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CASE REPORT

X-linked agammaglobulinemia, a case report

Agammaglobulinemia asociada al cromosoma X, reporte de un caso

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ABSTRACT

Introduction: X-linked agammaglobulinemia is a primary immunodeficiency caused by mutations in the Bruton tyrosine kinase gene, predominantly affecting males. It is characterized by the absence of B lymphocytes and extremely low levels of serum immunoglobulins. This leads to vulnerability to recurrent bacterial infections starting at six months of age, following the loss of maternal antibodies.
Case Presentation: a fourteen-month-old infant presented with fever, respiratory distress, and a history of otitis, pneumonia, and gastroenteritis since seven months of age. Physical examination revealed the absence of tonsillar tissue and palpable lymph nodes. Studies confirmed nearly undetectable immunoglobulins (IgG: 45 mg/dL, IgA: < 5 mg/dL, IgM: < 5 mg/dL, IgE: Indetectable) and a virtual absence of B lymphocytes. Genetic sequencing detected a mutation in the Bruton tyrosine kinase gene. The patient began lifelong immunoglobulin replacement therapy.
Conclusions: early diagnosis through medical history and physical examination is crucial to avoid serious complications. Although treatment improves quality of life, the risk of chronic lung damage persists.

Keywords: Primary Immunodeficiency; Recurrent Infections; X-linked.

RESUMEN

Introducción: la agammaglobulinemia asociada al cromosoma X es una inmunodeficiencia primaria causada por mutaciones en el gen de la tirosina quinasa de Bruton, que afecta predominantemente a varones. Se caracteriza por la ausencia de linfocitos B y niveles extremadamente bajos de inmunoglobulinas séricas. Esto provoca una vulnerabilidad a infecciones bacterianas recurrentes a partir de los seis meses de edad, tras la pérdida de anticuerpos maternos.
Presentación del caso: un lactante de catorce meses presentó fiebre, dificultad respiratoria y antecedentes de otitis, neumonía y gastroenteritis desde los siete meses. El examen físico reveló ausencia de tejido amigdalino y ganglios linfáticos palpables. Los estudios confirmaron inmunoglobulinas casi indetectables (IgG: 45 mg/dL, IgA: < 5 mg/dL, IgM: < 5 mg/dL, IgE: Indetectable) y ausencia virtual de linfocitos B. La secuenciación genética detectó una mutación en el gen de la tirosina quinasa de Bruton. El paciente inició terapia de reemplazo con inmunoglobulina de por vida.
Conclusiones: el diagnóstico temprano mediante la historia clínica y el examen físico es crucial para evitar complicaciones graves. Aunque el tratamiento mejora la calidad de vida, persiste el riesgo de daño pulmonar crónico.

Palabras clave: Agammaglobulinemia, Cromosoma X; Infecciones Recurrentes; Inmunodeficiencia Primaria.

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INTRODUCTION

X-linked agammaglobulinemia, also known as Bruton's agammaglobulinemia or simply XLA (X-linked agammaglobulinemia), represents one of the most emblematic and best-characterized primary immunodeficiencies in the history of clinical immunology. First described more than seven decades ago by the American pediatrician Ogden Bruton in 1952, this disease constitutes the prototype of pure B-cell deficiency and has served as a fundamental model for understanding the molecular mechanisms underlying the development and maturation of these essential cells of the adaptive immune system.[1,2]

XLA is a rare type of primary immunodeficiency (PID) characterized by a block in the differentiation of pre-B lymphocytes into mature B cells, leading to a virtual absence of antibodies and peripheral B cells. Its low incidence, estimated globally at between 1 in 200,000 and 1 in 500,000 live male births, makes this case report particularly significant. The presentation of detailed clinical cases is essential for raising awareness among frontline medical staff (pediatricians and family physicians), given that delayed diagnosis—often due to a low index of suspicion—leads to irreversible organ damage, particularly bronchiectasis caused by recurrent infections.[3]

