Autoimmune Cytopenia(s) might be initial presentation of Primary Immunodeficiency and Immune Dysregulation Disorder

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Introduction

•Primary immunodeficiency is a common diagnosis among patients with autoimmune cytopenia. Autoimmunity and immune dysregulation causing immune cytopenias might be an initial presentation in some patients.

•Here we describe 2 patients with autoimmune cytopenias and one them was eventually diagnosed with ALPS (Autoimmune lymphoproliferative syndrome) and the other with CVID(Common variable immunodeficiency).

•ALPS is characterized by dysregulation of the immune system due to inability to regulate lymphocyte homeostasis through the process of lymphocyte apoptosis. Autoimmunity is a common feature and is typically limited to the hematopoietic system but can involve other organs such as liver and kidneys. Combinations of cytopenias that occur concomitantly or /and sequentially are typically with Coomb's positive autoimmune hemolytic anemia and ITP.

•CVID is a primary immunodeficiency characterized by impaired B cell differentiation or function with defective immunoglobulin production. Autoimmune cytopenias are a more common presenting disorder in children than adults and maybe the initial manifestation. ITP and hemolytic anemia or combinations of these disorders were present in 33% of pediatric onset CVID patients with evidence of autoimmunity.

Case

•**Patient 1:** 19y/o female who was admitted 4 years ago with severe anemia. Work up showed H/H 6.7/19, retic 8%. Antibody screen positive, warm, and cold autoantibodies, Mycoplasma IgG and IgM were positive. She was diagnosed with autoimmune hemolytic anemia. She had 4 recurrences and was treated with systemic steroids with a positive response. No history of recurrent infections but had chronic lymphopenia off steroids. Immune work up showed low CD4, increased double negative T-cells (17%). Genetic testing for ALPS was negative but she met criteria for ALPS type3. She was started on Sirolimus 6mo ago and is maintaining a stable hemoglobin.

•**Patient 2:** 15y/o male with chronic refractory ITP, who also had history of AIHA, achieved remission after a course of IVIG at age 5. At age 9, he was diagnosed with ITP. He was treated with steroids, IVIG and rituximab over the course of 2 years. He remained in remission for 3 years but recently developed chronic ITP. Immunology work up revealed very low IgG and IgA, low naïve T cells, significantly decreased class switched memory B cells and absent plasmablasts. He had the classical findings of common variable immunodeficiency and was started on IgG replacement therapy and sirolimus, after the completion of short steroid course for chronic ITP.

Discussion

•Patient 1 was diagnosed due to a history of recurrent episodes of autoimmune hemolytic anemia and chronic lymphopenia even off steroids.

•Patient 2 was diagnosed due to sequential cytopenias and evidence of hypogammaglobulinemia

•Both patients were initially treated with steroids but with the confirmed diagnoses they were started on sirolimus

•They have been able to maintain stable and normal counts on this steroid sparing therapy without significant side effects.

Conclusion

•Patients with a history of chronic or multilineage immune cytopenias should be investigated further for autoimmune disorders or an underlying immune deficiency/immune dysregulation. Immunoglobulin substitution and steroid sparing therapy are fundamental in these patients. Early diagnosis may reduce treatment failure, morbidity, mortality, and long-term steroid therapy associated adverse effects.

References

1.Neven B, Magerus-Chatinet A, Florkin B, et al. A survey of 90 patients with autoimmune lymphoproliferative syndrome related to TNFRSF6 mutation. Blood 2011; 118:4798.

2.Price S, Shaw PA, Seitz A, et al. Natural history of autoimmune lymphoproliferative syndrome associated with FAS gene mutations. Blood 2014; 123:1989.

3.Baloh C, Reddy A, Henson M, et al. 30-Year Review of Pediatric- and Adult-Onset CVID: Clinical Correlates and Prognostic Indicators. J Clin Immunol 2019; 39:678.

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