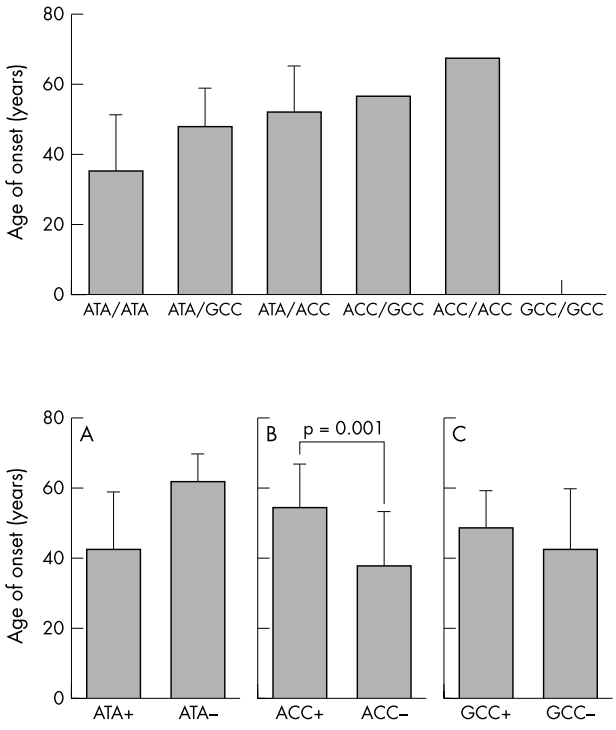

Figure 1 The effect of interleukin 10 (IL10) genotypes (upper part) on age at onset in Japanese patients with primary SS. (Lower part) Age at onset (mean and SD) is shown among the carriers and non-carriers of the IL10 ATA haplotype (panel A), ACC haplotype (panel B), and GCC haplotype (panel C), respectively.

sex, the presence of sicca symptoms, Schirmer test, salivary flow, or anti-Ro and anti-La antibodies (data not shown).

Our results suggested that the presence of the ATA haplotype and the absence of the ACC haplotype of the IL10 gene were associated with an increased sucseptibility to primary SS. Moreover, IL10 gene promoter region polymorphism affected the age at onset of SS, and supported evidence that variation in the age at onset of SS was genetically determined. We also clarified the association between IL10 gene polymorphisms and serum IgG levels. Brennan *et al* reported that a raised IgG level had a high specificity and high positive predictive value for SS.[10] IL10 gene polymorphism may become a useful predictor of SS.

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REFERENCES

1 **Nakken B**, Jonsson R, Bolstad AI. Polymorphisms of the Ro52 gene associated with anti-Ro 52-kd autoantibodies in patients with primary Sjögren's syndrome. *Arthritis Rheum* 2001;**44**:638–46.
2 **Perrier S**, Coussediere C, Dubost JJ, Albuisson E, Sauvezie B. IL-1 receptor antagonist (IL-1RA) gene polymorphism in Sjögren's syndrome and rheumatoid arthritis. *Clin Immunol Immunopathol* 1998;**87**:309–13.
3 **Hulkkonen J**, Pertovaara M, Antonen J, Pasternack A, Hurme M. Elevated interleukin-6 plasma levels are regulated by the promoter region polymorphism of the IL6 gene in primary Sjögren's syndrome and correlate with the clinical manifestations of the disease. *Rheumatology (Oxford)* 2001;**40**:656–61.
4 **Bolstad AI**, Wargelius A, Nakken B, Haga HJ, Jonsson R. Fas and Fas ligand gene polymorphisms in primary Sjögren's syndrome. *J Rheumatol* 2000;**27**:2397–405.
5 **Mullighan CG**, Heatley S, Bardy PG, Lester S, Rischmueller M, Gordon TP. Lack of association between mannose-binding lectin gene polymorphisms and primary Sjögren's syndrome. *Arthritis Rheum* 2000;**43**:2851–2.
6 **Wang Z**, Morinobu A, Kanagawa S, Kumagai S. Polymorphisms of the mannose binding lectin gene in patients with Sjögren's syndrome. *Ann Rheum Dis* 2001;**60**:483–6.
7 **Kumagai S**, Kanagawa S, Morinobu A, Takada M, Nakamura K, Sugai S, *et al*. Association of a new allele of the TAP2 gene, TAP2*Bky2 (Val577), with susceptibility to Sjögren's syndrome. *Arthritis Rheum* 1997;**40**:1685–92.
8 **Morinobu A**, Kanagawa S, Koshiba M, Sugai S, Kumagai S. Association of the glutathione S-transferase M1 homozygous null genotype with susceptibility to Sjögren's syndrome in Japanese individuals. *Arthritis Rheum* 1999;**42**:2612–15.
9 **Hulkkonen J**, Pertovaara M, Antonen J, Lahdenpohja N, Pasternack A, Hurme M. Genetic association between interleukin-10 promoter region polymorphisms and primary Sjögren's syndrome. *Arthritis Rheum* 2001;**44**:176–9.
10 **Brennan M T**, Sankar V, Leakan R A, Kleiner D, Atkinson J C, Wilkinson W E, *et al*. Risk factors for positive minor salivary gland biopsy findings in Sjögren's syndrome and dry mouth patients. *Arthritis Rheum* 2002;**47**:189–95.