North American (USIDNET) and European (ESID) registries show that in these regions, antibody deficiencies account for more than 50 % of PID diagnoses, with XLA being one of the most emblematic forms of agammaglobulinemia, with a consistent global distribution that reinforces the need to implement early screening in male patients with a suggestive family history or recurrent infections following the decline in maternal antibodies (after 6 months of age).[4,5]

The Latin American Registry (LASID) presents data from the Latin American Society for Immunodeficiencies (LASID) registry, highlighting that although significant underreporting occurs in our region, antibody deficiencies continue to account for the majority of reported cases. Collaboration through LASID is vital for standardizing diagnostic criteria and improving survival in Latin American patients, where access to immunoglobulin replacement therapies has historically been a logistical challenge.[6]

In Cuba, the management of these conditions has been systematized through the National Registry of Primary Immunodeficiencies, coordinated by the Institute of Hematology and Immunology (IHI). As reported by Macías et al.[7] in their studies on the epidemiology of PIDs in the country, antibody-predominant deficiencies represent the most frequent diagnostic subgroup. These studies have made it possible to centralize epidemiological surveillance and improve access to immunological and molecular diagnostics, despite global technological limitations. In our province of Villa Clara, care for patients with suspected PID is governed by established national protocols. The referral institution, the "José Luis Miranda García" University Pediatric Clinical and Surgical Hospital, works in a network with the IHI to ensure continuity of care. Local epidemiological surveillance focuses on early identification through medical history and warning signs (recurrent infections, absence of tonsils, family history), ensuring that every suspected case is promptly referred to tertiary care facilities for confirmatory diagnosis and initiation of replacement therapy (IVIG or SCIG), which is the cornerstone for improving the quality of life of these patients in our healthcare system.[7]

The aim of this article is to describe the clinical and therapeutic aspects of X-linked agammaglobulinemia.

CASE REPORT

A 14-month-old male patient was admitted to the Pediatric Emergency Department and presented with acute respiratory symptoms characterized by a fever of 39,5 °C that had persisted for two days, severe productive cough, lethargy, and signs of respiratory distress.

Physical examination

- The vital signs included a temperature of 39,5 °C, a heart rate of 160 bpm, a respiratory rate of 45 bpm, and an oxygen saturation (SpO2) of 88 % on room air.
- General Appearance: Acutely ill pediatric patient, lethargic, with evident signs of respiratory distress (nasal flaring and subcostal retractions).
- Head and neck: Otoscopy revealed bilaterally opaque and bulging tympanic membranes. Notable is the absence of tonsillar tissue (hypoplastic/invisible palatine tonsils). No cervical, submandibular, or axillary lymph nodes are palpable, an unusual finding in the context of an acute and severe infectious condition.
- Chest and lungs: Auscultation revealed right basal crackles and decreased vesicular breath sounds in the lower third of the right hemithorax.
- Abdomen: Soft, depressible, without hepatosplenomegaly.

Personal medical history (PMH)

Perinatal (0 months): Uncomplicated pregnancy. She was born at term (39 weeks) via spontaneous vaginal delivery. Birth weight: 3,200 g. Nutritional and Developmental (0–6 months): Exclusively breastfed until 6 months. The child appeared healthy at this stage. Immunizations (2–6 months): Vaccination schedule up to date. These include live attenuated vaccines such as rotavirus. Although no serious systemic complications occurred, prolonged diarrhea was reported following the second dose.

Infectious (7–14 months): Coinciding with weaning, a pattern of recurrent infections began:

- 7, 8, and 12 months: Three episodes of acute otitis media. The patients were treated on an outpatient basis with amoxicillin-clavulanic acid (40 mg/kg/day for 10 days).
- 9 months: One episode of community-acquired pneumonia (CAP) requiring hospitalization. The child received intravenous antimicrobial therapy with ceftriaxone (50 mg/kg/day) for 7 days, with a favorable outcome.
- 10 and 13 months: Two episodes of prolonged acute gastroenteritis. During the second episode, *Giardia lamblia* was isolated and treated with metronidazole (15 mg/kg/day for 5 days).

