Cyclic Neutropenia in Common Variable Immunodeficiency

The case report on cyclic neutropenia in a case of common variable immunodeficiency (CVID) was interesting(1). The authors have done well in controlling the infections and symptoms over a three year period.

Detailed studies of patients with so-called cyclic neutropenia have revealed involvement of monocytes, lymphocytes, reticulocytes and platelets as well(2). Hence the term cyclic hematopoiesis is more appropriate. These parameters have not been mentioned in the reported case. There is also no mention of whether the child had organomegaly. This is relevant because patients with cyclic neutropenia and splenomegaly have been reported to benefit from splenectomy. Incidentally, splenomegaly is also seen in 45% CVID cases(3).

Patients with CVID usually present in 2nd and 3rd decade of life. Characteristically these patients have normal or increased B lymphocytes which are defective. Though PIII A stimulation was defective, the number of B lymphocytes were actually decreased. This would go in favor of autoantibodies (against T and B lymphocytes plus neutrophils in this case); in which case CD4 and CD8 ratio should be decreased (usually due to increase in T suppressor cells)(4). Unfortunately, helper and suppressor T lymphocyte subsets were not analysed in this case. In fact the T lymphocytes were identified using resetting with sheeps RBCs—a test which identifies only that lymphocyte subset having epitope reactive to monoclonal antibody CD2.

Along with autoantibodies against neutrophils and lymphocytes, other autoimmune diseases can also be present with CVID (like autoimmune hemolytic anemia, idiopathic thrombocytopenia, SLE, chronic active hepatitis, rheumatoid arthritis, etc). With the hypothesis put forth in the discussion, why were antiplatelet antibodies and Coomb's test not done? The other theory of a persistent viral infection would hardly explain cyclic neutropenia and is, therefore, untenable.

Lastly, I am unable to understand the following line in the case report, "...serum G. CSF, 3 days prior to the ANC being zero, showed a slight elevation 'in vitro' CFU-C assay". How was serum G. CSF measured? What is 'slight elevation' in 'in vitro' CFU-C assay?

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REFERENCES


Reply

The term cyclic hematopoiesis is more appropriate—yes, we would agree. However, due to the relatively long half life of red cells and platelets compared with neutrophils, anemia and significant thrombocytopenia are not seen and are difficult to document(1). Since this was not documented in our case we preferred to use the term cyclic neutropenia.

This child had no organomegaly. The negative findings were not mentioned to keep the case report short. Splenectomy is without benefit for cyclic neutropenia and common variable immunodeficiency (CVID). Anyway, we would certainly hesitate to consider splenectomy for a 1 1/2 year old child due to the obvious risk of infective complications in a young immunocompromised infant.

CVID syndrome describes a highly heterogeneous group of patients with hypogammaglobulinemia, decreased ability to produce antibodies after antigenic stimulation and variable degrees of T-cell impairment(2). Patients with CVID can present in infancy and childhood, or during the second and third decades of life. B-cell numbers can be normal, increased or absent. T-cell analysis in some patients demonstrates decreased numbers of CD3 and CD8 cytotoxic/suppressor T-cells leading to an increased CD4:CD8 ratio(3). Since T-lymphocyte subsets were not studied in this case, this discussion would be redundant.

This child had isolated neutropenia with the Hb and platelet counts being normal and the antiplatelet antibodies and Coomb's test were negative. We would disagree with Parikh that a persistent viral infection could not explain cyclic neutropenia. In fact, recurrent granulocytic aplasia as clinical presentation of a persistent parvovirus B19 infection has been reported(4). Parvovirus B19, with minor genetic alterations or other similar viruses might be cytotoxic not only to erythroid progenitor cells but also to other hematopoietic progenitor cells. This may result in dysregulation of myeloid...