

## NOTES

# Adenosine Deaminase Deficiency and Purine Nucleoside Phosphorylase Deficiency in Common Variable Immunodeficiency

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**The clinical presentations of adenosine deaminase deficiency and purine nucleoside phosphorylase deficiency are widely variable and include clinical and immunologic findings compatible with common variable immunodeficiency. The screening of 44 patients with common variable immunodeficiency failed to identify any individuals with deficiencies of these enzymes.**

Common variable immunodeficiency (CVID) is a primary immunodeficiency disease characterized by hypogammaglobulinemia, functional antibody deficiencies, and, in some patients, associated defects in T-cell function (5, 6, 17). Clinical findings commonly include sinopulmonary infections, gastrointestinal infections, autoimmune and inflammatory disorders, and a high frequency of lymphoreticular and gastrointestinal malignancies (5, 6, 17). In most patients, the etiology of CVID is unknown.

Adenosine deaminase (ADA) and purine nucleoside phosphorylase (PNP) are enzymes of the purine salvage pathway (7). Complete deficiency of ADA is the cause of approximately one-quarter to one-third of the reported cases of autosomal recessive severe combined immunodeficiency (2). Deficiency of PNP typically causes T-cell immunodeficiency, which is associated in some cases with autoimmune and neurologic diseases (9). However, the clinical presentations of both ADA deficiency and PNP deficiency are widely variable and include clinical and laboratory findings compatible with CVID (3, 7, 8, 10–12, 14–16, 18).

Therefore, it is possible that some individuals diagnosed with CVID actually have an underlying ADA or PNP deficiency. The ability to determine the specific etiology of CVID in an individual patient is important to his or her care, since it may allow for genetic counseling and more specific treatment options, such as polyethylene glycol-ADA replacement therapy (7). Accordingly, we screened a population of patients with CVID for ADA and PNP deficiencies.

All patients seen in the immunodeficiency clinics of the Johns Hopkins Hospital, the Children's Hospital of Philadelphia, and the Wake Forest University Physicians' Clinic of The Bowman Gray School of Medicine from 1 July 1995 through 31

December 1996 who fulfilled the World Health Organization criteria for CVID (13) had erythrocyte ADA and PNP levels in their erythrocyte lysates determined at the Duke University School of Medicine as previously described (1). One additional patient with CVID who had died, but who had had ADA and PNP levels determined previously, was included in the study.

A total of 44 patients with CVID were evaluated for ADA and PNP deficiencies (Table 1). Twenty-three percent of the patients were diagnosed with CVID before the age of six. Just over 90% of the patients presented with recurrent infections. Forty-four percent of the patients had either opportunistic infections, autoimmune disorders, or sarcoidosis. Lymphopenia was fairly common, occurring in 50% of the patients. Of the 35 patients tested, 46% had abnormalities of T-cell number and/or function and 37% had decreased CD4 counts. None of the patients had neurologic disease. The levels of ADA and PNP in the 44 patients all fell within the normal range as established with 111 non-ADA- and non-PNP-deficient individuals.

Individuals with ADA or PNP deficiency have presented with a spectrum of immunologic findings. For example, although the original description of ADA deficiency was for infants with severe combined immunodeficiency, subsequent patients have been described as having both later clinical presentations and milder immunodeficiencies (8, 12, 14–16, 18). Similarly, although PNP deficiency was initially classified as an isolated deficiency in T-cell function, individual patients have presented with low levels of immunoglobulins and decreased antibody function (3, 10, 11). Thus, some patients with ADA or PNP deficiency have had clinical presentations compatible with CVID. Importantly, those "atypical" ADA- and PNP-deficient patients with late presentations compatible with CVID have usually had abnormalities of T-cell number and/or function. Conversely, a significant proportion of CVID patients, including those in the present study, have had lymphopenia and/or clinical and laboratory evidence of T-cell deficiency, in addition to their hypogammaglobulinemia, and thus have had some im-

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TABLE 1. Characteristics of 44 patients with CVID

Characteristic	No. of patients
Male .....	15
Female .....	29
Age at diagnosis (yr)	
0-5 .....	10
5-20 .....	14
>20 .....	20
Recurrent infections .....	40
Autoimmune diseases .....	14
Sarcoidosis .....	3
Opportunistic infections .....	5
Lymphopenia .....	22
T-cell abnormalities <sup>a</sup> .....	16

<sup>a</sup> T-cell abnormalities of number and/or function were assessed in 35 patients.

munologic findings in common with patients who are ADA or PNP deficient.

The screening of a population of 44 CVID patients for ADA and PNP deficiencies failed to identify any individuals with deficiencies of these enzymes. A previous study of 17 patients with CVID also failed to identify any patients with ADA or PNP deficiency (4). Although it remains possible that individual ADA- or PNP-deficient patients could present with findings consistent with CVID, these studies demonstrate that it is likely to be an uncommon occurrence. Nevertheless, patients with CVID who have features compatible with the milder clinical phenotypes of ADA and PNP deficiencies should be tested for deficiencies of these enzymes.

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