Nijmegen-breakage syndrome

GENERAL INFORMATION

Description:

Nijmegen breakage syndrome is an autosomal recessive chromosomal instability syndrome characterised by short stature, progressive microcephaly with loss of cognitive skills, ovarian failure in females and immunodeficiency. NBS is also associated with an increased risk of cancer, particularly lymphomas. Mutations of the NBS1 gene are detected in nearly all patients.

Alternative names:

- NBS
- Microcephaly - immunodeficiency - lymphoreticuloma
- Seemanova syndrome type 2

Classification:

- DNA breakage associated syndromes and DNA epigenetic modification syndromes
  - DNA-breakage-associated syndromes

Inheritance:

Autosomal recessive

OMIM:

- #251260 Nijmegen breakage syndrome gene; NBS1
- *602667 NBS1 GENE; NBS1

Cross references:

Phenotype related immunodeficiencies:

- IDR factfile for Nijmegen-breakage syndrome
- IDR factfile for Bloom syndrome

Incidence:

Incidence is not known.

CLINICAL INFORMATION

Description:

Patients generally have lower than normal birth weight and are small for gestational age. If not present from birth, microcephaly develops during the first months of life and progresses to severe microcephaly. Growth failure during the first two years of life results in height that is usually less than the 3rd centile by two years of age. The linear growth rate tends to be normal after two years of age, but patients remain small for age. As the microcephaly progresses, the facial features tend to become distinct, with sloping forehead, upslanting palpebral fissures, prominent midface, long nose, and small jaw. The ears may be large. Developmental milestones are attained at the usual time during the first year. In later infancy and early childhood, borderline delays in development and hyperactivity may be observed. Intellectual abilities tend to decline over time and most children tested after the age of seven years have mild to moderate mental retardation. The children are described as having a cheerful, shy personality with good interpersonal skills. Respiratory infections are the most common. Recurrent pneumonia and bronchitis may result in pulmonary failure and early death. Chronic diarrhea and urinary tract infections may also occur. According to Wegner et al (1999), 25 of the 70 patients (35%) reported to date have developed malignancies between the ages of one and 34 years. Twenty-two of the 25 were lymphomas, of which 19 occurred before the age of 15 years. Nine out of 19 were B-cell lymphomas; 1/19 was a T-cell lymphoma. Three patients developed solid tumors: glioma (at 12 years), rhabdomyosarcoma (at four years), medulloblastoma (at eight years). Wegner et al (1999) report a high incidence of primary ovarian failure in both prepubertal girls with NBS and adolescent and post-adolescent women with NBS, as evidenced by elevated gonadotrophin levels in both groups and primary amenorrhea and lack of secondary sexual

Diagnosis:

Diagnostic laboratories:

Clinical:

- Nijmegen breakage syndrome, ORPHANET
- Nijmegen breakage syndrome, eMedicine

Genetic:

- Nijmegen Breakage Syndrome, clinical testing, GeneTest
- Nijmegen Breakage Syndrome, research testing, GeneTest

Therapeutic options:

- Nijmegen breakage syndrome, eMedicine

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies
- Molecular and Clinical Studies of Primary Immunodeficiency diseases, ClinicalTrials.gov

GENE INFORMATION

Names:

HUGO name: NBS1
Alias(es): AT-V1, AT-V2, ATV, NBS, nibrin, Nijmegen breakage syndrome, Nijmegen breakage syndrome 1 (nibrin)

Localization:

Chromosomal Location:

8q21

Maps:

NBS1 (Map View)

Variations / Mutations:

- ; Nijmegen Breakage Syndrome Mutation Database

Other gene-based resources:

Ensembl: ENSG00000104320, GENATLAS: NBS1, GeneCard: NBS1, UniGene: 492208, Entrez Gene: 4683, euGenes: 4683, GDB: 9598211

PROTEIN INFORMATION

Description:

Other features:

Expression pattern for human:

Tissue	Exp. (%)	Clones
foreskin, melanocyte	7.12	6:13478
grade-2-chondrosarcoma	6.06	1:2639
bladder	5.36	6:17890
prostate, epithelium	5.16	3:9299
uterus, epithelium	4.84	4:13207
whole embryo, mainly head	4.64	1:3442
pancreas, islet	4.41	1:3625
kidney, pooled	4.32	2:7404
foveal and macular retina	3.95	1:4045
lung epithelial cells tissue nos 359-368	3.66	1:4366

OTHER RESOURCES

Societies:

General:

- International Patient Organization for Primary Immunodeficiencies
- Immune Deficiency Foundation
- NIH/National Institute of Allergy and Infectious Diseases
- European Society for Immunodeficiencies