Cigarette smoking, TB, and TNF inhibitors

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Accompanying the tremendous excitement about the introduction of TNF inhibitors into the clinic has been caution about potential adverse events that may be associated with the use of these potent immunomodulators. Increased susceptibility to certain infections, particularly *Mycobacterium tuberculosis* (TB), has been a particular concern.[1] Data from animal studies suggest that TNF has a central role in host defence against TB, in part related to effective granuloma formation.[2] For infliximab, 277 cases of TB had been reported world wide through August 2002 among more than 365 000 patients treated. Interestingly, although about 75% of infliximab use has been in the United States, more than two thirds of the reported TB cases were from outside the USA, mainly from the European Union. Part of the reason for this discrepancy may relate to a higher incidence of latent TB infection in the EU. However, we suggest that cigarette smoking may also be a relevant factor. In 2000, just over 23% of adults in the USA were current cigarette smokers, compared with about 30% of European adults (http://www.cdc.gov/tobacco; http://www.cisid.who.dk/tobacco—accessed

29/8/03). It has recently been shown that acetylcholine can inhibit the release of macrophage TNFα and attenuate inflammatory responses.[3] The inhibition is through a post-transcriptional mechanism that is dependent on the α7 subunit of the nicotinic acetylcholine receptor on human macrophages. Nicotine is a potent agonist of these α7 receptors, providing some explanation for the immuno-modulatory effects of cigarette smoking in conditions such as ulcerative colitis.[4] Interestingly, an association between tobacco smoking and TB has been noted in patients from southern India, with an odds ratio among smokers of 2.48 (95% confidence interval 1.42 to 4.37).[5] Unfortunately, information on smoking histories among patients with RA and TB treated with TNF inhibitors is not readily available from pharmacovigilance data. Among the varied deleterious effects cigarette smoking has on pulmonary funtion, it can damage the respiratory mucosa, thereby impairing host resistance to infection. Interestingly, it has recently been noted in a trial of anakinra that patients with underlying pulmonary disease seemed to be at a particular risk for developing pneumonia.[6] Therefore, rheumatologists ought to elicit a smoking history and advise stopping smoking among patients with RA, particularly those being considered for treatment with TNF inhibitors.

