To the editor:

Is hemophagocytic lymphohistiocytosis an autoimmune disease?

Arkwright et al recently reviewed the association of autoimmunity with several inherited immunodeficiency diseases. It has been suggested that most if not all autoimmune diseases are initiated by response to a single self-antigen. Mackay and Rosen defined an autoimmune disease as a clinical syndrome caused by the activation of T and/or B cells in the absence of an ongoing infection or other discernible cause. In many cases of autoimmune diseases, autoantibodies are produced and may serve as markers of the antigen-specific B- and T-cell response.

In the context of X-linked lymphoproliferative disease (XLP) and other inherited immunodeficiency diseases, Arkwright et al for the first time included also the immunologic disorder “hemophagocytic lymphohistiocytosis (HLH)” as an autoimmune phenomenon. HLH is characterized by uncontrolled T-lymphocyte and macrophage activation. Unrestricted release of inflammatory cytokines, such as interferon and tumor necrosis factor, is a prominent feature of primary and secondary HLH, including the Epstein-Barr virus–related form.

According to common classifications, HLH does not fulfill the criteria of an autoimmune disease (ie, an immune reaction to a more or less defined self-antigen).

We wonder, that Arkwright et al defines autoimmunity only as a bystander tissue damage due to suboptimal, chronic immune response to persisting opportunistic infection. Due to this definition, all chronic infectious disease in immune-deficient subjects would be classified as autoimmune phenomena.

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References

To the editor:

Autoimmunity in severe combined immunodeficiency (SCID)

Arkwright et al are to be complimented for their review on autoimmunity in human primary immunodeficiency diseases. While they emphasized the role of opportunistic infections, which are common in primary immunodeficiency (PID) states in the development of autoimmune disorders, we would like to draw attention to a completely different pathogenic pathway. Indeed, the apparent paradox of immunodeficiency and autoimmunity coexisting in the same patient is not a real one. Recently, Candotti et al pointed out that many components of the immune system have complex functions, which often play both positive and negative roles.

In order to illustrate this point, we would like to report on 2 cases of severe combined immunodeficiency (SCID) with autoimmune diseases. SCID was not mentioned in Arkwright et al’s review as a predisposing condition to autoimmunity. Furthermore, at this young age, opportunistic infections do not seem to be related to the autoimmune phenomena. In both cases, stem cell transplantation corrected both the immunodeficiency and the autoimmune conditions.

The first patient is a 2-month-old boy whose condition was diagnosed as Omenn syndrome. Genetic analysis revealed a 1886C>T mutation in RAG1. At diagnosis he had extended erythrodermatia with scaling on his entire body. He also had no hair on his scalp or body as is described in Omenn syndrome. Immunophenotyping from peripheral blood showed CD3 93%, CD20 2%, CD4 26%, and CD8 68%. Proliferation studies revealed marked decreased response to various mitogens. Immunoglobulin levels were very low for IgA, IgG, and IgM, whereas the IgE level was increased to 74 IU. Skin biopsy was...
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