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Clinical report

Root dentin anomaly and a *PLG* mutation

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ABSTRACT

We report a Thai girl affected with plasminogen deficiency, Type I. Ligneous conjunctivitis was first observed when she was one-month-old. The newly recognized findings include tapered incisor roots as a result of thin root dentin, generalized short tooth roots, and mandibular prognathism. Mutation analysis of *PLG* demonstrated homozygous c.1193G>A missense mutation. The parents were heterozygous for c.1193G>A mutation. The c.1193G>A mutation is novel and predicted to cause amino acid substitution p.Cys398Tyr. Thin root dentin in the patient who was affected with *PLG* mutation and immunolocalization of *Plg* during early root development in mice imply the role of plasminogen in root dentin formation.

1. Introduction

Plasminogen deficiency, Type I (OMIM#217090) or inherited severe hypoplasminogenaemia is a rare autosomal recessive disorder of the plasminogen gene (*PLG*) characterized by severely impaired extravascular fibrinolysis leading to ligneous fibrin-rich pseudomembrane formation on mucosa. The most common clinical manifestation is ligneous conjunctivitis (80%), a rare form of chronic conjunctivitis characterized by the formation of pseudomembranes on the palpebral surfaces of the eyes mainly on the tarsal conjunctivae and progress to thick, white or yellow-white masses that replace the normal mucosa. Ligneous gingivitis or periodontitis (destructive membranous periodontitis) (34%), ligneous laryngitis, ligneous vaginitis (8%), and congenital occlusive hydrocephalus have also been reported in patients affected with plasminogen deficiency. No genotype–phenotype correlation has yet been described. Intrafamilial clinical variability has been reported [Klammt et al., 2011; Tefs et al., 2006]. Here, we report a Thai girl affected with type I plasminogen deficiency, ligneous conjunctivitis, thin root dentin, tapered incisor roots, generalized short tooth roots, and a novel *PLG* mutation.

2. Case report

We report a 10-year-old Thai girl who came to the Departments of Ophthalmology and Pediatrics, Faculty of Medicine, Chiang Mai University for the treatment of ligneous conjunctivitis (Fig. 2A). She was the third child of Karen tribe parents in northern Thailand. There was no history of consanguinity. However, the parents' families have lived in the same village for many years. Both parents, the older brother, and sister were healthy. The patient's birth weight was 2600 g (<10 centile). The birth length and OFC at birth were not available, but were said to be unremarkable. Bilateral eyelid drooping was observed since she was one-month-old. Parents brought her to see an ophthalmologist (N.T.) for the first time when she was four months old. At the initial examination,

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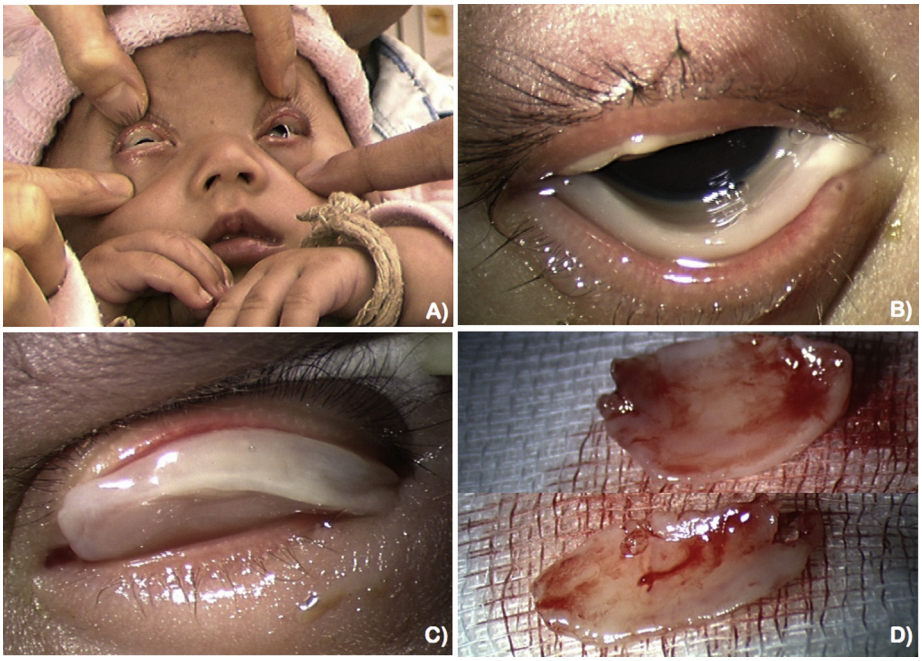

