Ligneous keratoconjunctivitis: a case report with predominantly corneal presentation

Ceratoconjuntivite lenhosa: relato de caso com apresentação predominantemente corneana

Leriéli Ferreira da Silva[1], **Victória Helena Stelzer Rocha**[1], **Eduardo Melani Rocha**[1], **Vívian Teixeira Sartori Carvalho**[1], **Bruno Fonzar Tannous**[1]

[1] Ophthalmology Department, Hospital das Clínicas de Ribeirão Preto, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, SP, Brazil.

How to cite:
Silva LF, Rocha VH, Rocha EM, Carvalho VT, Tannous BF. Ligneous keratoconjunctivitis: a case report with predominantly corneal presentation. Rev Bras Oftalmol. 2025;84:e0057.

doi:
https://doi.org/10.37039/1982.8551.20250057

Keywords:
Streptococcus pyogenes; Epithelium, corneal; Coinfection; Conjunctivitis; Keratoconjunctivitis; Chronic disease; Child

Descritores:
Streptococcus pyogenes; Epitélio corneano; Coinfecção; Conjuntivite; Ceeratoconjuntivite; Doença crônica; Criança

Received on:
July 25, 2024

Accepted on:
June 12, 2025

Corresponding author:
Eduardo Melani Rocha
Ophthalmology Department
Avenida dos Bandeirante, 3.900, 12° andar, Monte Alegre
Zip code: 14048-900 – Ribeirão Preto, SP, Brazil
E-mail: emrocha@frmp.usp.br

Institution:
Departamento de Oftalmologia, Hospital das Clínicas de Ribeirão Preto, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, SP, Brazil.

Conflict of interest:
no conflict of interest.

Financial support:
no financial support for this work.

ABSTRACT

Ligneous conjunctivitis is a rare chronic disease described as membranous keratoconjunctivitis that may be associated with systemic manifestations. It is associated with congenital plasminogen deficiency. In this case report, we describe the case of a 3-year-old male child who was diagnosed with ligneous conjunctivitis that mimicked gonococcal conjunctivitis after secondary infection with *Streptococcus pyogenes*. The patient had a bilateral pre-tarsal conjunctival membrane and a fibrous membrane extremely adherent to the corneal epithelium in the left eye, associated with intense purulent sensation. A plasminogen activity test was performed using a result of 36%, with the reference value being between 75 and 150%. The treatment consisted of 14 sessions of plasmapheresis, resulting in an improvement in the appearance of the cornea and conjunctiva."

RESUMO

A conjuntivite lenhosa é uma doença crônica rara descrita como ceratoconjuntivite membranosa que pode estar associada a manifestações sistêmicas. Está associada à deficiência congênita de plasminogênio. Neste relato de caso, descrevemos o caso de uma criança do sexo masculino, de 3 anos de idade, diagnosticada com conjuntivite lenhosa que mimetizava conjuntivite gonocócica após infecção secundária por Streptococcus pyogenes. O paciente apresentava membrana conjuntival pré-tarsal bilateral e membrana fibrosa extremamente aderente ao epitélio corneano no olho esquerdo, associada a intensa sensação purulenta. Foi realizado teste de atividade do plasminogênio com resultado de 36%, sendo o valor de referência entre 75 e 150%. O tratamento consistiu em 14 sessões de plasmaférese, resultando em melhora da aparência da córnea e da conjuntiva.

INTRODUCTION

Ligneous keratoconjunctivitis (LK) is the most common clinical manifestation of type I congenital plasminogen (PLG) deficiency (PLGD-I), also known as hypoplasminogenemia, which is an autosomal recessive systemic disorder.[1-4] The disorder causes low plasminogen antigen and activity levels and the degree of reduction of the PLG plasma level is variable, with a PLG activity ranged from 4% to 51% (normal range 75 to 120%).[4]

Its characteristic feature is the formation of pseudomembranes containing fibrin in the tarsal conjunctiva, which may involve corneal involvement. Diagnostic and treatment tools are not standardized and are currently poorly available. We report a case of ligneous conjunctivitis with good response to plasmapheresis.[4,5]

CASE REPORT

Male patient, 3 years and 8 months old, who was admitted to the Ribeirão Preto Emergency Unit, at the Hospital das Clínicas de Ribeirão Preto of the Faculdade de Medicina de Ribeirão Preto of the Universidade de São Paulo, on December 27, 2022.

