Clonal Hematopoiesis in the Short Telomere Syndromes

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The short telomere syndromes represent a spectrum of premature aging disorders. Telomere length is the primary driver of disease severity and immuno-hematopoietic and pulmonary disease are the most common manifestations. While patients with short telomere syndromes have lower than expected prevalence of common cancers, there is an increased risk of myelodysplastic syndrome and acute myeloid leukemia (MDS/AML) with 15% lifetime incidence. These MDS/AML diagnoses are generally limited to adults with nearly all cases diagnosed after age 40. Short telomere-related MDS/AML evolve on a background of myeloid clonality. Among adults with short telomere syndromes who do not have MDS/AML, clonal hematopoiesis is common and occurs two decades earlier than in the general population. Short telomere-related clonal hematopoiesis has a unique spectrum of recurrently mutated genes. Here, I will focus on the clonal hematopoiesis profile of short telomere syndromes and demonstrate how it may be used to stratify MDS/AML risk especially prior to lung transplantation.