Research Days

May 6th, 11:30 AM - 1:30 PM

Case series: Bone marrow failure in teen siblings with unique RPS19 variant

Alexandra Prosser

Title: Case series: Bone marrow failure in teen siblings with unique RPS19 variant

Submitting/Presenting Author (must be a trainee): Alexandra Prosser
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☐ Medical Student
☐ **Resident/Psychology Intern (≤ 1 month of dedicated research time)**
☐ Resident/Ph.D/post graduate (> 1 month of dedicated research time)
×☐ **Fellow**

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Other authors/contributors involved in project: Erin Hall

IRB Number: N/A

Describe role of Submitting/Presenting Trainee in this project (limit 150 words):

Primary author of the case series abstract.

Background, Objectives/Goal, Methods/Design, Results, Conclusions limited to 500 words
(Below--words 364, character count with spaces 2584)

Case series: Bone marrow failure in teen siblings with unique RPS19 variant
Background: Upon diagnosis of aplastic anemia, inherited bone marrow failure syndromes and acquired etiologies must be considered. Investigating causality is particularly important when multiple family members are affected. It is also essential to identify novel causative genetic variants of bone marrow failure to direct treatment in these patients.
Objectives: To describe the diagnosis and management of siblings who presented two weeks apart with severe pancytopenia and were diagnosed with severe aplastic anemia.
Methods: The first patient is a 13-year-old non-binary female who presented with severe pancytopenia on routine labs. Bone marrow biopsy revealed marked hypocellularity (0-10%) with hypoplasia. The second patient is their 16-year-old brother who presented two weeks later with new-onset petechial rash and was found to also have pancytopenia. His bone marrow biopsy demonstrated variable cellularity (10-70%), but after months of transfusion-dependence he met criteria for severe aplastic anemia. Laboratory evaluation for acquired etiologies such as infection was negative. Both patients had taken fluoxetine, but otherwise no potential medical triggers or environmental exposures were identified. Upon genetic evaluation, both patients were found to have a heterozygous variant of unknown significance of *RPS19* (c.-163>T). Although this variant has not been classified as pathogenic, three other variants in the 5' untranslated region of RPS19 have been reported in patients with Diamond Blackfan Anemia (DBA). In contrast to classic DBA, these patients did not present in infancy or have the typical phenotypic characteristics of disease. Given lack of other identified etiologies, however, an inherited bone marrow failure syndrome was presumed.
Results: With suspected genetic predisposition, matched sibling donor transplant was deferred and the patients underwent a matched unrelated donor bone marrow transplant with reduced-intensity

conditioning. Our first patient remains well without complications and our second patient has recovered from peripheral neuropathy and urticarial vasculitis.
Conclusions: With these cases, we aim to share a unique presentation of aplastic anemia that reveals a potentially novel pathogenic variant as well as to provide our approach to medical management in pediatric aplastic anemia in the setting of uncertainty. Identification of other patients with bone marrow failure and this genetic variant will be important to determine its pathogenicity.