The patient presented with abundant and thick ocular secretions, ocular irritation, and photophobia in both eyes, which worsened in the left eye. Approximately 1 week before, he had been treated with tobramycin for 5 days, without any improvement in his condition. There was partial improvement in symptoms with the use of ciprofloxacin + dexamethasone eye drops for 1 day. The accompanying responsible for the patient reported the presence of thick secretion and previous frequent episodes of conjunctivitis, of lesser intensity, since birth, previous diagnosis of allergic conjunctivitis, long-term use of cromoglicato disodico eye drops, and the habit of removing membranes with a cotton swab.

The responsible denied other systemic comorbidities, parental consanguinity, genetic diseases, or similar cases in the family. He has siblings without any comorbidities.

Clinical and biomicroscopic examinations

The patient presented with bilateral upper tarsal conjunctival membranes, chemosis and conjunctival hyperemia, transparent cornea on the right eye (Figure 1A), and corneal opacity on the left eye (Figure 1B)secondary to adhesion of membranes and fibrin, presence of purulent secretion in the left fornix. On physical examination, he had aphthous lesions in the oral cavity.

Laboratory exams

He presented negative serologies for hepatitis B and C, HIV, HTLV and syphilis, positive ocular secretion culture for multi-sensitive *Streptococcus pyogenes* (December 28, 2022), biopsy of the fibrin plaque covering the cornea (January 2, 2023): fragments of fibrin-leukocyte material, with the presence of numerous neutrophils and reactive epithelial cells; January 12, 2023: tissue plasminogen activator inhibitor 22 ng/dL (within normal limits); activated plasminogen 36% (reduced), figures 2 and 3.

Histopathology

Biopsy of January 2, 2023, presented with fragments of fibrino-leukocyte material, with the presence of numerous neutrophils and reactive epithelial cells.

Treatment

Initially, the patient was treated empirically for suspected bacterial or gonococcal conjunctivitis. After the pediatric team ruled out the hypothesis of gonococcal conjunctivitis and child abuse, and the culture result of the corneal and conjunctival membrane was positive for multi-sensitive *S. pyogenes*, we adjusted the antibiotic according

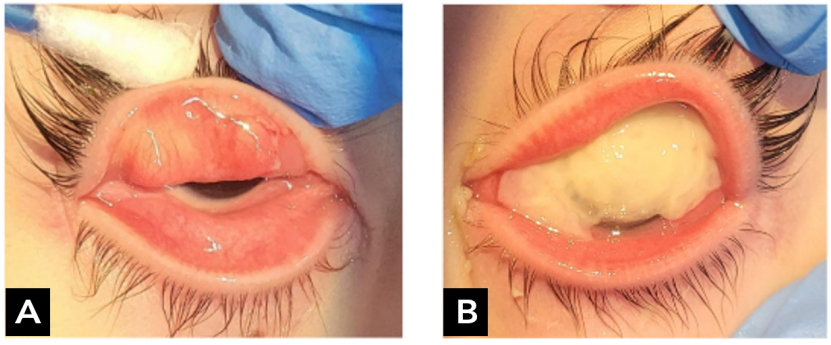

Figure 1. Patient's right (A) and left (B) eye on December 30, 2022.

