Erythema Nodosum and Acute Q Fever: Report of a Case with Granulomatous Hepatitis and Immunological Abnormalities

Sir,

We present a patient in whom acute Q fever infection appeared with fever and granulomatous liver involvement. The unusual aspects of this case included the appearance of erythema nodosum (EN) and transient immunological abnormalities during seroconversion to *Coxiella burnetii*. Resolution of all these manifestations was achieved with tetracycline therapy.

A 38-year-old man from a rural area was hospitalized with a history of fever reaching 40°C for 5 days, with general malaise. No previous history of drug intake was obtained. Physical examination showed only hepatomegaly. Routine laboratory investigations showed a high erythrocyte sedimentation rate (102 mm/h) and slightly elevated liver enzymes. Cultures of blood, urine and stools were negative. Serologic investigations were negative for hepatitis virus, cytomegalovirus, herpes simplex, Epstein-Barr virus, HIV, *Brucella*, *Salmonella*, mycoplasma and syphilis. Q fever serology (IgM against phase II *C. burnetii* antigen on an indirect immunofluorescence test) was negative on the 2nd day after admission.

On the 6th hospital day, the sudden onset of bilateral tender nodules on the anterior aspects of the legs and dorsa of the feet was evident. Both ankles were swollen and painful. The patient was not taking any medication. Skin biopsy showed only a subcutaneous involvement with a septal inflammation. Lymphohistiocytic cells predominated, with rare neutrophils. Granulomas or fat lobule involvement were not observed. Based on these data, a diagnosis of acute EN was made. At the same time, a seroconversion to Q fever agent was detected, later reaching 1/2,560. Liver biopsy showed granulomatous hepatitis. Repeated chest radiograms were always normal, as was echocardiogram. Immunologic studies were also made. ANA, rheumatoid factor and complement were normal or negative. Circulating immune complexes were positive. Polyclonal IgG and IgM cryoglobulins and circulating anticoagulant antibodies were also detected. A diagnosis of acute Q fever was made and therapy with tetracycline (2 g/day) was started on the 8th day after admission and maintained for 2 weeks. Acetylsalicylic acid was also given for 1 week. After treatment, fever, general malaise and liver enzymes returned to normal in less than 1 week; nodules were slow, resolving in 3 weeks. Q fever serology became negative, as did immunological abnormalities after 4 months. The evolution of Q fever serology was: January 4: (-); January 10: 1/40; January 26: 1/640; February 8: 1/2,560; March 4: 1/80; May 12: (-).

We present further evidence that EN and simultaneous immunological abnormalities may appear during acute Q fever infection. In our opinion, these findings are a true complication of acute Q fever rather than a merely coincidental event, due to: (1) the chronologic correlation between the appearance of Q fever and that of EN and immunological abnormalities; (2) the resolution of all these disorders after tetracycline therapy; (3) the absence of other etiologic factors; (4) evidence that EN is frequently a hypersensitivity reaction to an infectious agent; (5) the existence of two other previously reported cases with EN in Q fever (1,2); (6) evidence of other sporadic cases of cutaneous hypersensitivity reactions in Q fever such as vasculitis (3), erythema annulare centrifugum (4), or temporal arteritis (5); (7) demonstrated evidence that non-specific immunological abnormalities may be induced during acute and chronic Q fever, such as: circulating anticoagulant or antiphospholipid antibodies (6,7); smooth muscle antibodies (8); antiplatelet antibodies (9); circulating immune complexes (2); cryoglobulins (9); or transient monoclonal gammopathies (2). Furthermore, it has been observed that these findings are more frequent if liver involvement is present (8), as in the case presented here.

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