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X-linked agammaglobulinemia (XLA) in a 7-years-old boy, Saint Paul's Hospital Millennium Medical College (SPHMMC), Addis Ababa, Ethiopia

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Abstract

X-linked agammaglobulinemia is a rare primary immunodeficiency syndrome characterized by absent mature B cells and recurrent infections. We report a 7-year-old male child who was diagnosed with X-linked agammaglobulinemia and bronchiectasis after presenting with recurrent pneumonia and otitis media.

Keywords: Agammaglobulinemia, Absent mature B cells, Bronchiectasis

Background

X-linked agammaglobulinemia (XLA), also called Bruton'sagammaglobulinemia is one of the first described primary humoral immunodeficiencies by Bruton in 1952(1).It is characterized by absent or profoundly reduced circulating mature B cells resulting in reduced levels of immunoglobulin, lack of specific antibody production, and recurrent infection (2-4). We are reporting this case since it is rare and we had a diagnostic and treatment challenge, which could enlighten others.

Case report

This 7-year-old boy presented at the age of 10 months to St Paul's Hospital Millennium Medical College (SPHMMC). By then, the complaint was fever and seizures. The pertinent investigation was cerebrospinal fluid (CSF) analysis, which showed 10 cells with 95% granulocytes. Gram staining of the CSF revealed gram-negative extracellular diplococci but CSF culture was negative. For meningitis, he was managed with parenteral antibiotics and discharged improved.

Afterward, he had 8 admissions, and all of them were for severe pneumonia, on average he had 2 hospitalizations per year. In all cases, he presented with fever, cough, and fast breathing. At each admission, he was treated with intravenous antibiotics. On the fifth admission, he had complicated pneumonia with empyema and took a prolonged course of antibiotics, and 6 months later bronchiectasis was established. Additionally, he has been having a follow-up for recurrent chronic suppurative otitis media since the age of one year. He has an older sibling, a healthy female, no family history of immunodeficiency disease or early male childhood death on the maternal side.

Physical examination during the last admission (at the age of 4 years and 6 months): He was in respiratory distress, with a PR of 150, RR of 64, T of 39.70 c^0, and saturation of 86% with room air. His weight was 15 kg, with a height of 97 cm, anthropometry has a moderate wasting and stunting, has left ear puss discharge. Tonsils were not visualized, has subcostal and intercostal retractions, course crepitation at the right posterior one-third of the lung.

Investigations

WBC 13,000 with 76% neutrophils and 20% lymphocytes, HIV status was negative , ESR and platelet counts are normal, CXR showed right lower lobe opacity, CT Scan of the chest-showed secular bronchiectasis, Immunoglobulin (IgG) <75 mg/dl (normal value 420-1200),Ig A < 10 mg/dl(normal value 18-150).The flow cytometry report of the child was done at Ethiopian Public Health Institution (EPHI) immunohematology laboratory exhibited an Absent CD 20 and CD 19 cells, which are markers of B lymphocytes with normal CD 3 and CD 4 cells indicating normal T lymphocytes.

Table 1: Flowcytometry report of the child, shows absent B lymphocyte (negative CD 19 and 20)

CD Marker	Lymphocytes %(45)
CD3	90
CD4	35
CD5	87
CD7	81
CD8	53
CD10	Neg
CD19	Neg
CD20	Neg
CD22	Neg

Discussions

XLA is an uncommon disorder with a worldwide incidence of 5 to 10 per million cases (5). It is caused by a mutation of the Bruton's tyrosine kinase (Btk) gene located on the long arm of the X-chromosome. This gene contributes to B cell maturation at the bone marrow level (6).About 40 % of X-linked agammaglobulinemia has a positive family history while 60 % of the XLA is a spontaneous mutation (7,8).

Since Immunoglobulin G (IgG) is transferred through the placenta, affected newborns will not show symptoms. The classic clinical presentation starts after 4-12 months of age with recurrent bacterial infection once placental transferred immunoglobulin's wanes (9, 10). Clinical manifestations include recurrent sinopulmonary infections and otitis media.The most common etiologies are encapsulated microorganisms like *Streptococcus pneumonia, Haemophilusinfluenzae,*

Staphylococcus aureus, and *Pseudomonas aeruginosa*; enteroviral infections are also common etiologies causing hepatitis and meningoencephalitis (11-13).

The average age of diagnosis with a family history of XLA is 2.6 years while without family history it may take 5.4 years (8).The diagnosis of XLA is based on a History of recurrent infection in a male child, family history of similar illness, the physical examination which may show absent tonsils, and immunofluorescent study showing absence or <2% of B lymphocyte and reduced immunoglobulin.Genetic testing shows mutation or a defect on the tyrosine kinase gene (9).

Regular lifelong immunoglobulin replacement is a safe and effective treatment strategy for these patients and they can lead a relatively normal life. Prophylactic and therapeutic antibiotics are also used as a treatment. Hematopoietic stem cell transplantation (HSCT) is an alternative treatment tried in a few cases of XLA (14, 15).

In our patient, after one episode of pyogenic meningitis, 4 admissions for severe pneumonia, and recurrent otitis media, we made the diagnosis of XLA at the age of three and half years. The age at presentation, the recurrent ear and chest infection with absent tonsils are typical of XLA in this boy. Most probably he has a spontaneous mutation since there is no maternal family member with the same issue. A limitation of this case report is the lack of genetic testing that is inaccessible in the country and costly to send samples abroad. But the reduced immunoglobulin levels and the absence of B cells from flow cytometry together with the history and physical examinations are sufficient evidence to make the diagnosis in this case.

Physical examination on the last follow-up, on October 12, 2021, his weight is 22-kilograms height of 116 cm with a BMI of 16.2 that is normal for his age with mild stunting. He has grade 2 clubbing and maintenance of his saturation around 91 to 92% with atmospheric air. The chest finding persisted with crepitation on the posterior lower one-third.

He has been taking prophylaxis cotrimoxazole, azithromycin, for the past three and half years and on chest physiotherapy received INH prophylaxis because of contact with a patient with Tuberculosis. For the past year, he has had no admission to the hospital and is being followed at the chest clinic in a relatively stable condition. Since IVIG cost is sky high, he is not on monthly prophylaxis; hence, we are left with supportive care and treatment of complications.

Conclusion

Primary immunodeficiency should be suspected and diagnosed in children with recurrent and atypical infections before a permanent sequela or life-threatening condition develops in the child.

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Conflicts of interest

The authors declare no conflicts of interest.

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