Fig. 1. Patient at age 4 months. A–D) Note bilateral edematous eyelids with whitish membranous deposits on the tarsal conjunctivae.

she had bilateral edematous eyelids with whitish pseudomembranous deposits on the tarsal conjunctivae (Fig. 1A–D). Ligneous conjunctivitis was diagnosed based on the characteristic clinical features. Her eyes were otherwise unremarkable. Her growth and development have been normal.

At age 4 months, she underwent pseudomembrane excision and was given topical and oral antibiotics (Fig. 2D,E). *Streptococcus viridans* and coagulase-negative *Staphylococcus* were isolated from eye discharge cultures. Histology of the excised membranes revealed thick amorphous material composed predominantly of mononuclear inflammatory cells, scattered polymorphonuclear cells and areas of fibrin, consistent with ligneous conjunctivitis. The subepithelial infiltrates of uniformly dense, eosinophilic, hypocellular material that resembled amyloid were observed. However, Congo red staining was negative indicating that these substances were not amyloid (Supplemental Fig. 1S A,B).

Due to a recurrence of pseudomembrane formation, topical corticosteroids and topical cyclosporine A were implemented [Tabbara, 2004]. The condition improved with longer remission period. The patient still required intermittent membrane excision. At age three years, plasma plasminogen functional activity was determined by a chromogenic assay (Berichrom Plasminogen; Dade Behring Diagnostics, Newark, DE, USA). The plasminogen functional activities of the patient and her mother were 15.2% and 78%, respectively (normal 75%–140%) [Tefs et al., 2006]. At three years of age, the patient developed thick pseudomembranes

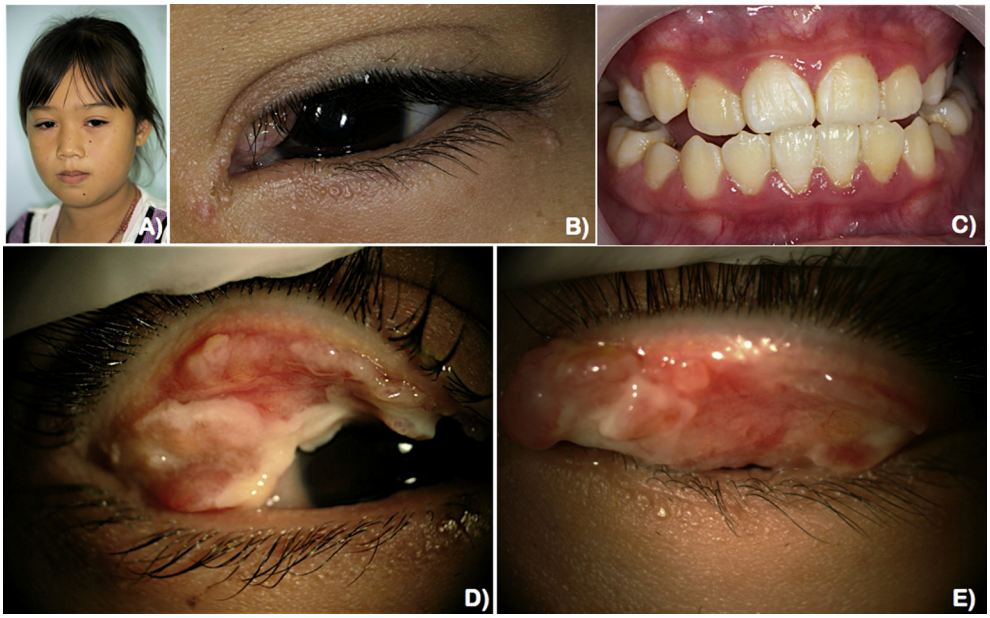

Fig. 2. A) Patient at age 10 years. B) Recurrence of ligneous conjunctivitis of the left eye. C) Edge to edge bite. Normal gingiva. C,D) Sessile pseudomembraneous lesions over the palpebral conjunctiva of both eyes at age 9 years.