Nijmegen Breakage Syndrome

Alternative Names
NBS
Ataxia-Telangiectasia Variant V1
AT-V1
Microcephaly with Normal Intelligence, Immunodeficiency, and Lymphoreticular Malignancies
Seemanova Syndrome II
Nonsyndromal Microcephaly, Autosomal Recessive, with Normal Intelligence Immunodeficiency, Microcephaly, and Chromosomal Instability
Berlin Breakage Syndrome
BBS
Ataxia-Telangiectasia Variant V2
AT-V2

WHO International Classification of Diseases
Congenital malformations, deformations and chromosomal abnormalities

OMIM Number
251260

Mode of Inheritance
Autosomal recessive

Gene Map Locus
8q21

Description
Nijmegen breakage syndrome is a rare autosomal recessive condition, which belongs to the DNA repair disorders. The hallmarks of Nijmegen breakage syndrome are microcephaly, a typical facial appearance, growth retardation, immunodeficiency accompanied by recurrent infections, chromosomal instability, X-ray hypersensitivity, and predisposition to malignancy. Additional features include skin abnormalities, particularly café-au-lait spots and vitiligo, and congenital malformations, particularly clinodactyly and syndactyly. Psychomotor development is usually normal or only mildly to moderately retarded despite severe microcephaly. About three quarters of the Nijmegen breakage syndrome patients are microcephalic at birth and the remainders become microcephalic within the first year of life. Severe microcephaly at birth may be associated with normal mental development and counterwise. Life expectancy is reduced because of their tendency to develop malignancies at a relatively young age and sometimes fatal infections.

Molecular Genetics
The gene responsible for Nijmegen breakage syndrome, NBS1, is located on chromosome 8q21. The NBS1 gene consists of 16 exons and spans approximately 50 kb of DNA. The gene encodes two transcripts of 4.4 and 2.4 kb that are expressed in all tissues examined and differ only in their site of polyadenylation. Both transcripts contain a single open reading frame coding for a protein of 754 amino acids with a predicted molecular weight of 85kd, called NIBRIN. All disease-causing alleles of the NBS1 gene identified to date are null alleles. The 657del5 mutation predominates, accounting for greater than 90% of all mutant alleles in Nijmegen breakage syndrome. All known Nijmegen breakage syndrome mutations are predicted to result in truncation of the NIBRIN protein.

Epidemiology in the Arab World

Kuwait
Teebi et al. (1987) described a large Arab kindred with frequent consanguineous marriages and eight cases in five sibships with microcephaly, peculiar facies, and normal intelligence. Of these cases, two died of an acute lymphoreticular malignancy or bronchopneumonia. Immunological and chromosomal studies carried out for the three affected living sibs were normal.
**United Arab Emirates**
Al Talabani et al. (1998) studied the pattern of major congenital malformations in 24,233 consecutive live and stillbirth in Corniche hospital, which is the only maternity hospital in Abu Dhabi, between January 1992 to January 1995. A total of 401 babies (16.6/1,000), including 289 Arabs, were seen with major malformation. Single gene disorders accounted for 24% of the cases, 76% were due to autosomal recessive disorders. In their study, Al Talabani et al. (1998) observed nine cases of familial microcephaly born to first cousin couples from United Arab Emirates. Recurrence was reported in the affected families. Al Talabani et al. (1998) concluded that their study was very close to representing the true incidence of congenital abnormalities in the whole United Arab Emirates, as they investigated over 98% of deliveries in Abu Dhabi, the capital of United Arab Emirates.

**References**

**Contributors**
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