Family medical history (FMH): No history of consanguinity. A suggestive clinical history is noted: a maternal uncle (the mother's brother) died at age 2 from pulmonary sepsis.

Given the family history of early death in a male due to infectious causes and the patient's APP, the case was previously evaluated by the Clinical Genetics service. The construction of the family tree pointed to an X-linked inheritance pattern, justifying the subsequent suspicion of primary immunodeficiency and guiding the diagnostic pathway.

Additional Tests (Chronological Order)

1. Chest X-ray (on admission) revealed evidence of lobar consolidation in the right lower lobe, which was consistent with acute pneumonia.
2. Complete blood count: Total white blood cells: 14,500/µL (reference range: 6,000–15,000/µL)
    - Neutrophils: 75 % | 10,875/µL (reference range: 25–60 % | 1,500–8,500/µL)
    - Lymphocytes: 20 % | 2,900/µL (reference range: 35–65 % | 3,000–9,500/µL)
    - Monocytes: 3 % | 435/µL (reference range: 2–8 % | 200–1,000/µL)
    - Eosinophils: 2 % | 290/µL (reference range: 1–5 % | 50–700/µL)
    - Basophils: 0 % | 0/µL (reference range: 0–1 % | 0–150/µL)
    - Hemoglobin concentration: 11,5 g/dL (reference range: 11,0–14,0 g/dL)
    - Platelets: 250,000/µL (reference range: 150,000–400,000/µL)
3. Blood culture (taken upon admission) revealed a positive result at 48 hours for *S. pneumoniae*.
4. Serum Immunoglobulin Levels (indicated due to suspected immunodeficiency):
    - IgG concentration: 45 mg/dL (reference range: 400–1,200 mg/dL) – Severely decreased.
    - IgA: < 5 mg/dL (reference range: 30–100 mg/dL) – Undetectable.
    - IgM: < 5 mg/dL (reference range: 40–140 mg/dL) – Undetectable.
    - IgE: Undetectable (reference range: < 60 IU/mL).
5. Flow Cytometry - Lymphocyte Subpopulations: This study was conducted in accordance with the protocol of the Institute of Hematology and Immunology (IHI) in Havana.
    - Total T cells (gated: CD3+/CD45+): 83 % | 2,407 cells/µL (reference range: 55–80 % | 1,500–4,000 cells/µL).
    - Helper T lymphocytes (gated: CD3+/CD4+/CD45+): 52 % | 1,508 cells/µL (Ref. range: 30–55 % | 1,000–2,500 cells/µL).
    - Cytotoxic T lymphocytes (gated: CD3+/CD8+/CD45+): 28 % | 812 cells/µL (Ref. range: 15–35 % | 500–1,500 cells/µL).
    - NK cells (gated: CD3-/CD16+CD56+/CD45+): 16 % | 464 cells/µL (reference range: 5–15 % | 150–700 cells/µL).
    - B lymphocytes (Gating: CD3-/CD19+/CD20+/CD45+): 0,05 % | 1,45 cells/µL (Ref. range: 10–25 % | 300–1,000 cells/µL) – Virtually absent.

Genetic Sequencing

The DNA sample was sent to and processed at the Center for Genetic Engineering and Biotechnology in Havana. A panel of primary immunodeficiencies was analyzed using next-generation sequencing (NGS), confirming a pathogenic mutation in the BTK gene (Bruton's tyrosine kinase), located on the X chromosome (Xq21,3-q22). A family study confirmed that the mother was a heterozygous carrier, establishing a definitive diagnosis of X-linked agammaglobulinemia (Bruton's disease).

Course and Treatment

Empirical intravenous antibiotic therapy was initiated with cefotaxime (1 g/4 mL vial) at a dosage of 150 mg/kg/day, which was administered in divided doses every 8 hours. The empirical treatment was subsequently supported by the results of blood culture susceptibility testing, which revealed the following:

- Susceptibility to cefotaxime (MIC <0,5 µg/mL), ceftriaxone, penicillin, and vancomycin.
- Resistant to: Erythromycin, Trimethoprim-Sulfamethoxazole.

