MYSM1 Deficiency; The Consequence of an Outdated Gene Panel

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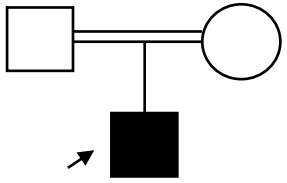
Background and Purpose

The autosomal recessive, bone marrow failure syndrome 4 (BMFS4), which is caused by bi-allelic variants in *MYSM1* gene has been well characterized when three unrelated families with BMFS4 have been reported back in 2018. Since then, several laboratories included *MYSM1* gene in their bone marrow failure gene panel. It has been reported recently that BMFS4 was successfully treated with allogeneic hematopoietic stem cell transplantation. We aim to emphasize the importance of reviewing all genes in a gene panel before requesting this gene panel testing.

Case Report and Methods

A 2 year and 6 month old Saudi boy to a consanguineous parents, was referred to our hospital at the age of 1 day suffering from acute respiratory distress syndrome, which required intubation. Since early days of life, he had pancytopenia, initially with anemia and leukopenia then thrombocytopenia. At the age of 2 months, he was admitted with acute pallor and very low hemoglobin with an impression of bone marrow failure. Blood transfusion was started along with inherited bone marrow failure work-up. A bone marrow failure gene panel analysis came out negative. He then required blood transfusion with frequent admissions every 3-4 weeks. His bone marrow aspiration/biopsy showed hypocellularity for age (Figure1). A Blood sample was sent for bone marrow failure gene panel analysis. After 6 months, another sample was sent for whole exome sequencing (WES).



c.1962del
p.(Trp654Cysfs*37)

Results

The NGS-based gene panel came out negative. For broader coverage, another blood sample was sent for WES analysis, which detected a frameshift homozygous variant c.1962del p.(Trp654Cysfs*37) in *MYSM1* gene, which was not included in the gene panel (Figure 2).

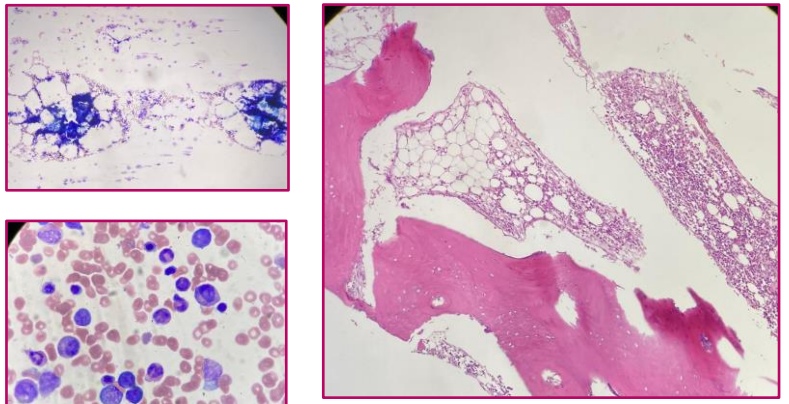


Figure 1

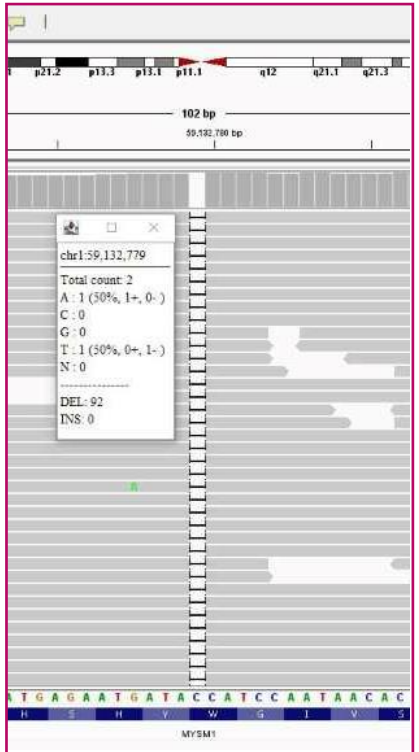


Figure 2

Conclusion

Not all laboratories update their gene panels after discovery of new genes. Thus, a careful revision of gene panels before sending a sample is highly recommended for diagnosing patients in a more timely manner and eventually for precise and better treatment.