May 11th, 11:30 AM - 1:30 PM

TNFAIP3: Evolving clinical picture from Autoinflammatory syndrome to Autoimmune lymphoproliferative syndrome

Esosa Adah MD
Children's Mercy

TTNFAIP3: Evolving clinical picture from Autoinflammatory syndrome to Autoimmune lymphoproliferative syndrome

Esosa Adah MD, Mary Nguyen MD, Nikita Raje MD, Julia Harris MD, Voytek Slowik MD

Introduction

Autoimmune lymphoproliferative syndrome (ALPS) is a rare genetic disorder of the immune system that affects children and adults. It can present with lymphoproliferation to lymphoid organs with the development of neutropenia, lymphopenia, and thrombocytopenia. Most cases are caused by either a germline or somatic mutation in the FAS, FASLG, or CASP10 genes that are involved in cell apoptosis. Tumor Necrosis Factor Alpha, Induced Protein 3 (TNFAIP3) is a protein coding gene associated with A20 haploinsufficiency.

Images

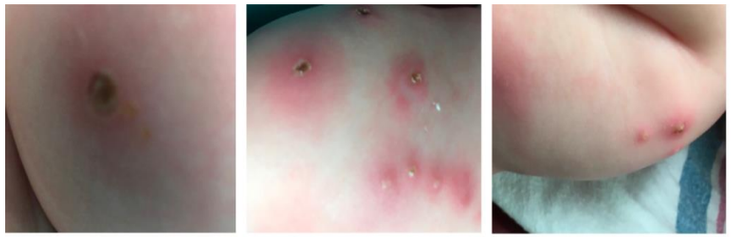

Figure 1. Rash on lower and upper extremities

Abstract

A 3-year-old female presented at 4-months old to the intensive care unit in shock with a vesiculopustular skin rash & indurated plaques on her extremities (see images) . Upon presentation, she was febrile and in respiratory failure requiring intubation. Infectious workup was unrevealing. Following discharge, genetic evaluation revealed heterozygous TNFAIP3 c.475del, p.Tyr159Metfs*57. Brain MRI/MRA/MRV were normal, EGD/colonoscopy showed chronic gastritis with normal biopsy, and eye exam showed no ocular inflammation. Immunology evaluation revealed T cell lymphopenia: CD3 1576 mm^3, CD4 1182 mm^3, CD8 368 mm^3, CD4−CD8− TCRαβ+ T cells (1.6 % T cells) with normal CD 19, NK cells, immunoglobulins, hib/tetanus titers, oxidative burst and lymphocyte proliferation to mitogen. At the age of 2, patient developed elevated AST/ALT (~300s-700 units/L) & pancytopenia 8 months later with physical findings of recurrent oral ulcers. Abdominal ultrasound remarkable for splenomegaly. Liver biopsy showed acute & chronic hepatitis with lymphocyte predominance, bile duct injury and bridging fibrosis. Bone marrow biopsy was negative for malignancy. Flow cytometry on peripheral blood had elevated CD4−CD8− TCRαβ+ (4.7% T cells), suggestive of ALPS. Fas mediated assay, sFASL, IL-10, IL-18 were obtained & pending.

Discussion

TNFAIP3 is known to present with autoinflammatory symptoms. Our case shows that patients with TNFAIP3 variants can have an evolving clinical picture that can include a spectrum of autoimmune lymphoproliferative syndrome - like disease. A hallmark finding of ALPS is a high proportion of CD4−CD8− TCRαβ+ T cells, called double-negative T cells. A 2017 case report revealed a 1 year old male with findings of bilateral cervical lymphadenopathy and hepatosplenomegaly. TNFAIP3, A20 was identified in this patient showing the ALPS-like phenotype with elevated double-negative T cells (5.1% T cells).

References

- Niaid.nih.gov.2021.*Autoimmune Lymphoproliferative Syndrome (ALPS)*.[online]Availableat:<https://www.niaid.nih.gov/diseases-conditions/autoimmune-lymphoproliferative-syndrome-alps> [Accessed 14 March 2021].
- UpToDate [Internet]. Uptodate.com [cited 20121]. Available from:https://www.Uptodate.com/contents/autoimmue-lymphoproliferative-syndrome-alps-clinical-features-and-diagnosis
- Takagi, M., Ogata, S., Ueno, H., Yoshida, K., Yeh, T., Hoshino, A., Piao, J., Yamashita, M., Nanya, M., Okano, T., Kajiwara, M., Kanegane, H., Muramatsu, H., Okuno, Y., Shiraishi, Y., Chiba, K., Tanaka, H., Bando, Y., Kato, M., Hayashi, Y., Miyano, S., Imai, K., Ogawa, S., Kojima, S. and Morio, T., 2021. *Haploinsufficiency of TNFAIP3 (A20) by germline mutation is involved in autoimmune lymphoproliferative syndrome*.

Children's Mercy KANSAS CITY

Additional partner logo may go here. To make inserted graphic transparent, FORMAT, Recolor, Set Transparent Color, place cursor over white spot of graphic and click.

UMKC School of Medicine