Conference Abstracts

Atypical Presentation of Shwachman-Diamond Syndrome in Three Brothers

Jennie Vagher, MS¹, Sagar Patel¹, Srinivas Tantravahi, MD¹

¹ Hematology and Hematologic Malignancies, Huntsman Cancer Institute, Salt Lake City, Utah, USA

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BACKGROUND

Pathogenic germline variants in *SBDS* gene are associated with Shwachman-Diamond syndrome (SDS). SDS is classically associated with bone marrow failure and exocrine pancreatic insufficiency and increased risk for developing myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML).^{1,2} We report three brothers without the classic clinical phenotype of SDS and history of MDS or AML in adulthood.

history or features suggestive of autosomal recessive predisposition syndrome.

CASE DISCUSSION

The proband presented with mild persistent neutropenia at age 38. Marrow evaluation showed a markedly hypocellular bone marrow (20%) without a definitive myeloid neoplasm. At age 40, the proband developed worsening cytopenias ([Figure 1](#)), and marrow confirmed MDS with excess blasts-2. He was treated with MUD allogeneic stem cell transplant (allo-SCT) and relapsed at day 100. Despite additional treatment, the patient progressed to AML and died at age 41. DNA Sequencing obtained cultured skin fibroblasts identified compound heterozygous pathogenic variants in the *SBDS* gene.

The proband's younger brother was diagnosed with MDS at age 21 and underwent allo-SCT. On day 100, he relapsed and had a second allo-SCT. Subsequently, the younger brother progressed to AML and died at age 22. The proband's older brother presented with pancytopenia at age 43, and marrow evaluation confirmed AML with myelodysplasia-related changes. He was refractory to initial induction chemotherapy and had no response to multiple salvage therapies, and ultimately died at age 44. Site-specific testing of cultured fibroblasts confirmed the same variants in the proband's older brother. SDS was not confirmed in the proband's younger brother.

CONCLUSION

This sibship supports an expansion of the SDS phenotype into adult-onset MDS or AML without classic SDS phenotype. Germline testing for predisposition to myeloid malignancies should be considered in all patients with early-onset MDS/AML, especially in the presence of positive family

Proband denoted with a small arrow. MDS, myelodysplastic syndrome. AML, acute myeloid leukemia. SDS, Shwachman Diamond syndrome affected. GT, genetic testing.

REFERENCES

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