In conjunction with this, intravenous immunoglobulin (IVIG) was administered at a dosage of 600 mg/kg. For chronic and outpatient management, the following was indicated:

- Replacement therapy: Monthly IVIG or weekly subcutaneous immunoglobulin (SCIG), with the goal of maintaining tr-trough IgG levels above 500–800 mg/dL and preventing severe infections.
- Precautions: Strict prohibition of live attenuated vaccines (e.g., oral polio, rotavirus, MMR, yellow fever).
- Monitoring: Periodic pulmonary evaluation (lung function tests and chest CT scans) was performed to monitor for the development of bronchiectasis.
- Genetic Counseling: Provided to the mother and extended family (aunts, sisters) to identify other potential carriers and for family planning.

The patient responded favorably. His fever subsided on the third day, and his oxygen requirement decreased progressively. He was discharged on the seventh day, and after 6 months of follow-up in a specialized clinic, he maintained adequate serum IgG levels without further hospitalization.

DISCUSSION

This clinical case provides a classic illustration of the presentation of X-linked agammaglobulinemia (XLA), highlighting the importance of warning signs for the early detection of antibody-deficient conditions. The infant's history—including three episodes of otitis media, severe pneumonia requiring intravenous antibiotics, and recurrent gastroenteritis—fully meets the criteria for clinical suspicion established by organizations such as the Jeffrey Model Foundation. The need for hospitalization and the use of parenteral antimicrobial therapy are critical indicators that should guide clinicians toward a thorough immunological evaluation.[8,9]

In the diagnostic process, it is essential to recognize that flow cytometry and genetic sequencing are not typically immediately available tools in the initial clinical setting. While awaiting these results, clinical reasoning should consider various differential diagnoses. Transient hypogammaglobulinemia of infancy (THI) is a common condition in this age group; however, unlike XLA, children with THI typically have circulating B lymphocytes and immunoglobulin levels that tend to normalize between 2 and 4 years of age.[10]

Another probable diagnosis is common variable immunodeficiency (CVID), although this usually manifests in later stages (generally after age 4 or in adulthood) and is frequently associated with normal or enlarged lymphoid tissue (lymphadenopathy or splenomegaly), which contrasts with the lymphoid hypoplasia observed in this patient. Likewise, hyper-IgM syndrome, which is characterized by a marked reduction in IgG and IgA but with normal or elevated IgM levels, should be considered; however, this was ruled out given the panhypogammaglobulinemia in this case.[8]

The patient's history followed the characteristic temporal pattern of XLA. The period of good health during the first 6 months of life reflects the protection conferred by maternal immunoglobulins transferred transplacentally, particularly IgG. The onset of recurrent bacterial infections at 7 months, coinciding with weaning and the degradation of maternal antibodies, is highly suggestive of primary humoral deficiency. Patients with XLA typically develop symptoms between 6 and 12 months of age, although approximately 60 % are diagnosed when they present with a severe, life-threatening infection.[11]

The pattern of infections is characteristic of XLA: three episodes of acute otitis media (the most common manifestation prior to diagnosis), pneumonia requiring hospitalization, and prolonged gastroenteritis with isolation of Giardia lamblia. Recurrent otitis media is reported in 88 % of patients with XLA in the USIDNET registry, while respiratory infections are the most commonly documented. Susceptibility to Giardia lamblia is characteristic of all antibody deficiencies and can cause chronic diarrhea, weight loss, and protein-losing enteropathy.[12]

Physical examination revealed two crucial findings that should have immediately raised suspicion of primary immunodeficiency: marked lymphoid hypoplasia (hypoplastic/invisible palatine tonsils) and the absence of palpable lymph nodes despite active infection. These findings contrast dramatically with what is expected in a child with an acute infection, where reactive lymphadenopathy would normally be observed. The absence of lymphoid tissue is a distinctive feature of XLA that distinguishes it from other immunodeficiencies, such as common variable immunodeficiency (CVID), where lymphoid tissue is normal in size or enlarged.[9]

