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Cancer Prone Disease Section

Mini Review

Familial monosomy 7 syndrome

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Identity

Alias: Familial leukemia or MDS associated with monosomy 7

Note: Monosomy 7 is seen in a variety of hematologic disorders:

1 - de novo myelodysplastic disorders (MDS) and ANLL.
2 - Therapy-related MDS and ANLL.
3 - Childhood myeloproliferative / myelodysplastic disorder commonly referred to as the childhood monosomy 7 syndrome, which is associated with a subset of juvenile myelomonocytic leukemia (JMML, JCML).
4 - MDS or ANLL associated with constitutional predispositions to myeloid leukemia including Fanconi anemia, congenital neutropenia, and neurofibromatosis type 1.
5 - Familial monosomy 7 syndrome- Rare familial cases of MDS or ANLL associated with either complete or partial monosomy 7 have been reported in 12 pedigrees.

Inheritance: In some pedigrees the pattern of involvement is compatible with an autosomal dominant inheritance pattern with incomplete penetrance.

Clinics

Phenotype and clinics

Disease: Hematologic disorder characterized by either marrow aplasia, dysplasia, or frank acute myeloid leukemia occurring in at least two siblings associated with either partial or complete loss of chromosome 7. The majority of reported cases of familial monosomy 7 present at an early age (20 out of 24 cases before age 20 years) with either MDS or ANLL.
Phenotype/cell of origin: Multipotential progenitor cell.
Epidemiology: There is an even male to female distribution. Median age at presentation age 8 years although adult presentations also have been reported.
Clinical features: The disease in some cases appears to associated with other mendelian disorders including probable Noonan's syndrome, cerebellar ataxia/atrophy, and Fanconi's anemia (monosomy 7 is also common in non-familial cases of MDS/ANLL arising in Fanconi's anemia and other constitutional disorders). Cytopenias and myelodysplasia in non-leukemic family members is common.
Pathology: The pathology is typical of MDS and ANLL.

Treatment

The number of reported cases makes it difficult to draw conclusions about appropriate therapy. Allogeneic transplantation from a related sibling is problematic because of the familial predisposition to hematologic malignancies.

Prognosis

The prognosis is poor. Nearly all reported patients have died of their disease.

Cytogenetics

Note
Complete or partial monosomy may be associated with other abnormalities including +8, 5q-, and t(1;7). Of the 12 reported cases, the lost chromosome 7 was shown to be of different parental origin in two.

Genes involved and proteins

Note
The available data suggest that the monosomy 7 contributes to oncogenesis by reduced gene dosage. Studies showing different parental origin of the deleted

chromosome argue against a possible tumor suppressor mutated on the retained chromosome. It has been proposed that the susceptibility locus or loci located on other chromosomes acts as a mutator that promotes chromosomal instability. In some pedigrees the pattern of involvement is compatible with an autosomal dominant inheritance pattern with incomplete penetrance.

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