EUROPEAN JOURNAL OF INFLAMMATION Vol. 12, no. 1, 201-202 (2014)

LETTER TO THE EDITOR

RHEUMATOID ARTHRITIS-LIKE DISORDER MIMICKING SERUM SICKNESS: DO NOT FORGET ACUTE B HEPATITIS!

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Received May 4, 2013 – Accepted December 3, 2013

We report on a patient who presented with a severe symmetric polyarthritis that was found to be part of the prodromal stage of acute hepatitis B. This syndrome is seen in a minority of cases, resembles serum sickness and parallels the duration and level of hepatitis B viremia. It is a type III immune complex reaction with complement consumption and activation which ultimately triggers inflammation and may also occur in the context of other infections, vaccines, and use of antibiotics or sera. We emphasize the need to search for acute B hepatitis in all patients with polyarthritis or other symptoms of serum sickness.

A 34-year-old man was referred to us because of joint swelling and increasing pain which affected his hands, wrists, elbows, knees and ankles, and became progressively more severe in the arms than in the legs. The patient rated 8 on a scale of 0 to 10, with 10 indicating the most severe pain; he was not taking regular medication other than ibuprofen and acetaminophen for pain relief, and had no known allergies or a personal or family history of rheumatological and autoimmune disorders; his previous medical history was otherwise unremarkable. On examination, the joints of the hands, wrists, elbows, knees and ankles were diffusely swollen and warm with no effusions, active and passive movement of the joints caused pain, there was no muscle edema or tenderness, and muscle strength was normal; he had no pyrexia, vital signs were normal, and the remainder of the examination was normal. Erythrocyte sedimentation rate was 85 mm/hr, C-reactive protein (CRP) 15 mg/dL (normal < 0.5), complement C3 80 mg/dL (normal 90-170), and C4 20 mg/dL (normal 20-65); blood levels of liver enzymes, the complement hemolytic activity (CHA) and the other laboratory studies were normal. Autoimmunity screening, including antinuclear, anti-double-stranded DNA and antineutrophil antibodies, rheumatoid factor, antibodies to cyclic citrullinated peptide, cryoglobulin, and serology for HIV type 1 and type 2, *Borrelia burgdorferi*, syphilis, and parvovirus B19 were negative.

The patient was lost to immediate follow-up. Three weeks later, he returned with profound malaise and jaundice but had completely recovered from joint symptoms. At that time, bilirubin was 8.6 mg /dL (normal < 1), with conjugated bilirubin 3.2 mg/dL, alanine aminotransferase 2877 U/L (normal 5-40), and aspartate aminotransferase 1951 U/L (normal 5-40), search for HBsAg, HBeAg, and anti-HBc-IgM was positive, anti-HBs and anti-HBe IgG and IgM were nonreactive, and circulating hepatitis B virus (HBV) DNA was 120 x 10^6 IU/ml. Testing for hepatitis C virus, Epstein-Barr virus, and cytomegalovirus (CMV) was negative. He was treated supportively and was discharged on the 27th day with no evidence of active arthritis or hepatitis and normal levels of bilirubin, aminotransferases,

Key words: polyarthritis, serum sickness, B hepatitis, extrahepatic manifestations

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1721-727X (2014)

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C3, C4 and CHA; HBsAg, HBeAg, and HBV DNA were negative, anti-HBs and anti-HBe antibody had become positive, and anti-HBc had converted to IgG. At the last follow-up visit one year later, the patient was symptomless with no clinical or laboratory evidence of active hepatitis. He did not report any arthritis flare-up after his liver function returned to normal.

We ruled out all other causes of polyarthritis and the subsequent clinical course led us to implicate acute HBV infection as the cause of polyarthritis in this case. This syndrome, which resembles serum sickness, was first described by Graves in 1843 (1) and is part of the prodromal stage of acute hepatitis B, however it is seen in less than one-third of patients presenting with acute hepatitis B (2, 3). Polyarthritis is usually symmetric, with an additive or migratory pattern, and may be associated with morning stiffness, precedes the icteric phase by several days to several weeks, and has a mean duration of approximately two to three weeks (2, 3). Systemic symptoms such as malaise, fatigue and generalized weakness are common, furthermore an urticarial rash can occur coincidentally with the arthritis in about a half of cases, furthermore erythematous macules, papules, and petechiae may also be found (2, 3). Of note, our patient had no skin manifestation of the syndrome. This prodrome of acute B hepatitis resolves completely before or at the onset of the icteric phase but, even though some patients may have a long-lasting polyarthritis, joint destruction remains an almost rare complication (2, 3). The course of this syndrome often parallels the duration and level of viremia as rapid clearance of the virus is often associated with a rapid resolution of the illness.

A type III immune complex (IC) reaction, with consumption of complement caused by circulating small, soluble ICs that activate the complement cascade and Fc receptors, ultimately triggers inflammation (4). These ICs are formed in the zone of excess of antigens, i.e. epitopes of HBsAg, HBc, viral DNA, and complement components which indicate that a prolonged phase of persistent antigenemia is needed for this serum sickness-like disorder to develop. This typically occurs in the prodromal stage of acute B hepatitis and more rarely in the context of other settings such as CMV or enterovirus infections, subacute endocarditis, infected shunts or tunneled catheters, injection of serum, exogen protein or vaccines, and treatment with antibiotics such as penicillin and sulfonamides.

This report is a reminder of an old syndrome with which many of us are still unfamiliar. We emphasize the need to search for acute B hepatitis in all patients with polyarthritis or other symptoms of serum sickness even if aminotransferases and bilirubin are normal at presentation.

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