These physical findings should facilitate early recognition of the disorder and are sufficiently specific to warrant immediate immunological testing.[13,14]

Laboratory tests confirmed the diagnostic criteria for XLA:

Severe hypogammaglobulinemia was defined as an IgG concentration of 45 mg/dL (normal 400–1200 mg/dL), with undetectable IgA and IgM concentrations (200 mg/dL). Particular attention to IgM is critical: although decreased IgG and IgA can be seen in children with constitutional delay in immunoglobulin production, low IgM combined with reduced IgA and IgG is almost always indicative of immunodeficiency.[15]

1. Virtually absent B lymphocytes: 0,1 % CD19+ cells (normal 10–20 %). This finding is pathognomonic of XLA and reflects the blockage of the differentiation of pro-B cells to pre-B cells caused by BTK mutation.[16]
2. Preserved cellular immunity: T lymphocytes (CD3+, CD4+, and CD8+) and natural killer (NK) cells were normal, confirming that this was a pure B-cell deficiency.[17]

The history of a maternal uncle who died at age 2 from pulmonary sepsis strongly suggests XLA in the family. Given the X-linked recessive inheritance pattern, the sisters of affected males have a 50 % chance of being carriers, and the sons of carriers have a 50 % chance of being affected. In 80–85 % of cases, the mother is a carrier of the mutation, while 15–20 % result from de novo mutations. Confirmation that Mateo's mother is a heterozygous carrier has important implications for family genetic counseling and future pregnancies.[18]

The current presentation of lobar pneumonia caused by Streptococcus pneumoniae is typical of XLA. Encapsulated bacteria, particularly S. pneumoniae and Haemophilus influenzae, are the pathogens most commonly implicated prior to diagnosis and may continue to cause sinusitis and otitis even after the initiation of immunoglobulin replacement therapy. A positive blood culture for S. pneumoniae confirms severe bacteremic infection, which represents one of the life-threatening complications leading to diagnosis in approximately 60 % of cases.[19]

A concerning aspect of this case is that the patient received live attenuated vaccines (rotavirus) according to the vaccination schedule and presented with prolonged diarrhea after the second dose. Although no serious complications were reported, this represents a significant risk. Patients with XLA are susceptible to persistent infections from live-virus vaccines; historically, 5–10

% of patients developed paralytic poliomyelitis associated with the oral live-attenuated virus vaccine before the availability of immunoglobulin replacement therapy. Prolonged postvaccination diarrhea could have been a manifestation of rotavirus vaccine infection. These retrospective findings underscore the importance of early diagnosis, ideally through neonatal screening, to avoid the administration of live vaccines in these patients.[20,21]

Acute treatment was appropriate: empirical intravenous antibiotic therapy with cefotaxime. This approach was based on national treatment protocols for severe community-acquired pneumonia (CAP) in pediatrics, which recommend third-generation cephalosporins for empirical coverage of the main encapsulated community pathogens (such as pneumococcus or H. influenzae), to which this patient is highly susceptible.(

Intravenous immunoglobulin (IVIG) was administered at a therapeutic dosage of 600 mg/kg to provide immediate antibodies against the active infection.[15,19] Although IVIG is fundamentally a replacement therapy, in the context of this severe infectious condition, it acts as a systemic adjuvant by providing an immediate load of opsonins and neutralizing antibodies against the ongoing infection, as supported by the indications in Cuba's National Formulary of Medicines for severe sepsis in immunocompromised patients.