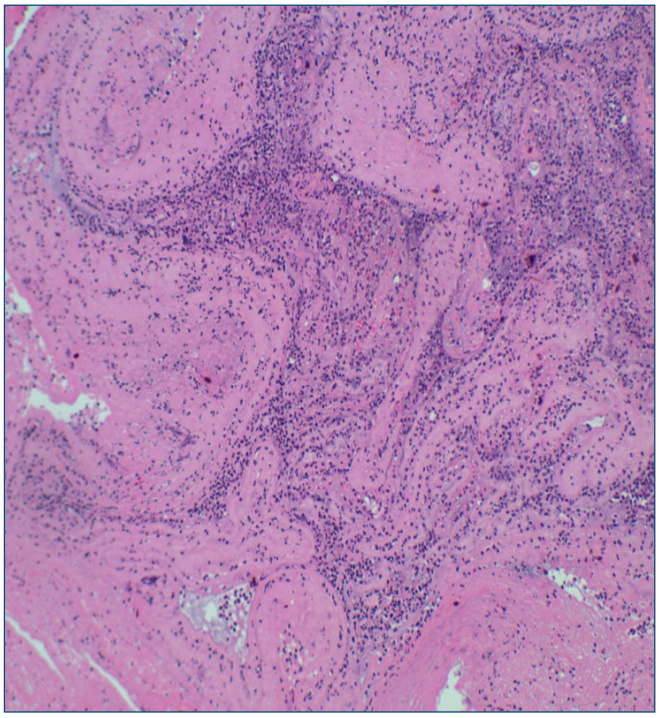

Figure 2. Biopsy of an ocular fragment on the cornea with 100x magnification.

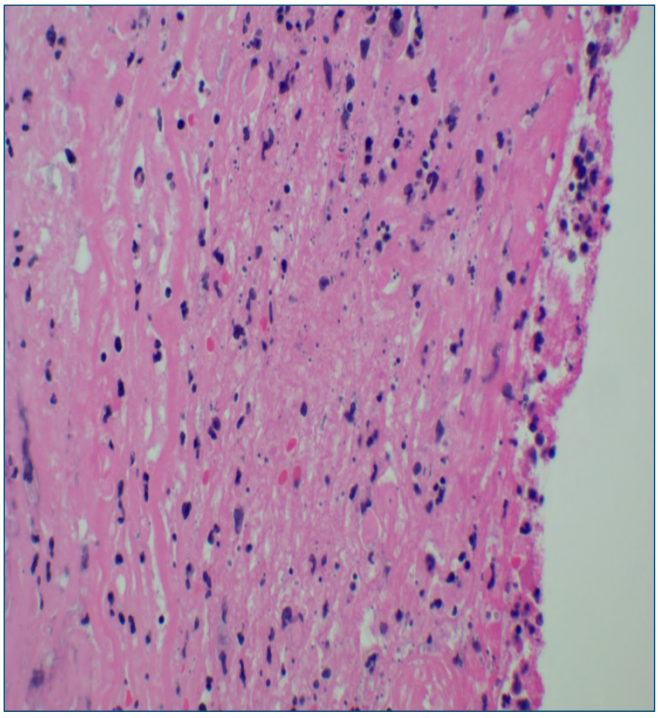

Figure 3. Biopsy of an ocular fragment on the cornea with 300x magnification.

to the test and initiated topical corticosteroids. However, the patient showed only partial improvement in symptoms after 10 days of treatment: reduction of bilateral upper tarsal conjunctival hyperemia, little reduction in the number of membranes in the bilateral upper tarsi, and presence of corneal opacity in the left eye, as well as corneal and bulbar membranes in the left eye. Thus, a decision was made to reduce the topical corticosteroid, discontinue the antibiotic, and maintain only intense lubrication of both eyes. In conjunction with the hematology team, the diagnosis of LK was made, based on laboratory and clinical examinations, and it was decided to start treatment with plasmapheresis.

The patient in this report underwent 14 plasmapheresis sessions, 8 sessions at weekly intervals and the last 5 monthly. The patient showed improvement in the appearance of his cornea and conjunctiva from the first month of plasmapheresis.

