CASE REPORT

Tranexamic acid-induced ligneous conjunctivitis with renal failure showed reversible hypoplasminogenaemia

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SUMMARY

Ligneous conjunctivitis is a rare severe conjunctivitis characterised by fibrin-rich, 'woody', pseudomembranes on the tarsal conjunctiva complicated by congenital hypoplasminogenaemia. A previous report suggested that ligneous conjunctivitis may result from tranexamic acid (TA)-induced 'secondary' hypoplasminogenaemia. However, the serum plasminogen level has not been confirmed in that scenario. We report for the first time a case of TA-induced ligneous conjunctivitis with reversible hypoplasminogenaemia. A 70-year-old woman developed a gastric ulcer that was treated with oral TA. After 5 weeks of treatment, the patient presented with bilateral pale yellow pseudomembranes on the palpebral conjunctivae. Haematological analysis showed hypoplasminogenaemia. We diagnosed ligneous conjunctivitis. TA was discontinued after 14 weeks after the gastric ulcer symptoms resolved. Six weeks after discontinuation of therapy, the pseudomembranes regressed and the serum plasminogen level returned to the normal range. TA should be considered a possible aetiology in the setting of unresolving ligneous conjunctivitis.

BACKGROUND

Ligneous conjunctivitis is a rare severe conjunctivitis characterised by fibrin-rich, 'woody', pseudomembranes on the tarsal conjunctiva complicated by congenital hypoplasminogenaemia. A previous report suggested that ligneous conjunctivitis may result from tranexamic acid (TA)-induced 'secondary' hypoplasminogenaemia. However, the serum plasminogen level has not been confirmed in that scenario. We report for the first time a case of TA-induced ligneous conjunctivitis with reversible hypoplasminogenaemia.

CASE PRESENTATION

A 70-year-old Japanese woman with chronic renal failure presented with a 3-day history of pain and pruritus in the left eye and was diagnosed with peripheral corneal infiltration, started on 0.5% levofloxacin hydrate and 0.1% fluorometholone drops. After 1 week with this therapeutic regimen, it had completely resolved. However, during this time the patient developed a gastric ulcer, and was treated with oral TA (Transamin, 750 mg/day). At 6 weeks after initial presentation to our clinic, which coincided with approximately 5 weeks of TA therapy, the patient presented with a 4-day history of bilateral severe eye pain. She had no other ophthalmic problems. Slit lamp examination was normal with the exception of bilateral pale yellow

pseudomembranes on the upper palpebral conjunctiva (figure 1). Dilated funduscopic examination was unremarkable bilaterally. Pseudomembranes were swabbed and cultured, and were found to be negative for bacteria. The lesions were resected bilaterally, and histopathological examination demonstrated fibrin accumulation and an inflammatory cell infiltrate. There was no evidence of fungi and staining for amyloid was negative. Plasma plasminogen activity was low at <25% (normal: 73–94%). A diagnosis of ligneous conjunctivitis was made, and treatment with daily topical cyclosporine (0.1%) was initiated. There were multiple recurrences and repeat resections of the pseudomembranes over a period of 9 weeks. Fourteen weeks after beginning TA, the drug was discontinued due to resolution of gastric ulcer symptoms. Topical cyclosporine was discontinued at 10 weeks after discontinuation of TA. At 6 weeks after discontinuing TA therapy, the pseudomembranes had almost completely regressed (figure 2). Plasma plasminogen activity had also returned to within the normal range at this time (74%). At 30 weeks after discontinuation of TA, there had been no recurrence of pseudomembranes.

INVESTIGATIONS

We could check the serum plasminogen level and pathological examination in a case of TA-induced ligneous conjunctivitis for the first time.