For chronic management, immunoglobulin replacement therapy is the cornerstone of treatment:[22]

- Dose: 300–800 mg/kg every 3–4 weeks for IVIG or 100 mg/kg weekly for subcutaneous immunoglobulin (SCIG).[22]
- Trough Level Goal: Maintain IgG >500–800 mg/dL, with an optimal target of ≥600 mg/dL.[19,22,23]
- Individualization: The dose should be adjusted on the basis of clinical response and trough levels, as there is significant variability in the half-life of IgG among patients.[24]

The decision to use weekly subcutaneous immunoglobulin at home is appropriate and reflects current practice. Both IVIG and SCIG have comparable efficacy, and the choice depends on factors related to patient and family convenience. SCIG offers the advantages of home administration, more stable IgG levels, and potentially fewer systemic adverse reactions.[16]

Although the patient responded favorably to initial treatment and did not require new hospitalizations at the 6-month follow-up, recognizing that XLA is associated with long-term risks even with optimal treatment is crucial.[12] Recurrent infections can lead to bronchiectasis and chronic obstructive pulmonary disease when adequate prophylactic treatment is not implemented. Recent cohort studies confirm that bronchiectasis remains a significant burden for these patients despite current best therapeutic efforts. Despite immunoglobulin replacement therapy, patients remain susceptible to systemic enteroviral infections, including enteroviral meningoencephalitis. Neurological manifestations are significant comorbidities associated with mortality.[12,25]

Although current therapy reduces early mortality, life expectancy remains reduced compared with that of the general population. In the USIDNET registry, infection-related mortality was reported in 71 % of deaths, with chronic lung disease as a frequent complication (53 %). The median age at death was 21 years.[12]

Although immunoglobulin replacement therapy is the current standard of care, it has inherent limitations: it lacks IgA and IgM, which places patients at theoretical risk for recurrent respiratory infections and the development of bronchiectasis. Hematopoietic stem cell transplantation (HSCT) is a potentially curative strategy, but it is not the standard of care because the associated risks must be balanced against the severity of XLA and the availability of other existing treatments. Gene therapy represents a promising future option, with murine models having demonstrated proof of concept.[26]

As a practical recommendation for general practitioners, this report highlights the importance of a thorough physical examination. The absence of palatine tonsils and palpable lymph nodes in a child with an active infection process is a physical finding strongly suggestive of a defect in B-cell maturation. In the presence of this sign, the physician must strictly refrain from administering live attenuated vaccines (such as rotavirus or oral polio), as they may trigger active disease, as suggested by the prolonged postvaccination diarrhea in this infant.[27]

Finally, it is necessary to acknowledge the limitations of this study. As this is a single-case report, its findings cannot be generalized to the entire population of patients with XLA, nor do they allow for definitive inferences of causality. Furthermore, the six-month follow-up is considerably short for evaluating the chronic course of the disease and the success of treatment in preventing long-term organ damage. Nevertheless, the detailed presentation of this case serves a vital educational purpose by raising awareness among healthcare professionals about a rare disease whose prognosis depends critically on early diagnosis.

CONCLUSIONS

This patient's presentation demonstrates that the early detection of X-linked agammaglobulinemia depends on a detailed medical history that identifies the onset of recurrent bacterial infections following the loss of maternal immunity. Physical examination, specifically the notable absence of tonsillar tissue and palpable lymph nodes despite active infectious processes, is a powerful and specific clinical tool for differentiating this disorder from other immune deficiencies.

The definitive diagnosis achieved through sequencing of the Bruton's tyrosine kinase gene not only validates the child's medical management but is also essential for identifying the mother as a carrier and providing essential genetic counseling for the family. Finally, the case highlights that while lifelong immunoglobulin replacement therapy allows for effective control of infections and an initial favorable course, maintaining continuous monitoring of pulmonary status and strictly prohibiting the use of live-virus vaccines to avoid serious long-term complications are vital.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

AUTHORSHIP CONTRIBUTION

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BIBLIOGRAPHIC REFERENCES

1. Rosen FS, Cooper MD, Wedgwood RJP. The Primary Immunodeficiencies. N Engl J Med. 1995;333(7):431-40. doi:10.1056/NEJM199508173330707

2. Ochs HD, Edvard Smith CI. X-Linked Agammaglobulinemia A Clinical and Molecular Analysis: Medicine (Baltimore). 1996;75(6):287-99. doi:10.1097/00005792-199611000-00001

