COMMON VARIABLE IMMUNODEFICIENCY (CVID) is considered one of the more common immune deficiencies, with a prevalence of between one in 25,000 and one in 50,000 people in the U.S.¹ It is categorized by low IgG antibody levels (usually less than 400 mg/dL), and low levels of IgM or IgA antibodies may also be present. Presentation of CVID can vary widely from patient to patient. Seventy percent to 80 percent of CVID patients present with sinopulmonary infections that are indicative of an immunodeficiency, but approximately 20 percent of CVID patients present with signs of autoimmunity instead, resulting in diagnostic delay.² The connection between CVID and autoimmunity is of great interest to researchers and, as such, is the subject of increased study.

Patients who present with autoimmune complications in addition to infections usually have a poorer prognosis than patients who present with infections alone.

Autoimmunity and Diagnostic Delay

Unlike other immunodeficiencies, patients are usually diagnosed with CVID in their 30s and 40s.² However, it is not uncommon for patients to go undiagnosed for six to eight years after the appearance of their first symptoms.² The “variable” in CVID is what contributes to diagnostic delay, which can result in years of delay in proper treatment. For instance, patients may be seen by their gastroenterologist for gastrointestinal issues, their pulmonologist for respiratory manifestations or their oncologist for cancer without a physician ever thinking to check for low IgG levels. And, while serum antibodies may be detected in autoimmune conditions,³ a diagnosis of autoimmunity will not preclude a diagnosis of CVID in a patient with an accompanying immune deficiency.

Autoimmunity occurs when the immune system fails to distinguish self from non-self. When this happens, the immune system attacks specific tissues through the production of auto-antibodies, thus causing autoimmunity.³ Paradoxically, autoimmunity is common in diseases of antibody deficiency, but how antibodies are produced against a patient’s own tissues when overall antibody production is impaired is unclear.² It has been suggested that both conditions may be related to genetic immune dysregulation.¹

Types of Autoimmunity in CVID

Charlotte Cunningham-Rundles, MD, David S. Gottesman professor of immunology at the Mount Sinai School of Medicine in New York, says that CVID patients can be categorized into two groups: those who present with infections and those who present with inflammatory or autoimmune conditions in addition to infections.¹ However, approximately 20 percent of CVID patients have some manifestation of autoimmunity in the absence of infection.²

Inflammatory and autoimmune conditions can range from gastrointestinal disease to inflammatory lung diseases and even cancer. In a large European study of 334 patients, 71 percent presented with one or more of these inflammatory and/or autoimmune manifestations, as well as infections, while the remainder presented with infections only.¹ In patients who present with both autoimmune manifestations and infections, the autoimmune manifestations are often the first to appear, thus contributing to diagnostic delay.²

The presentation of autoimmune manifestations in CVID patients may be just as variable as the presentation of CVID itself. Although autoimmune conditions that affect solid organs do occur in CVID patients, most studies recognize the blood conditions idiopathic thrombocytopenic purpura (ITP) and autoimmune hemolytic anemia (AIHA) as the most common concomitant autoimmune manifestations.
in CVID.\textsuperscript{1,2} It is estimated that 5 percent to 8 percent of CVID patients also have ITP and/or AIHA.\textsuperscript{2} Rheumatologic conditions have been known to occur in up to 10 percent of CVID patients and may include the involvement and destruction of one or many joints.\textsuperscript{2} Autoimmune or inflammatory gastrointestinal disease may be present in between 6 percent to 10 percent of CVID patients, and is particularly difficult to treat.\textsuperscript{2} Lymphoma and other cancers are also recognized as a complication of CVID. In an Australian study of 416 CVID patients, the incidence of malignancies was four times as common as in the general population.\textsuperscript{3}

The CVID-Autoimmunity Prognosis

Patients who present with autoimmune complications in addition to infections usually have a poorer prognosis than patients who present with infections alone. In fact, inflammatory and autoimmune conditions are recognized as being responsible for most of the morbidity and mortality in CVID.\textsuperscript{1} In a U.S. study of 473 CVID patients, those who had one or more inflammatory or autoimmune complications were 11 times more likely to die during the 40-year follow-up period than patients who had infections only.\textsuperscript{4} This number is still less than what is seen among the general population, and survival in CVID has improved significantly over time. The majority of patients in this study were able to live normal, active lives with appropriate treatment. And, improved diagnosis and treatment options are likely to continue this positive trend.\textsuperscript{4}

Due to the variability in the presentation of CVID and the resulting morbidity and mortality from the inflammatory and autoimmune complications that can accompany it, CVID patients must be carefully monitored for signs and symptoms of autoimmune or inflammatory conditions to ensure the best possible prognosis. Unfortunately, other than monitoring IgG levels, there is not much consensus on the best way to follow up with CVID patients. It is suggested that periodic blood panels, examinations of lung function, monitoring of gastrointestinal symptoms and investigation of any general health complaints will be helpful in the diagnosis of problems that can arise in CVID patients due to autoimmunity.\textsuperscript{1} It is also hoped that disease management will help reduce the serious complications that can lead to CVID morbidity and mortality. ■

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References