

Letters to the Editor

nonlateral joint involvement, which have been reported to be very low in the overall literature (5-7). Another unusual feature in our case history was the dramatic clinical picture. The absence of a skin rash, on the contrary, cannot be considered an unexpected finding, since its prevalence in a pediatric population with B19-associated arthritis has been recently reported to be lower than 50% (5).

In this case the overall clinical picture, the laboratory tests demonstrating abnormal indices of inflammation and the rapid response to anti-inflammatory therapy could suggest the hypothesis of a rheumatic-like disease. It is known that both in children and adults B19 infection has been implicated as a possible triggering factor of autoimmune diseases affecting the joints, connective tissue and large and small vessels, thus confirming that B19 may contribute to the induction of autoimmune reactions (8, 9). Therefore, we can underline, on the basis of our atypical case report, the conclusions by Oguz *et al.* (5) that B19 IgM have to be searched for in children who present with acute monoarthritis, whatever the clinical picture and localization.

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Comparison of serum IgE levels between female and male SLE patients, with reference to gender differences in the incidence of SLE

Sirs,

Several studies have been performed to investigate the importance of the serum IgE level in systemic lupus erythematosus (SLE) (1-3). It has been reported that serum IgE levels are significantly higher in the active stage of SLE when compared with the level during remission (1). Our recent study of 51 patients with SLE (45 women and 6 men) revealed significantly higher IgE levels in SLE patients compared with normal controls (450.5 ± 1136 IU/ml in 51 SLE patients vs. 72.7 ± 87 IU/ml in 391 controls, $p = 0.007$) independent of disease activity (2). In general, the IgE level in SLE patients does not appear to be related to the development of atopic diseases (3).

As shown in Table I, 7 out of 12 male patients (58%) in our SLE cohort showed high serum IgE levels (> 250 IU/ml) compared with normal controls (normal 250 IU/ml). In contrast, 21% (10/47) of our female SLE patients showed high IgE levels (> 250 IU/ml). There was a significant difference in the prevalence of high serum IgE levels between male and female SLE patients ($p = 0.011$ by the chi-squared test performed with SPSS software; Chicago, USA). In contrast, a significant difference was not observed in the average amounts of IgE levels between male and female SLE patients (399 ± 372 IU/ml in 12 male patients vs. 330 ± 755 IU/ml in 47 female patients, $p = 0.66$), probably because certain female patients showed extremely high levels of IgE. In our male patients, no significant correlation was observed between IgE and other serum parameters such as immunoglobulins (IgG, IgA, and IgM) and autoantibodies. Thus,

their high serum levels of IgE did not seem to result from polyclonal B cell activation. A history of atopic disease in 12 male patients was only obtained in one patient.

The prevalence of SLE is significantly higher in females than in males, and this is probably due to promotion of the immune response by sex hormones (especially estrogen), including the production of several cytokines (such as interleukin (IL)-1, -6, and -10) and antibodies mediated by these T helper-2 (Th-2) cytokines (4). Estrogens are also reported to contribute to an increase in the transcription of autoantigens (5), such as human endogenous retroviruses (HERV) that may be a plausible causative agent of SLE (6). Thus, female hormones such as estrogen appear to cause a decrease in the threshold for responsiveness to autoantigens and/or production of autoantigens, and that this is related to a higher incidence of SLE in females. In addition, DNAmethylation seems to play an important role in the induction of autoimmunity in SLE. Low levels of cytosine methylation (indicated by low activity of DNA methyltransferase-1 (DNMT-1), a methylation-regulating enzyme) in the regulatory sequences of DNA leads to transcriptional activation of genes, and DNA methylation is decreased in both male and female SLE patients (7). DNAhypomethylation (implied by low DNMT-1 activity) is thought to contribute to hyperresponsiveness to autoantigens in SLE patients and to the production of autoantigens, including HERV (7). It has been reported that IgE production is contributed by DNA hypomethylation and is also enhanced by estrogens (8, 9). The levels of IgE production mediated by IL-4 are known to be closely associated with the estrogen level (4). Thus, high IgE levels in male SLE patients may reflect stronger hyperresponsiveness due to DNAhypomethylation that is not related to the influence of sex hormones.

Further precise clinical and/or laboratory investigations of male SLE, as well as female patients with the postmenopausal onset of SLE (10), may make an important contribution to elucidation of the reason for the gender bias of this disease.

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Table I. Serum IgE levels in male and female SLE patients.

| Sex | No. of pts. | IgE | | Pvalue (male vs. female) |
|--------|-------------|-----------------------|-------------------------|--------------------------|
| | | High (> 250 IU/ml) | Low (≤ 250 IU/ml) | |
| Male | 12 | 7 (58%) | 5 (42%) | < 0.05 |
| Female | 47 | 10 (21%) | 37 (79%) | |

IgE was measured by chemiluminescent enzyme immunoassay (CLEIA; Fuji Levio Co., Inc. Tokyo, Japan).

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Announcements

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Stresa, Italy, 20-22 September 2004

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1ST EUROPEAN COURSE ON CAPILLAROSCOPIC AND RHEUMATIC DISEASE

Genoa, Italy, 10-12 September 2004

Purpose: An introductory clinical and practical course on the role of capillaroscopy in Raynaud's phenomenon and rheumatic diseases.

Scientific secretariat: Prof. Maurizio Cutolo, MD, Division of Rheumatology DIMI, Univer-

sity of Genova, Italy. E-mail: mcutolo@unige.it

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IV INTERNATIONAL CONFERENCE ON SPONDYLOARTHROPATHIES

Gent, Belgium, 7-9 October 2004

Topics: Innate immunity: Toll-like receptors and chronic inflammation, HSPs as activators of innate immunity, NK receptors and the immune response, gene expression profiles
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XI INTERNATIONAL CONFERENCE ON ANTIPHOSPHOLIPID ANTIBODIES

Sydney, Australia, 14-18 November 2004

For complete information on the meeting, please visit the website: <http://www.xith-icaa2004.unsw.edu.au/sydney/index.html>

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Royal College of Physicians, London, UK

3-5 March 2005

Chairman: Professor David Isenberg, MD, FRCP

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