Not All That Swells is Cancer: Lymphadenopathy as a Marker for CVID

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Intro: CVID is the most common form of severe antibody deficiency found in both children and adults. It is characteristically defined by an impairment of B cell differentiation resulting in a defective production of immunoglobulins. Age of onset ranges between 20 and 40. Patients with CVID are often afflicted with recurrent bacterial infections of the sinopulmonary and GI tract. Splenomegaly and lymphadenopathy are additional common findings, and the former is closely associated with granulomatous disease.

Case: 24M with history of psoriasis and nephrotic syndrome presented with abdominal pain, nausea, vomiting, and fever for two days. Of note, the nephrotic syndrome was present during childhood and resolved after treatment with tacrolimus and prednisolone. He was hypotensive and febrile on initial presentation with physical exam findings significant for psoriatic plaques and diffuse lymphadenopathy which have been present for two years. He was found to have Neisseria Meningitidis bacteremia along with splenomegaly noted on CT. Labs were significant for leukocytosis with neutrophil predominance, mild eosinophilia, CKD3a, and proteinuria, but albumin was normal. Due to his diffuse lymphadenopathy, there was concern for lymphoma. However, lymph node biopsy was negative for malignancy. Instead, it was notable for follicular hyperplasia and paracortical expansion. Extensive immunologic workup revealed hypogammaglobulinemia in the setting of proteinuria, low CH50, and hypocomplementemia. B cell subset analysis was performed, and the results were a severe reduction in class switched memory B cells (CD27+, IgD-, IgM-) correlating with granulomatous disease along with increased transitional B cells (CD38, IgM+) correlating with lymphadenopathy. He received the Tdap vaccine a year prior, and repeat titers were negative. He was also administered PPSV23, and titers post administration showed no response indicating failure versus loss of protection. A primary immunodeficiency panel revealed only variants of unknown significance.

Discussion: This patient fits the criteria for CVID due to his hypogammaglobulinemia, lack of vaccine response, and lack of an alternative genetic immunodeficiency. His presentation is unique in that he did not have a history of recurrent acute otitis media or sinopulmonary bacterial infections. He had a remote history of buttock abscesses requiring antibiotics twice but was relatively healthy until he presented with disseminated Neisseria Meningitis. It is interesting to note his history of nephrotic syndrome since renal involvement in CVID is rare. In contrast, hypogammaglobulinemia is a frequent finding in steroid-responsive nephrotic syndrome due to urinary loss of proteins resulting in decreased production of IgG and IgA. However, since his albumin was normal it is less likely that he has a recurrence of his nephrotic syndrome. Given that the patient's primary immunodeficiency panel was negative, the next step would be to perform wide exome sequencing to definitively determine whether he has a primary versus secondary hypogammaglobulinemia.