

Ankylosing Spondylitis and Allied Diseases in Adults and Children

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Ankylosing spondylitis (AS) is a human leukocyte antigen (HLA)-B27-associated disease that is characterized by chronic progressive inflammation in the axial joints and entheses (the ligaments and tendon attachments in bone). The disease has late involvement in other organs including the eyes, lungs, skin and kidney. Juvenile-onset spondyloarthropathies (JSpAs) are a group of HLA-B27-associated disorders in children and teenagers younger than 16 years of age, and which are characterized by asymmetric arthritis and enthesitis largely in the lower limbs. JSpAs encompass several well-defined disease entities including seronegative enthesopathy and arthropathy (SEA) syndrome,¹ reactive arthritis, Reiter disease, inflammatory bowel disease-associated arthropathies, psoriatic arthropathy and juvenile ankylosing spondylitis (JAS). Unlike adult-onset AS (AAS), JAS typically presents as inflammation around entheses. It is also highly associated with the HLA-B27 antigen.² As much as 90% of JAS patients have been detected to have HLA-B27, but only about 60% of children with JSpAs have been found to be HLA-B27-positive. Nevertheless, the presence or absence of HLA-B27 cannot be regarded as a reliable criterion to establish or refute diagnosis of JAS.² In many patients, the specific diagnosis remains "undifferentiated", with some of them fulfilling criteria for SEA syndrome³ or more bizarre presentations of undifferentiated spondyloarthropathy. Over time, some of these children with undifferentiated spondyloarthropathy develop definite sacroiliitis, fulfilling the criteria for JAS.⁴ It has been estimated that JAS accounts for about 20% of JSpAs.

In general, spondyloarthropathy (SpA) rarely occurs before the second decade of life. On the other hand, typical AAS usually starts at around 15 years of age. JAS is much more common in boys than in

girls, but the other subsets of JSpAs have a more equal sex distribution. A family history of similar presentations is frequently present, even in those who do not have HLA-B27 antigen.⁵ A prospective pediatric rheumatology registry for JSpAs and other rheumatic diseases has shown incidences of 53% for juvenile rheumatoid arthritis, 13% for JSpAs, 10% for vasculitides, 6% for systemic lupus erythematosus, 5% for isolated Raynaud's phenomenon, 5% for dermatomyositis/polymyositis and 2% for scleroderma among 1,742 children who were diagnosed with rheumatic diseases.⁶ Thus, well-recognized juvenile rheumatoid arthritis accounted for more than half of the pediatric patients with rheumatic presentation. Over time, there would be patients with JSpAs turning out to have rheumatoid arthritis. However, those data may be biased by the failure of many children with mild SpA to be properly recognized and referred to rheumatologists.

The International League Against Rheumatism has proposed another term for this group of diseases in young age, i.e. juvenile idiopathic arthritides (JIAs),^{7,8} which must fulfill at least 2 of the following criteria including tenderness in a sacroiliac joint and/or inflammatory spinal pain, presence of HLA-B27 antigen, 1st- or 2nd-degree next-of-kin with medically confirmed HLA-B27-associated disease, anterior uveitis associated with pain, red eyes, photophobia, or onset of arthritis after the age of 8 years in boys. In these proposed diagnostic criteria, 2 of the conditions should be excluded to diagnose JIA, i.e. psoriasis recognized in the patient's 1st- or 2nd-degree next-of-kin or the presence of systemic arthritis.

Except for joint inflammation and enthesitis, patients with JSpAs may also frequently present with extra-articular symptoms in the eyes, gut, skin and



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mucosa. These include uveitis,⁹ scleritis, secondary amyloidosis, Henoch-Schönlein purpura, IgA nephropathy and secondary sicca syndrome. Despite the difficulties in diagnosing and differentiating JSpAs from other juvenile arthritides, there has been significantly increased recognition and reporting of this group of diseases in recent years.

The prevalence, incidence, or clinical features of AAS or its relevance to SpA in Taiwan has not been well recognized, although scattered studies regarding the clinical manifestation and their genetic background have been sporadically reported.¹⁰⁻¹² In the November 2009 issue of the *Journal of the Chinese Medical Association*, Lin et al¹³ report a comparison between AAS and JAS. They analyzed 169 patients with AS, among whom 47 patients were recognized to have JAS at presentation. Both groups of patients had similar sex distribution, duration in delay of diagnosis and duration of the natural disease course. The JAS patients tended to develop initial inflammation around entheses or peripheral joints, while AAS patients had their initial manifestations in the axial joints. These findings were similar to those reported previously for Caucasians.^{1,2} In particular, onset of both JAS and AAS frequently coincided with overzealous physical exercise or physical trauma, indicating that the pathogenetic mechanism of SpA may be quite different from that of rheumatoid arthritis, which is characterized by intense lymphocyte infiltration in the synovium. On the other hand, this might be alternatively interpreted as the reason for delay in diagnosis. Indeed, the onset of SpA symptoms early in the second decade coincides with a period of steeply increased sports activity. Children with SpA are therefore commonly thought to have recurrent sprains or strains, resulting in ignorance of the true diagnosis.

Regarding the late manifestations in extra-articular organs, IgA nephropathy seemed to occur more frequently in JAS patients. It is unclear whether this was caused by longer incubation time for the development of renal inflammation in JAS patients or other unidentified environmental and genetic factors. After all, the sample size was too small to draw a definite conclusion. The drawback of the present investigation is that Lin et al were unable to include patients followed-up in the pediatric clinic. This dilemma was similar to that encountered previously by a pediatric rheumatology registry in New England.⁶ It might have led to underestimation of the JAS incidence in the 169 studied patients. In addition, the prevalence of rheumatoid

factor in serum or actual rheumatoid activity in these patients was not known. Previous investigations have shown that a substantial percentage of JIA or JSpA patients will eventually evolve to full-blown rheumatoid arthritis. This cohort of 169 patients deserves further long-term follow-up and evaluation to observe the disease outcome and complications. Nevertheless, their data may still shed some light on the study of juvenile arthritis because the true incidence and prevalence of SpA in Taiwan is still unknown.

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