A Young Woman with Diffuse Skin Lesions

(See pages 195–196 for the Photo Quiz.)

Figure 1. Computed tomography of the chest demonstrates long, dilated bronchi (short arrow), as well as the cystic “signet ring” lesions (long arrow), which are consistent with bronchiectasis.

Diagnosis: common variable immunodeficiency (CVID) with epidermodysplasia verruciformis-like lesions.

Epidermodysplasia verruciformis was classically described as a genetic condition involving diffuse warty skin lesions due to human papillomavirus (HPV), such as those seen in Figure 1. However, it has also been associated with both acquired immune defects, such as human immunodeficiency virus infection and organ transplantation, and primary immunodeficiencies, such as CVID, X-linked hyper-immunoglobulin (Ig) M immunodeficiency syndrome, and Wiskott-Aldrich syndrome, among others [1–4]. Interestingly, it has been described in both immunodeficiencies that involve T cells and those that involve B cells. The presence of epidermodysplasia verruciformis–like lesions should initiate a search for an underlying immune defect.

In this patient, thoracic high-resolution computed tomography (HRCT) revealed diffuse lymphadenopathy, consolidation in the right middle lobe, and lingula with bilateral bronchiectasis (Figure 1). An abdominal CT demonstrated mild hepatomegaly and retroperitoneal lymphadenopathy, and a sinus CT revealed pansinusitis. Nitro blue tetrazolium test and complement levels (CH50, C3, and C4) were normal. Immunoglobulin quantitative study revealed the following results: IgG, 296 (normal range, 800–1800); IgM, 35 (normal range, 50–400); IgA, 13 (normal range, 50–350); IgE, 0.67. Flow cytometric analysis of peripheral blood mononuclear cells demonstrated 80% CD3+ cells, 23% CD4+ cells, 58% CD8+ cells, and 6% CD19+ cells, with a CD4+/CD8+ cell ratio of 0.4. The blood group was O+, and blood isoagglutinins (anti-A and anti-B) were not detectable. Polymerase chain reaction of the warty lesions had results that were positive for HPV type 33.

A diagnosis of CVID was confirmed by the patient’s clinical history, demonstration of low levels of all immunoglobulin classes, absence of isoagglutinins, decreased CD4+/CD8+ cell ratio, generalized lymphadenopathy, hepatomegaly, thrombocytopenia, bilateral bronchiectasis, and pansinusitis.
CVID is a heterogeneous immune disorder with a prevalence of 1 case per 25,000 individuals that is distributed in a bimodal pattern of age (1–5 years of age and 18–25 years of age). Patients have markedly reduced levels of IgG and IgA or IgM with impaired antibody responses despite the presence of B cells, which is attributable to the defective B cell differentiation and immunoglobulin secretion. As a result, patients experience recurrent bacterial pneumonia and bronchiectasis, which are seen in 30%–50% of patients and are an important cause of morbidity and mortality [5–7]. Sinusitis—acute and chronic—is in 30%–50% of patients and are an important cause of morbidity and mortality [5–7]. Sinusitis—acute and chronic—is very common [8].

T cell abnormalities include a low CD4+/CD8+ T cell ratio and impaired responses to mitogens and antigens [5, 9]. Absence of isoagglutinins was a good clue to the confirmation of the diagnosis, in addition to test results that were negative for antibody to hepatitis B surface antigen (despite vaccination for hepatitis B virus). Considering the high incidence of autoimmune disorders in patients with CVID, the thrombocytopenia in our patient was likely the first clinical manifestation of CVID, and splenectomy was not indicated. A review of 326 patients with CVID found that 11% had a history of ideopathic thrombocytopenic purpura, autoimmune hemolytic anemia, or Evans’ syndrome [10].

Regarding epidermodysplasia verruciformis in CVID, a report has shown that wart lesions have resolved after administration of subcutaneous immunoglobulin [11]. Our patient was discharged from the hospital with monthly intravenous immunoglobulin to prevent respiratory infections [12]. At present, she is in good condition, and her platelet count (∼100,000 platelets/µL) and IgG levels (500 mg/dL) are in acceptable ranges. Although the respiratory symptoms have been markedly alleviated, the skin lesions remain, and we plan to administer subcutaneous immunoglobulin to our patient.

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