3. Rivière JG, Franco-Jarava C, Martínez-Gallo M, Aguiló-Cucurull A, Blasco-Pérez L, Paramonov I, et al. Uncovering Low-Level Maternal Gonosomal Mosaicism in X-Linked Agammaglobulinemia: Implications for Genetic Counseling. Front Immunol. 2020;11:46. doi:10.3389/fimmu.2020.00046

4. Kindle G, Alligon M, Albert MH, Buckland M, Edgar JD, Gathmann B, et al. Inborn errors of immunity: manifestation, treatment, and outcome – an ESID registry 1994-2024 report on 30,628 patients. Allergy and Immunology; 2025. http://medrxiv.org/lookup/doi/10.1101/2025.02.20.25322586 doi:10.1101/2025.02.20.25322586

5. Pickett G, Motazedi T, Kutac C, Cahill G, Cunnigham-Rundles C, Fuleihan RL, et al. Infection Phenotypes Among Patients with Primary Antibody Deficiency Mined from a US Patient Registry. J Clin Immunol. 2021;41(2):374-81. doi:10.1007/s10875-020-00916-1

6. Villavicencio MF, Pedroza LA. Diagnosis of primary immunodeficiency diseases in the developing world: the need for education and networking with the developed world. Curr Opin Pediatr. 2019;31(6):835-42. doi:10.1097/MOP.0000000000000834

7. Macías-Abraham C, Marsán V, Sánchez M, Ustariz C, Alfonso M, Adams Y, et al. Registro cubano de inmunodeficiencias primarias. Rev Cuba Hematol Inmunol Ía Hemoter. 2017;36. https://revhematologia.sld.cu/index.php/hih/article/download/791/751/5127?hl=es-ES

8. Rawat A, Jindal AK, Suri D, Vignesh P, Gupta A, Saikia B, et al. Clinical and Genetic Profile of X-Linked Agammaglobulinemia: A Multicenter Experience From India. Front Immunol. 2021;11. doi:10.3389/fimmu.2020.612323

9. Eldeniz FC, Gul Y, Yorulmaz A, Guner SN, Keles S, Reisli I. Evaluation of the 10 Warning Signs in Primary and Secondary Immunodeficient Patients. Front Immunol. 2022;13:900055. doi:10.3389/fimmu.2022.900055

10. Chen XF, Wang WF, Zhang YD, Zhao W, Wu J, Chen TX. Clinical characteristics and genetic profiles of 174 patients with X-linked agammaglobulinemia: Report from Shanghai, China (2000–2015). Medicine (Baltimore). 2016;95(32):e4544. doi:10.1097/MD.0000000000004544

11. Rondón-Carrasco J, Morales-Vázquez CL, Rosabal-Pérez K, Rondón-Carrasco J, Morales-Vázquez CL, Rosabal-Pérez K. Papel inmunológico de la lactancia materna en la prevención de enfermedades. Rev Cienc Médicas Pinar Río. 2024; 28(2). http://scielo.sld.cu/scielo.php?script=sci_abstract&pid=S1561-31942024000200022&lng=es&nrm=iso&tlng=es

12. O'Toole D, Groth D, Wright H, Bonilla FA, Fuleihan RL, Cunningham-Rundles C, et al. X-Linked Agammaglobulinemia: Infection Frequency and Infection-Related Mortality in the USIDNET Registry. J Clin Immunol. 2022;42(4):827-36. doi:10.1007/s10875-022-01237-1

13. van Schouwenburg P, Unger S, Payne KJ, Kaiser FMP, Pico-Knijnenburg I, Pfeiffer J, et al. Deciphering imprints of impaired memory B-cell maturation in germinal centers of three patients with common variable immunodeficiency. Front Immunol. 2022;13:959002. doi:10.3389/fimmu.2022.959002 PubMed PMID: 36275744; PubMed Central PMCID: PMC9582261.

14. Ransmayr B, Bal SK, Thian M, Svaton M, van de Wetering C, Hafemeister C, et al. LTβR deficiency causes lymph node aplasia and impaired B cell differentiation. Sci Immunol. 2024;9(101):eadq8796. doi:10.1126/sciimmunol.adq8796 PubMed PMID: 39576873; PubMed Central PMCID: PMC7618087.

