, but negativity for cANCA (ANCA, cytoplasmic pattern), myeloperoxidase and proteinase 3. Of interest, the patient’s son subsequently developed polyarteritis nodosa.

Case 2 was a 26-yr-old woman who presented with Wegener’s granulomatosis and then RA 15 yr later. In August 1965, she developed almost complete consolidation of both lungs with cavitation following dental extraction 6 weeks earlier. Antibiotics made no difference. A transbronchial lung biopsy was performed, showing focal areas of necrosis with eosinophils and giant cells in the surrounding granulation tissue, consistent with Wegener’s granulomatosis. Oral prednisolone was commenced and on discharge 2 weeks later her chest X-ray was clear. Maintenance treatment was with low-dose prednisolone and hydroxychloroquine. The latter was stopped 1 yr later, but attempts to stop the steroids led to further lung cavitations and gum discharge, resolving on restarting therapy.

In 1980, she developed a swollen right MCP. Three years later her wrist became swollen, with an erythrocyte sedimentation rate (ESR) of 21 mm/h. In 1984, she developed MCP and wrist synovitis, with restriction of flexion, reduced grip strength and prolonged morning stiffness. Blood tests showed ESR 92 mm/h and positivity for rheumatoid factor. X-rays of hands and feet showed marked periarticular osteoporosis with metatarsophalangeal head erosions, and knee X-rays showed narrowing of the joint spaces. Her symptoms improved with Indocid (indometacin), cyclophosphamide and prednisolone. pANCA was positive in December 1992, but became negative in 1994. There was no recurrence of the Wegener’s granulomatosis, but she went on to require a right knee arthroplasty in 1992 and debulking of right wrist synovium in March 1999.

Overlap syndromes with RA have been reported frequently, but overlap with Wegener’s granulomatosis appears to be rare. The immunological profile in our patients is interesting as both were positive for pANCA rather than cANCA, which is more usually associated with Wegener’s granulomatosis. Myeloperoxidase antibodies were negative in case 1, suggesting atypical ANCA with a determined antigen. The positive pANCA in case 2 predated routine testing for myeloperoxidase or proteinase 3. Theoretically, the antigen could be the same in both cases. A study has shown that positivity for pANCA in RA indicates severe basic disease with increased inflammatory activity [7]. However, data suggesting that ANCA positivity enhances the risk of vasculitis is contradictory [8]. There is small value in ANCA testing unless systemic vasculitis is suspected. pANCA can be a significant and independent predictor of RA-associated nephropathy [7]. Neither of our cases developed renal complications. Wegener’s granulomatosis can mimic other rheumatological conditions, and follow-up studies suggest that it starts as a localized vasculitis. A diagnosis of RA should be considered if joint disease becomes problematic in Wegener’s granulomatosis, rather than considering it a joint manifestation of the disease.
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Accepted 19 October 2001

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