Age of onset in successive generations of patients with a spondyloarthritis

Juvenile spondyloarthritis (JSPA) is as yet not a fully defined disorder, but can be considered as a juvenile form of the adult spondyloarthritis (SPA). Preliminary criteria for the latter have been proposed, the tip of the iceberg being ankylosing spondylitis. These criteria are also applicable for JSPA. The clinical presentation of JSPA may differ from adult onset SPA, but eventually a considerable percentage of patients with JSPA will develop a clinical picture indistinguishable from adult SPA. Ankylosing spondylitis has a strong association with the presence of the HLA-B27 antigen. The risk for a first degree HLA-B27 positive relative of a patient with ankylosing spondylitis developing that disease is about 20%. The prevalence of SPA in parents of children with early onset pauci-articular chronic arthritis than in the general population was reported previously. Possibly, the prevalence of SPA among parents with a child with SPA might also be higher than in the general population. We report that there is a tendency towards an earlier onset of SPA in the next generation.

Seven index patients were seen in the paediatric rheumatology clinic and presented with JSPA according to the European Spondyloarthropy Study Group (ESSG) criteria, around the age of 10 (table). The age of onset in the children varied from 5 to 10 years (mean 8.3) and in the parents from 21 to 42 years (mean 31.1). The year of onset is the year the first complaints relating to the SPA were noticed. The clinical picture of the juvenile patients consisted of an asymmetric, IgM rheumatoid factor negative oligoarthritis with a predilection for joints in the lower extremities combined with features of enthesis. Symptoms of inflammation of the lower lumbar spine were rare at presentation. All the children carried the HLA-B27 antigen. One of the parents of these seven index patients developed SPA (retrospectively diagnosed) according to the ESSG criteria in their third or fourth decade.

There may be several explanations for our observation. It could be a coincidental finding or biased by our daily practice: a parent might pay more attention to joint or back complaints when his/her child is diagnosed as having JSPA. It might also be explained by a simultaneous infection in the presence of the HLA-B27 antigen in the family members of two generations. A marked discrepancy between the calendar years of onset for the children and parents pleads against temporal clustering. Another explanation might be genetic anticipation, which has been clearly delineated in some diseases, where there is a tendency for the disease to start earlier in successive generations over subsequent generations. This phenomenon has been described in several monogenic neurodegenerative disorders and possibly exists in familial rheumatoid arthritis. Recent studies have suggested that factors other than genetic factors may be associated with SPA. A variation in age of onset (5-81 years) was noted in one multicase family with a tendency towards an earlier age of onset in successive generations.

Extended studies of HLA and non-HLA genes are required to answer the question whether the phenomenon of genetic anticipation occurs in SPA.

As unstable trinitucleotide repeats have been described in neurodegenerative diseases correlating with the clinical phenotype of genetic anticipation it may be worth looking for unstable genetic elements in familial SPA.

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Quinine induced lupus-like syndrome and cardiolipin antibodies

A large number of drugs are known to cause a clinical syndrome resembling systemic lupus erythematosus. The antihistaminergic agents, quinidine has frequently been reported to cause such a syndrome. Additionally, the presence of cardiolipin antibodies has been described in patients receiving phenothiazine, procainamide, and ethosuximide. Quinidine is an antimalarial drug analogue to quinidine that can also produce several autoimmune abnormalities, but a lupus-like syndrome and production of cardiolipin antibodies induced by this drug have not been previously described. We report a case of well documented quinidine induced lupus-like syndrome in which cardiolipin antibodies were also found.

A 30 year old white woman was admitted to our hospital in May 1994 because of fever, chills, and diaphoresis of three days' duration. Six weeks before admission the patient had been on vacation in Cameroon, but she did not take any prophylaxis for malaria. Physical examination was unremarkable at time of admission except for fever up to 40°C. Laboratory examinations disclosed a packed cell volume of 0.37, haematocrit 11%, and normal white cell count of 3.8 \times 10^9/\text{l} (76% neutrophils, 20% lymphocytes, 4% monocytes), and platelet count of 150 \times 10^9/\text{l}. Thrombocytosis and hyperferritinaemia were noted. The patient was diagnosed as having malaria and treated with quinine sulphate 600 mg three times daily.

Forty eight hours into treatment the patient became afibrile and a thick smear became negative for malaria. The patient complained of dyspnoea and constant retrosternal chest discomfort, and developed a systolic murmur with an ejection click. The murmur was best heard over the precordium with a thrill of 1+ and a grade I-2 murmur extending through the aortic area.

A 2-dimensional echocardiogram showed severe mitral regurgitation with multiple small vegetations, moderate tricuspid regurgitation and thickening of all the valves. An antemortem diagnosis of endocarditis with quinidine induced lupus-like syndrome was made.

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