15. Smith CE, Berglöf A. X-Linked Agammaglobulinemia. En: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Amemiya A, editores. GeneReviews®. Seattle (WA): University of Washington, Seattle; 1993. http://www.ncbi.nlm.nih.gov/books/NBK1453/ PubMed PMID: 20301626.

16. Sun D, Heimall JR, Greenhawt MJ, Bunin NJ, Shaker MS, Romberg N. Cost Utility of Lifelong Immunoglobulin Replacement Therapy vs Hematopoietic Stem Cell Transplant to Treat Agammaglobulinemia. JAMA Pediatr. 2022;176(2):176. doi:10.1001/jamapediatrics.2021.4583

17. Buckley RH. Primary Immunodeficiency Diseases Due to Defects in Lymphocytes. Mackay IR, Rosen FS, editores. N Engl J Med. 2000;343(18):1313-24. doi:10.1056/NEJM200011023431806

18. Jain A, Govindaraj GM, Edavazhippurath A, Faisal N, Bhoyar RC, Gupta V, et al. Whole genome sequencing identifies novel structural variant in a large Indian family affected with X-linked agammaglobulinemia. Bandapalli OR, editor. PLOS ONE. 2021;16(7):e0254407. doi:10.1371/journal.pone.0254407

19. Lackey AE, Ahmad F. X-Linked Agammaglobulinemia. En: StatPearls. StatPearls Publishing; 2023. https://www.ncbi.nlm.nih.gov/books/NBK549865/ PubMed PMID: 31751055.

20. Blom M, Duintjer AJ, Jamee M, De Gier M, Bloomfield M, Klocperk A, et al. Self-reported Clinical Outcomes and Quality of Life in Agammaglobulinemia: the Importance of an Early Diagnosis. J Clin Immunol. 2025;45(1):125. doi:10.1007/s10875-025-01904-z

21. Nishimura A, Uppuluri R, Raj R, Swaminathan VV, Cheng Y, Abu-Arja RF, et al. An International Survey of Allogeneic Hematopoietic Cell Transplantation for X-Linked Agammaglobulinemia. J Clin Immunol. 2023;43(8):1827-39. doi:10.1007/s10875-023-01551-2 PubMed PMID: 37454339.

22. Research C for BE and. BIVIGAM. FDA. 2024. https://www.fda.gov/vaccines-blood-biologics/approved-blood-products/bivigam

23. Maarschalk-Ellerbroek LJ, Hoepelman IM, Ellerbroek PM. Immunoglobulin treatment in primary antibody deficiency. Int J Antimicrob Agents. 2011;37(5):396-404. doi:10.1016/j.ijantimicag.2010.11.027

24. Peddi NC, Vuppalapati S, Sreenivasulu H, Muppalla SK, Reddy Pulliahgaru A. Guardians of Immunity: Advances in Primary Immunodeficiency Disorders and Management. Cureus. 2023;15(9):e44865. doi:10.7759/cureus.44865 PubMed PMID: 37809154; PubMed Central PMCID: PMC10560124.

25. Cinicola BL, Uva A, Leonardi L, Moratto D, Giliani S, Carsetti R, et al. Case Report: A Case of X-Linked Agammaglobulinemia With High Serum IgE Levels and Allergic Rhinitis. Front Immunol. 2020;11. doi:10.3389/fimmu.2020.582376

26. Shillitoe BMJ, Gennery AR. An update on X-Linked agammaglobulinaemia: clinical manifestations and management. Curr Opin Allergy Clin Immunol. 2019;19(6):571-7. doi:10.1097/ACI.0000000000000584

27. Chear CT, Ismail IH, Chan KC, Noh LM, Kassim A, Latiff AHA, et al. Clinical features and mutational analysis of X-linked agammaglobulinemia patients in Malaysia. Front Immunol. 2023;14:1252765. doi:10.3389/fimmu.2023.1252765 PubMed PMID: 37809070; PubMed Central PMCID: PMC10560089.