

Bruton's agammaglobulinemia

Identity

Other names X-linked agammaglobulinemia (XLA)

Inheritance X-linked disorder occurring in males; frequency of XLA is about 0.3-0.6/10⁵.

Clinics

Phenotype and clinics immunological deficiency, first described in 1952, manifest from late infancy and typically resulting in frequent bacterial infections commencing in the second half of the first year of life: tonsils and lymph nodes are very small; marked decrease of serum immunoglobulins of all isotypes (maternal IgG gives some protection in early infancy)

Neoplastic risk probably slight; in a 1963 paper, two patients with lymphoma were reported and reference was made to two adults with hypoglobulinemia who also had lymphomas; recent surveys of XLA patients do not reveal any cases of lymphoma; however, long-term vigilance needs to be maintained; at least seven cases of adenocarcinoma of the gastrointestinal tract in young adults with XLA have been reported; other malignancies have also been reported, but it is not clear whether they occur with an increased frequency

Treatment vigorous antibiotic therapy and regular injections of immunoglobulin

Prognosis good, on survival into early adulthood

Other findings

Note absence of plasma cells in bone marrow and lymph nodes (the latter lack germinal centres) resulting in an almost complete lack of humoral immunity due to a failure of early B-lymphocyte development; normal myeloid and T-cell function: extremely deficient production of antibodies to all antigens

Genes involved and Proteins

Gene Name BTK (Bruton's tyrosine kinase)

Location Xq21.3-Xq22

DNA/RNA

Description encoded in 19 exons spanning 37 kb

Protein

Description Btk is a 659 amino-acid cytoplasmic tyrosine kinase

Expression is expressed at all except the terminally differentiated plasma cell stage of B-cell development

Function it is a member of a small family of src-related hematopoietic kinases and, like them, has several interaction domains that allow it to bind to other components of signal-transduction pathways; unlike other src family members, Btk family members have a pleckstrin homology (PH) domain which is followed by a proline rich region that binds to the SH3 region of several src family members

Mutations

Germinal over 300 different mutations in Btk have been identified; only about 50% of patients with the clinical and laboratory findings of XLA have a family history of immunodeficiency; most of the remaining patients are the first manifestation of a new mutation in Btk; most mutations are single base-pair substitutions that result in premature stop codons, splice defects, or amino-acid substitutions. 5-10% of patients with XLA have gross alterations in the BTK gene (usually deletions) detectable by Southern-blot analysis; most amino-acid substitutions in Btk render the protein unstable and markedly reduced or absent

External links

[OMIM](#) [300310](#)

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