At the end of the treatment, the visual acuity of the right eye was 0.8, while the left eye retained only light perception. On biomicroscopy, the right eye showed conjunctival fornices without lesions, clear bulbar conjunctiva, transparent cornea, formed anterior chamber, trophic iris, and transparent lens. The left eye showed clear bulbar conjunctiva, fornices without lesions, corneal scar opacity (corneal keloid), and conjunctivalization of the cornea. The anterior chamber was formed, but it was difficult to evaluate more details because of corneal opacity. Figure 4 shows the eyes of the patient photographed on January 10, 2024, after the treatment described above.

Figure 4. Patient's right (A) and left (B) eye on January 10, 2024.

DISCUSSION

Surgical excision of pseudomembranes alone only provides short-term interruption and can also be a trigger for recurrence.[2,4,6] The treatments described without PLG, such as cyclosporine, steroids and heparin, do not help control the disease or prevent it.[6]

The administration of fresh frozen plasma (FFP) has been shown to be able to reduce pseudomembranous lesions, but the fact that repeated infusions are necessary can be uncomfortable for the patient.[4,7,8] Congenital plasminogen eye drops can be administered more easily and have been found to be effective in several case studies.[4,9,10]

The reported case, in addition to its rarity, presents a serious condition due to the total involvement of the cornea on the left eye and the possibility of amblyopia in the medium and long term.

The disease usually begins as acute, bilateral, membranous, or pseudomembranous conjunctivitis in childhood. Occasionally, it may be associated with corneal involvement that can progress to perforation and loss of the globe.[11] In patients with predisposition or PLGD, the injury can be triggered by triggers such as post-ocular trauma, post-ocular surgery, autoimmune reaction, hypersensitivity or secondary response to viral or bacterial infection, or other systemic infection. The most related etiological agents are *Staphylococcus aureus* and *Haemophilus influenzae*.[12]

The chronic phase is characterized by the appearance of a relatively asymptomatic conjunctival granuloma that recurs despite all forms of treatment.[11]

It is important to highlight that, as it is a rare disease, there are difficulties in both diagnosis and therapy. Diseases that result in the deposit of foreign material in the body, such as amyloidosis or lipoid proteinosis, are among the differential diagnoses. Congenital plasminogen deficiency may be suspected in early childhood, with conjunctival involvement, a history of respiratory infections and/or recurrent cervicitis, and the presence of stromal fibrin deposits on direct immunofluorescence.[3] The suspicion must be confirmed by a decrease in plasminogen activity in plasma and by genetic study of the PLG gene by complete sequencing (next generation sequencing or Sanger) to detect and describe the genetic changes responsible for the appearance of this disease in each patient and their family despite subsequent genetic counseling.[13,14] The difficulty in obtaining such tests also restricts the agility in confirming the diagnosis.

The treatment of these patients is challenging as there is no gold standard treatment described because of the rarity of the pathology. In this manner, several topical and systemic treatments are used, such as those recorded in the literature. Among the therapies, surgical removal of lesions has been indicated when there are local problems, but it can be a trigger for new lesions.[13] The use of stanozolol or danazol, anabolic steroids, can normalize plasminogen levels, as described in a therapeutic trial.[15] The use of fresh plasma transfusions has been described with good results, especially when combined with systemic corticosteroids[16]. The use of human plasminogen may represent a modality with encouraging results, but it also requires more clinical studies.[1]

Tunay et al. demonstrated that topical application of FFP was effective in a case report of a 6-month-old infant with pseudomembranous lesions, mainly in the tarsal conjunctiva, since 2 months of age.[10] Corroborating the effectiveness of topical FFP, Tabbara et al. also demonstrated positive results in subconjunctival applications in patients with ligneous conjunctivitis.[9]

According to Pergantou et al., topical and systemic application of FFP is effective in treating and preventing the recurrence of ligneous conjunctivitis.[17]

We observed that in a University Hospital with many resources and references, we faced obstacles in obtaining diagnostic laboratory tests and access to treatment, such as the handling of FFP eye drops. Despite these limitations, we believe that plasmapheresis is a reasonable plan for the treatment of ligneous conjunctivitis, if plasminogen eye drops is not available.