DISCUSSION

Ligneous conjunctivitis is a rare form of chronic conjunctivitis characterised by the development of fibrin-rich, 'woody' (eg, ligneous) pseudomembranes on the tarsal conjunctiva.¹ Corneal involvement is a common complication with this condition, and may lead to blindness as a result of scarring, vascularisation, keratomalacia and corneal perforation.¹ The diagnosis of ligneous conjunctivitis is made based on the clinical appearance and histopathological demonstration of fibrinous pseudomembranes with inflammatory cell infiltrate.¹ Infectious causes for pseudomembrane formation must be ruled out prior to diagnosing ligneous conjunctivitis.¹ Low plasma plasminogen activity further confirms the diagnosis.¹ Herein, we describe a case of recurrent ligneous pseudomembrane formation resulting from treatment with TA, an antifibrinolytic agent. The clinical and laboratory findings were consistent with a diagnosis of ligneous conjunctivitis. The relationship between hypoplasminogenaemia and ligneous conjunctivitis

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Figure 1 Upper palpebral conjunctiva after 6 weeks of tranexamic acid use. Pale yellow, thick pseudomembranes were observed in both eyes.

has been firmly established in the past.¹ A low plasmin activity leads to membrane or pseudomembrane formation due to inadequate fibrinolysis.² Activation of the fibrinolytic system depends on the zymogen plasminogen, a serine protease present in the plasma.³ Plasminogen is predominantly produced by the liver and circulates in the blood. It is converted to plasmin by tissue-plasminogen activator or urokinase-type plasminogen activator.⁴ Plasmin plays an important role in intravascular and extravascular fibrinolysis, wound healing and tissue remodelling.³ The main substrate for plasmin is fibrin and an absence of plasmin leads to pathological clot formation.⁵ Congenital plasminogen deficiency is an autosomal recessive disorder that has a variety of systemic manifestations, including gingivitis, renal calculi, vulvovaginitis, respiratory disease, otitis media and hydrocephalus among others. However, ligneous conjunctivitis is by far the most common clinical manifestation of hypoplasminogenaemia.¹ As our patient had no family history of hypoplasminogenaemia, and there were no other systemic manifestations, a congenital plasminogen deficiency was deemed unlikely. Additionally, serum plasminogen activity rose to within the normal range after cessation of TA.

TA is a synthetic derivative of the amino acid lysine that has been used for the treatment of multiple types of bleeding diatheses, including intraoperative or postoperative bleeding, menorrhagia and pulmonary or renal haemorrhage. It has also been used in cases of oral mucosal aphthae associated with stomatitis and pharyngolaryngitis.⁶ TA exerts its antifibrinolytic effect by blocking the interaction of plasmin with fibrin by blocking the lysine binding sites on the kringle domains of plasmin. This prevents the formation of the fibrin–plasmin complex, thus mitigating fibrinolysis.^{2–6} Interestingly, Diamond *et al*⁷ previously

suggested that the drug could potentially cause ligneous conjunctivitis via its antifibrinolytic effects. Herein, we report for the first time a case of ligneous conjunctivitis associated with reduced serum plasminogen activity that resolved upon cessation of TA therapy, which seems to support the concept that the antifibrinolytic property of this drug may lead to the development of this type of conjunctivitis in some patients.

There is only one report of ligneous conjunctivitis associated with TA,⁷ although TA is a widely used drug.⁶ We hypothesise that our patient may have been at increased risk for the adverse effects of TA secondary to renal dysfunction. The drug is metabolised in the kidney, and some reports have suggested that the drug effects may be increased in patients with renal impairment.⁶ Hence, although the patient was taking the usual therapeutic dose of TA, her blood levels may have been significantly higher. Hence, we suspect that the ligneous conjunctivitis was a manifestation of increased circulating levels of TA. Consistent with this hypothesis, resolution of signs and symptoms only occurred after discontinuation of TA. The use of TA should be considered as a possible aetiology in the setting of unresolving ligneous conjunctivitis. Moreover, caution should be exercised in the use of TA as it may contribute to the development of ligneous conjunctivitis that is not amenable to typical treatment modalities.

Learning points

- ▶ Tranexamic acid (TA) is the antifibrinolytic agent which may cause pseudomembranous disease such as ligneous conjunctivitis in a patient with renal failure.
- ▶ It is important to examine the levels of plasma plasminogen activity after making diagnosis with pseudomembranous conjunctivitis such as ligneous conjunctivitis.
- ▶ One should confirm the previous dosing history of TA when one examines ligneous conjunctivitis.

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Competing interests None.

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Figure 2 Upper palpebral conjunctiva 6 weeks after discontinuing tranexamic acid. There is dramatic improvement with only minimal pseudomembrane present at the left upper palpebral fornix of the conjunctiva.

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