Systemic-onset juvenile idiopathic arthritis and HLA-B27 juvenile-onset undifferentiated spondyloarthritis in the same patient

Sir,

In 2008, Akkoc and co-workers reported the cases of 4 adult patients suffering from coexisting spondyloarthritis (SpA), in particular ankylosing spondylitis (AS) and undifferentiated axial SpA, and adult-onset Still’s disease (AOSD) (1). In a recent article published in *Clinical and Experimental Rheumatology*, Hornoff and Burgos-Vargas (2) reminded us that up to 11% of patients with juvenile-onset AS and 6% of those with juvenile-onset undifferentiated SpA (3-6) may meet criteria for systemic-onset juvenile idiopathic arthritis (SoJIA) (6, 7), previously known as Still’s disease, during active periods of disease. Since 2003, we have been following up a boy suffering from HLA-B27 positive juvenile-onset SpA (2-5) who developed SoJIA (7), which we want to report briefly. He is one of the fourteen children with B27-positive enthesitis-related arthritis (ERA) we are following up with the aim to establish how many of them will develop axial involvement (8).

The patient was first seen in April 2003, when he was twelve-years-old, due to the onset of arthritis involving both shoulders. His medical and family history were negative for SpA and the other HLA-B27-associated syndromes. Physical examination revealed tenderness and limitation of both joints. Noteworthy laboratory evaluation included an erythrocyte sedimentation rate (ESR) (Westergren) of 47 mm/h and a C-reactive protein (CRP) of 142 mg/L (normal <5). HLA typing showed A2, A28, B13, B27, Cw2 and Cw6. Magnetic resonance imaging (MRI) of the shoulders showed joint effusion together with subacromial bursitis and tenosynovitis of the long head of the biceps brachii. Pelvis radiographs showed normal sacroiliac joints. A diagnosis of B27-positive ERA was made (6). In the following months, the patient developed enthesitis of the flexor carpi radialis together with extensor tenosynovitis of the right wrist. The patient was treated with nimesulide at a dose of 50 mg twice a day together with extensor tenosynovitis of the right wrist. The patient was treated with nimesulide at a dose of 50 mg twice a day and the disease spontaneously went in remission after three months.

In November 2007, the boy was admitted with the fever. Examination showed splenomegaly and cervical lymphadenopathy. Notable laboratory evaluation included ESR 71 mm/h, CRP 124 mg/L, ferritin 6870 ng/ml (normal range 20–200), white blood cell count of 32,000 cells/mm³ with neutrophilia, gamma-glutamyl transpeptidase (GGT) 102 U/L (nv <61), alanine aminotransferase (ALT) 97 U/L (nv <40). Ultrasound showed enlarged spleen and cervical lymph nodes and echocardiography demonstrated pericardial effusion and thickening. A diagnosis of SoJIA (6, 7) was made and the patient was given 50 mg/day of prednisone together with 75 mg/day of indomethacin with only a slight partial improvement of symptoms. Due to the persistence of the disease, methotrexate at a dose of 15 mg/week was added without any success.

In the following months, the patient was given anakinra at a dose of 1.5 mg/day. Recent studies suggested that anakinra can be useful in patients with SoJIA who have failed to respond to standard therapy (9). The patient had an excellent response to anakinra with resolution of fever and musculoskeletal symptoms. After two months, all laboratory findings were normal and the daily dose of prednisone was initially reduced to 25 mg/day. In July 2008, while on 5 mg/day of prednisone, fever and generalised pain, more severe at the neck and the superior left arm, reappeared and responded to increasing the prednisone dose up to 35 mg/day. Laboratory examination showed a CRP of 2.5 mg/L. In the following months, the prednisone dose was progressively tapered to the current dose of 2.5 mg/day and symptoms have not reappeared so far.

Our patient developed B27-positive ERA (6) when he was 12 and a clinical picture of SoJIA (7) when he was 16. The latter cannot be considered a systemic involvement of SpA because the typical features of SOJIA are present. Therefore, our patient is suffering from two different diseases. The diagnosis of SoJIA, which is today considered an autoinflammatory disease, could be made even if our patient did not have clear joint swelling and, for this reason, he did not meet the ILAR classification for this disease (6). It is well ascertained that SoJIA may occur for months and years without arthritis (10). It is possible that our patient has not developed arthritis so far since he is still on therapy with methotrexate and anakinra 22 months after the onset of the disease. In any case, other illnesses mimicking SoJIA including infectious diseases, connective tissue diseases, vasculitis, inflammatory bowel diseases, and malignancies have been excluded (7). In addition, the macrophage activation syndrome (MAS) (11) was excluded for the absence of cytopenia, hypertriglyceridemia, intravascular coagulation, central nervous system manifestations and for the presence of increased ESR.

There is general agreement that SoJIA and AOSD are part of the same clinical spectrum (10). However, the clinical classification criteria for each were elaborated independently and differ significantly. The major classification criteria for AOSD include arthralgia or arthritis of a two weeks duration or longer, a spiking fever of 39°C or higher lasting for at least 1 week, the characteristic rash and leukocytosis (12, 13). As already stated, the ILAR criteria consider arthritis as a condition sine qua non for the diagnosis of SoJIA (7). In addition, these criteria consider exclusions, one of these being the presence of arthritis in an HLA-B27 positive male beginning after the 6th birthday. According to the ILAR criteria, patients meeting criteria for two categories (SoJIA and ERA in our patient) should be classified as suffering from undifferentiated arthritis since systemic features in ERA patients exclude such diagnosis and HLA-B27 in systemic patients exclude the diagnosis of SoJIA. It should be remembered that classification criteria are built for epidemiological, clinical, therapeutic and basic science studies and have a limited diagnostic utility (14, 15).

In conclusion, the case of our patient confirms the observation by Akkoc et al. on the possible coexistence in the same patient of SpA and AOSD (1) and extends this possibility to the younger patients.

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References

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