X-linked Agammaglobulinemia

Subjects: Genetics & Heredity
Contributor: Bruce Ren

X-linked agammaglobulinemia (XLA) is a condition that affects the immune system and occurs almost exclusively in males.

genetic conditions

1. Introduction

X-linked agammaglobulinemia (XLA) is a condition that affects the immune system and occurs almost exclusively in males. People with XLA have very few B cells, which are specialized white blood cells that help protect the body against infection. B cells can mature into the cells that produce special proteins called antibodies or immunoglobulins. Antibodies attach to specific foreign particles and germs, marking them for destruction. Individuals with XLA are more susceptible to infections because their body makes very few antibodies.

Children with XLA are usually healthy for the first 1 or 2 months of life because they are protected by antibodies acquired before birth from their mother. After this time, the maternal antibodies are cleared from the body, and the affected child begins to develop recurrent infections. In children with XLA, infections generally take longer to get better and then they come back again, even with antibiotic medications. The most common bacterial infections that occur in people with XLA are lung infections (pneumonia and bronchitis), ear infections (otitis), pink eye (conjunctivitis), and sinus infections (sinusitis). Infections that cause chronic diarrhea are also common. Recurrent infections can lead to organ damage. People with XLA can develop severe, life-threatening bacterial infections; however, affected individuals are not particularly vulnerable to infections caused by viruses. With treatment to replace antibodies, infections can usually be prevented, improving the quality of life for people with XLA.

2. Frequency

XLA occurs in approximately 1 in 200,000 newborns.

3. Causes

Mutations in the *BTK* gene cause XLA. This gene provides instructions for making the BTK protein, which is important for the development of B cells and normal functioning of the immune system. Most mutations in the *BTK* gene prevent the production of any BTK protein. The absence of functional BTK protein blocks B cell development

and leads to a lack of antibodies. Without antibodies, the immune system cannot properly respond to foreign invaders and prevent infection.

3.1 The gene associated with X-linked agammaglobulinemia

- BTK

4. Inheritance

This condition is inherited in an X-linked recessive pattern. The gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes. In males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In females (who have two X chromosomes), a mutation would have to occur in both copies of the gene to cause the disorder. Because it is unlikely that females will have two altered copies of this gene, males are affected by X-linked recessive disorders much more frequently than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

About half of affected individuals do not have a family history of XLA. In most of these cases, the affected person's mother is a carrier of one altered *BTK* gene. Carriers do not have the immune system abnormalities associated with XLA, but they can pass the altered gene to their children. In other cases, the mother is not a carrier and the affected individual has a new mutation in the *BTK* gene.

5. Other Names for This Condition

- agammaglobulinemia
- Bruton's agammaglobulinemia
- congenital agammaglobulinemia
- hypogammaglobulinemia
- XLA

References

1. Conley ME, Farmer DM, Dobbs AK, Howard V, Aiba Y, Shurtleff SA, Kurosaki T. A minimally hypomorphic mutation in Btk resulting in reduced B cell numbers but no clinical disease. Clin Exp Immunol. 2008 Apr;152(1):39-44. doi:10.1111/j.1365-2249.2008.03593.x.
2. Howard V, Greene JM, Pahwa S, Winkelstein JA, Boyle JM, Kocak M, Conley ME.The health status and quality of life of adults with X-linked agammaglobulinemia.Clin Immunol. 2006 Feb-Mar;118(2-3):201-8.

3. López-Herrera G, Vargas-Hernández A, González-Serrano ME, Berrón-Ruiz L,Rodríguez-Alba JC, Espinosa-Rosales F, Santos-Argumedo L. Bruton's tyrosinekinase--an integral protein of B cell development that also has an essential rolein the innate immune system. J Leukoc Biol. 2014 Feb;95(2):243-50. doi:10.1189/jlb.0513307.
4. Plebani A, Soresina A, Rondelli R, Amato GM, Azzari C, Cardinale F, Cazzola G,Consolini R, De Mattia D, Dell'Erba G, Duse M, Fiorini M, Martino S, Martire B,Masi M, Monafo V, Moschese V, Notarangelo LD, Orlandi P, Panei P, Pession A,Pietrogrande MC, Pignata C, Quinti I, Ragno V, Rossi P, Sciotto A, Stabile A;Italian Pediatric Group for XLA-AIEOP. Clinical, immunological, and molecularanalysis in a large cohort of patients with X-linked agammaglobulinemia: anItalian multicenter study. Clin Immunol. 2002 Sep;104(3):221-30.
5. Smith CIE, Berglöf A. X-Linked Agammaglobulinemia. 2001 Apr 5 [updated 2016Aug 4]. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K,Amemiya A, editors. GeneReviews® [Internet]. Seattle (WA): University ofWashington, Seattle; 1993-2020. Available fromhttp://www.ncbi.nlm.nih.gov/books/NBK1453/
6. Väliaho J, Smith CI, Vihinen M. BTKbase: the mutation database for X-linkedagammaglobulinemia. Hum Mutat. 2006 Dec;27(12):1209-17. Review.
7. Winkelstein JA, Marino MC, Lederman HM, Jones SM, Sullivan K, Burks AW, ConleyME, Cunningham-Rundles C, Ochs HD. X-linked agammaglobulinemia: report on aUnited States registry of 201 patients. Medicine (Baltimore). 2006Jul;85(4):193-202.

Retrieved from https://encyclopedia.pub/entry/history/show/13844