Last but not least, the fact of listening to the caregiver and valuing their report once again shows us that careful anamnesis helps medicine develop diagnostic hypotheses with greater chances of being correct.

REFERENCES

1. Aslan D, Akata RF. The search for new approaches to treating type 1 plasminogen deficiency. Pediatr Blood Cancer. 2018;65(4). doi: 10.1002/pbc.26922
2. Bauer M, Koinzer S, Oschlies I, Claviez A, Tiede K, Roider J, Nölle B. Conjunctivitis lignosa [Ligneous conjunctivitis]. Ophthalmologe. 2016;113(5):416-9. German.
3. Dimopoulos D, Zacharioudakis A, Kazamias G, Danilatou V, Katerini D, Nodarakis M, Koutentaki ME, Koutentakis P. Ligneous conjunctivitis associated with type I plasminogen deficiency: A rare case. Eur J Ophthalmol. 2022;32(5):NP1-NP4.
4. Sartori MT, Bartuli A, Siboni SM, Leonardi A, Valente P, Secci J, Cortellessa F, Caputo R. Ligneous conjunctivitis and use of human plasminogen eyedrops: The Italian experience. Haemophilia. 2023;29(2):681-4.
5. Martins TG, Martins TG, Martins DG, Kuba MC. Tratamento de conjuntivite lenhosa com soro heterólogo. einstein (São Paulo). 2019;17(3):eRC4714.
6. Schuster V, Seregard S. Ligneous conjunctivitis. Surv Ophthalmol. 2003;48(4):369-88.
7. Yurttaser Ocak S, Bas E. Treatment of ligneous conjunctivitis with fresh

frozen plasm in twin babies. J AAPOS. 2021;25(1):50-2. doi:
8. Watts P, Agha SH, Mameesh M, Conor P, Ganesh A, Al-Mujaini A, et al. Fresh frozen plasma (Octaplas) and topical heparin in the management of ligneous conjunctivitis. J AAPOS. 2019;23(1):42-45.e1.
9. Tabbara KF. Prevention of ligneous conjunctivitis by topical and subconjunctival fresh frozen plasma. Am J Ophthalmol. 2004;138(2):299-300.
10. Tunay ZÖ, Özdemir Ö, Acar D, Gül E, Akbay S. Successful treatment of ligneous conjunctivitis with topical fresh frozen plasma in an infant. Arq Bras Oftalmol. 2015;78(5):318-9
11. Spencer LM, Straatsma BR, Foos RY. Ligneous conjunctivitis. Arch Ophthalmol. 1968;80(3):365–7.
12. Rouatbi A, Chebbi A, Bouguila H. Ligneous conjunctivitis due to plasminogen deficit: Diagnostic and therapeutic approach. With literature review. J Fr Ophtalmol. 2018;41(10):916-9.
13. Magdaleno-Tapial J, Hernández-Bel P, Valenzuela-Oñate C, Gimeno-Ferrer F, Rodríguez-López R, Hernández-Bel L, et al. Congenital plasminogen deficiency with long standing pseudomembranous conjunctival and genital lesions. JAAD Case Rep. 2018;5(1):44-6.
14. Shimabukuro M, Iwasaki N, Nagae Y, Nakagawa Y, Ohtori Y, Inoue Y, Tano Y. Ligneous conjunctivitis: a case report. Jpn J Ophthalmol. 2001;45(4):375-7.
15. Mannucci PM, Kluft C, Traas DW, Seveso P, D'Angelo A. Congenital plasminogen deficiency associated with venous thromboembolism: therapeutic trial with stanozolol. Br J Haematol. 1986;63(4):753–9.
16. Shapiro AD, Nakar C, Parker JM. Plasminogen replacement therapy for the treatment of children and adults with congenital plasminogen deficiency. Blood. 2018;131(12):1301–10.
17. Pergantou H, Likaki D, Fotopulou M, Katsarou O, Xafaki P, Platokouki P. Management of ligneous conjunctivitis in a child with plasminogen deficiency. Eur J Pediatr. 2011; 170(10):1333-6.