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Cancer Prone Disease Section

Mini Review

Diamond-Blackfan anemia (DBA)

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This article is an update of: Punnett HH. Diamond-Blackfan anemia (DBA). Atlas Genet Cytogenet Oncol Haematol.1999;3(3):160.

Identity

Inheritance: Genetic heterogeneity; majority of cases autosomal dominant, occasionally with variable expression (incomplete dominance) manifesting as mild anemia or only macrocytosis and/or elevated erythrocyte adenosine deaminase activity (eADA) in transmitting parent or in siblings; some cases apparently autosomal recessive, not linked to 19q.

Clinics

- Chronic constitutional aregenerative anemia with absent or decreased red cell precursors in bone marrow.
- Macrocytosis elevated fetal hemoglobin and increased eADA.
- Physical abnormalities in about 40% of DBA cases including craniofacial and thumb abnormalities, atrial or ventrucular septal defects, short stature, mild retardation, etc.
- Hematologic malignancy: in 2.5% of all reported cases of DBA; primarily ANLL with no FAB preference but also ALL, Hodgkin's disease.
- Solid tumors include carcinoma of liver, stomach, osteogenic sarcoma.
- Age of malignancy onset from 2 to 43 years.
- Disease-related and treatment-related factors, i.e., allosensitization and iron overload, contribute to malignancy.

Treatment

Corticosteroids, transfusion, bone marrow transplant.

Evolution

Some patients enter remission, with or without corticosteroid therapy.

Prognosis

Median survival: 38 years.

Genes involved and Proteins

RPS19

Location: 19q13.2

Protein

Description: Ribosomal protein S19; ribosomal proteins are a major component of cellular proteins. In general their function(s), aside from being part of the ribosome, are unknown. However, RPS19 protein was shown to be essential for 18S rRNA maturation and 40S subunit synthesis. Haplo-insufficiency of the protein encoded by the mutated gene is a likely mechanism underlying the pathogenesis of DBA.

Mutations

Germinal: 62 different heterozygous mutations in RPS19 were identified and reported in 113 of the 457 (about 25%) DBA probands. They were non-sense, frameshift, splice site and missense mutations. Several patients had disease-associated chromosomal abnormalities in DBA region, including t(X;19), t(8;19), and 19q microdeletions.

RPS24

Location: 10q22.3

DNA/RNA

Description: ribosomal protein S24.

Mutations

Germinal: Three heterozygous mutations in RPS24 (two nonsense and one splice site mutations causing premature termination codons and skipped exon, respectively) were identified among 185 RPS19-negative DBA probands (about 2%).

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