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REFERENCES

1 **Keane J**, Gershon S, Wise RP, Mirabile-Levens E, Kasznica J, Schwieterman WD, *et al*. Tuberculosis associated with infliximab, a tumor necrosis factor α-neutralizing agent. *N Engl J Med* 2001;**345**:1098–104.
2 **Mohan VP**, Scanga CA, Yu K, Scott HM, Tanaka KE, Tsang E, *et al*. Effects of tumor necrosis factor alpha on host immune response in chronic persistent tuberculosis: Possible role for limiting pathology. *Infection Immunity* 2001;**69**:1847–55.
3 **Wang H**, Yu M, Ochani M, Amella CA, Tanovic M, Susarla S, *et al*. Nicotinic acetylcholine receptor α7 subunit is an essential regulator of inflammation. *Nature* 2003;**421**:384–8.
4 **Floto RA**, Smith KGC. The vagus nerve, macrophages, and nicotine. *Lancet* 2003;**361**:1069–70.
5 **Kolappan C**, Gopi PG. Tobacco smoking and pulmonary tuberculosis. *Thorax* 2002;**57**:964–6.
6 **Fleischmann RM**, Schechtman J, Bennett R, Handel ML, Burmester GR, Tesser J, *et al*. Anakinra, a recombinant human interleukin-1 receptor antagonist (r-metHuIL-1ra), in patients with rheumatoid arthritis. *Arthritis Rheum* 2003;**48**:927–34.

Large synovial cysts originating from the sternoclavicular joints in a patient with rheumatoid arthritis

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Synovial cysts in rheumatoid arthritis (RA), most common in the popliteal fossa,[1 2] have also been described in proximity to several other rheumatoid joints,[3–9] but never the sternoclavicular joints.

CASE REPORT

We here describe, for the first time, the development of unusually large synovial cysts, from the disproportionately small sternoclavicular joints, in a 58 year old man, with a 27 year history of severe, seropositive, erosive, destructive, deforming, nodular RA. Over the years he had been treated, albeit erratically, with several disease modifying antirheumatic drugs (DMARDs), but he had been poorly followed up.

Seven months ago, while receiving D-penicillamine 500 mg/day and methylprednisolone 2 mg/day, he presented with a 10 cm long and 5 cm thick, fluctuant, non-tender, sausage-like mass over the right clavicle, and a smaller one, about 5 cm long over the left clavicle, developed gradually over one month. Routine haematology and biochemistry were normal. A purified protein derivative (PPD) skin test was negative.

A chest computed tomomographic (CT) scan (fig 1A) showed sclerosis and subchondral and marginal erosions in the manubriosternal and both sternoclavicular and first costosternal articulations. The posterior sternal surface was largely eroded, and the cancellous portion transformed to a smooth walled cavity, filled up with soft tissue. The overlying anterior thoracic wall soft tissues contained several cystic lesions, 1–6 cm in diameter, arranged parallel to the two lateral sternal borders. The four upper costovertebral joints (not shown) were similarly affected. Paracentesis of the right mass yielded a turbulent dark yellow fluid, with white blood cells (WBCs) 40.5×10^9/l (82% polymorphonuclear cells (PMNs)), sugar of 80 mg/l and no malignant cells. Direct stains and cultures for common and acid fast bacteria and fungi were negative. An open biopsy of the wall of the mass on the right showed granulomatous fibrous tissue, with no evidence of malignancy and negative culture. After a repeat paracentesis with similar results, three months later, an injection, with a long acting corticosteroid preparation, of both masses was performed. Two months later, the left mass disappeared and that on the right was significantly reduced, confirmed by a second CT scan (fig 1B). This scan disclosed further excessive destruction of the left glenohumeral joint and a 6 cm synovial cyst, just anteroinferior to that, under the left upper thoracic muscles. A magnetic resonance imaging (MRI) scan confirmed, additionally, that the cysts contained only fluid, whereas their walls showed enhancement after the administration of paramagnetic medium, suggesting active inflammation (figures not shown). Furthermore, MRI showed that the soft tissue eroding the upper part of the sternum had broken into the anterior mediastinum, in close contact with the anterior pleura. Although the whole area was examined meticulously by MRI, in more than two planes, no communication of the cysts with the proximal or remote joints was demonstrated.

DISCUSSION

The synovial origin of the described lesions was strongly supported by (*a*) their cystic nature confirmed by CT and