DISEASE FLARE IN JUVENILE RHEUMATOID ARTHRITIS FOLLOWING INTESTINAL INFECTION

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Introduction:
Various infections have been linked to autoimmune disease both in humans and animal models. Enteric bacteria have been associated with reactive arthritis.

Case report:
A 19-year-old man, with sero-negative polyarticular juvenile rheumatoid arthritis for 6 years, well controlled on sulfasalazine for 2 years, presented with acute flare up of arthritis of both knees, both ankles, right wrist and right shoulder joint of 5-day duration. He was confined to bed due to severe pain in knees and ankles. One week prior to the onset of this flare, he had suffered from dysentery (8-10 loose stools/day, mixed with blood) for 2 days, was treated with ciprofloxacin and metronidazole. There was no skin rash, redness of eyes, oral ulcers or back pain. There was no past history of similar episodes. Examination revealed pallor, normochromic anemia (Hb 7.5 g/dL), raised inflammatory parameters (erythrocyte sedimentation rate- 56 mm fall in first hour), normocytic, normochromic anemia (Hb 7.5 g/dL), raised inflammatory parameters (erythrocyte sedimentation rate- 56 mm fall in first hour, C-reactive protein 3.5 mg/dL), platelets 4.5x10^5 /mm^3, and normal renal and liver function tests. Stool examination was negative for ova, cyst blood or leucocytes. Levels of C3d bound immune complexes in the serum (29 µg/ml) and in the synovial fluid (65 µg /ml) were high EIA (normal <1.2 µg / ml). Levels of IgA rheumatoid factor (IgA RF) in polyethylene glycol-precipitated immune complexes isolated from serum (14.3 arbitrary units /ml) and synovial fluid (7.95 arbitrary units/ml) were high (EIA normal < 1.56 arbitrary units). However, IgM RF could not be detected in the immune complexes using EIA. He improved with oral diclofenac sodium (150 mg/d) and injection methyl prednisolone 60 mg in the right knee joint; on follow-up hemoglobin increased to 12 g/dL over the next 6 weeks. The flare subsided of gastro-intestinal infection and exacerbation of arthritis, which had been in sustained remission in our patient, may be coincidental. It may, on the other hand, reflect a cause and effect relationship. Increased levels of C3d bound immune complexes, and of IgA RF in the immune complexes in the serum and synovial fluid provide indirect evidence for triggering role of intestinal infection, though we failed to identify the organism that caused dysenteric illness. Increased level of IgA RF has been described in patients with Lyme arthritis. Another possibility is that the patient had reactive arthritis in a setting of pre-existing Juvenile rheumatoid arthritis, however the joint involvement in lower limbs was symmetrical, unlike classical reactive arthritis. Several microbial agents like borrelia, brucella, and leptospirosa can trigger in a polyarticular illness, similar to that seen in this patient.

It is interesting that, in our patients joints were involved during the flare were the same as had been originally affected, it is therefore, possible that the original disease and the flare were caused by either the same microbial agent or those that share cross reactive epitopes. An infectious etiology has often been considered but never proven for JRA. Of the three types of JRA (based on onset), systemic onset subgroup is most likely to have an infectious etiology. However, in some cases of polyarticular type of JRA, re-exposure to influenza A H2N2 was postulated as a precipitating factor in disease development. Similarly, pauciarticular JRA has been linked to rubella, parvovirus, adenovirus and mycoplasma infections. Enteric infection like Yersinia enterocolitica is a common cause of reactive arthritis in childhood. Increased levels of C3d-bound immune complexes and of IgA RF in immune complexes in our patient at the time of disease exacerbation point towards a crucial role of immune complexes in the pathogenesis of acute synovitis. The analysis of microbial agent in the immune complexes could have provided further insight as to the cause of his flare.

References: