• Letter to the Editor •

Ascher syndrome: a rare case of blepharochalasis combined with double lip and Hashimoto's thyroiditis

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Dear Editor,

I am Dr. Yao Fu, from the Department of Ophthalmology, Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China. I write to present a rare case of Ascher syndrome.

Ascher syndrome was described first in 1920, presenting as a combination of blepharochalasis, double lip, and non-toxic goitre[1]. It is considered to be a rare, sporadic, benign condition and usually has onset during puberty. Although hormonal influences and autosomal dominant inheritance have been involved in some cases[2], its etiology remains largely unknown. The report is in accordance with the Declaration of Helsinki Ethical Principles. The patient has given her consent for her images and related clinical information to be reported in this journal.

A 28-year-old female patient consulted the Department of Ophthalmology complaining of bilateral canthal adhesions between her upper and lower eyelids. The patient had the first edema attack in her upper eyelids at age 14 and gradually developed lax eyelids and bilateral canthal adhesions. She underwent bilateral blepharoplasty and lateral canthotomy 7 years ago. However, the lateral canthal adhesions recurred soon thereafter.

The palpebral fissure length was: 25 mm OD, 26 mm OS. The palpebral fissure height was: 9.5 mm OD, 10.5 mm OS. Physical examination found bilateral blepharophimosis, lateral canthal adhesion, double upper lip, and pseudoappearance of the overaction of lateral rectus in both eyes (Figure 1). No orbital fat prolapse or lacrimal gland prolapse was found. The best corrected visual acuity was: 1.0 OU. No abnormality in the ocular fundus or vitreous was found. A thyroid function test revealed normal serum free triiodothyronine, free thyroxine, and thyroid-stimulating hormone levels but increased thyroglobulin antibody (TGAb, 557.4 IU/mL; normal: 0-115 IU/mL) and thyroid peroxidase antibody (TPOAb, 51.6 IU/mL; normal: 0-9 IU/mL). Immunological laboratory tests revealed an increased immunoglobulin E (IgE) level (205 IU/mL; normal: 0-100 IU/mL). Thyroid ultrasonography revealed neither thyroid enlargement nor nodules.

Based on the clinical and laboratory findings, the patient presented Ascher syndrome and Hashimoto's thyroiditis. She therefore underwent bilateral lateral canthoplasty. Because the patient did not intend to correct the double lip at the time, only a biopsy of the buccal mucosa was taken during the surgery. Verhoeff's elastic stain of the eyelid (Figure 2A) revealed a loss of elastic fibers. Verhoeff's elastic stain of the biopsy of the buccal mucosa (Figure 2B) revealed very few elastic fibers and dehiscence of the elastic fibers. Whole exome sequencing of both the patient and her mother revealed none of specific gene mutations related to blepharochalasis. Postoperative images are shown in Figure 3. No specific treatment was done for the thyroid problem, and the patient was asked to follow up with thyroid hormone and thyroid antibody testing regularly.

Blepharochalasis is a rare syndrome characterized by recurrent episodes of painless eyelid edema and represents progressive skin laxity and atrophy due to decreased elastic fibers. The upper eyelids are usually involved, with an appearance of atrophy, wrinkles, and often discoloration of the skin[3], which is present in approximately 80% of Ascher syndrome cases. In our case, the patient presented with a lateral canthal reattachment, a rounded deformity of the lateral canthal angle, and a horizontally shortened palpebral fissure. Her inner intercanthal distance and interpupillary distance were normal. We assume that this happened due to dehiscence of the lateral canthal tendon from the orbital tubercle secondary

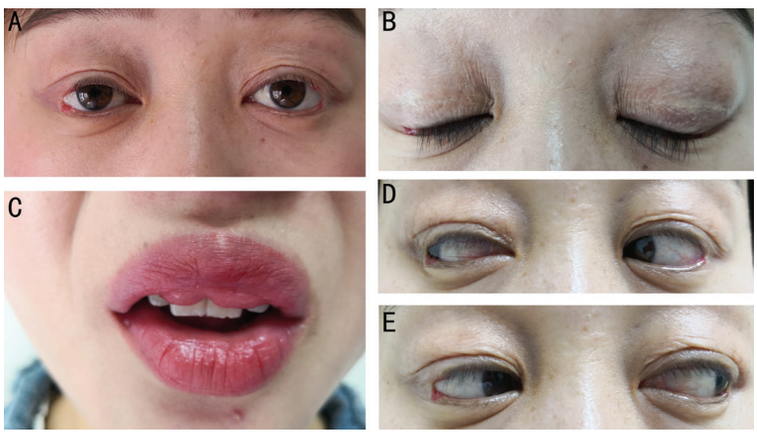

Figure 1 Bilateral blepharochalasis (A, B), double lip (C) and pseudoappearance of the overaction of the lateral rectus (D, E).

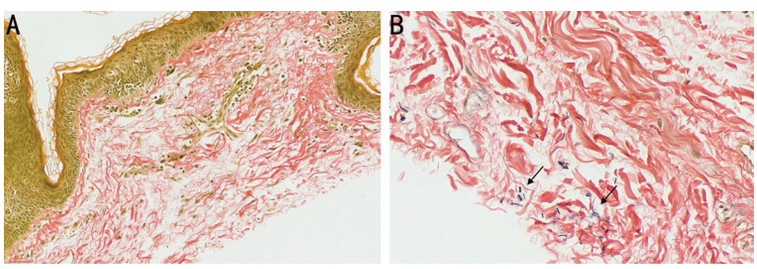

Figure 2 Verhoeff's elastic stain showed loss of elastic fibres in eyelid (A, 20×) and very few short elastic fibers (arrow) in buccal mucosa (B, 40×).

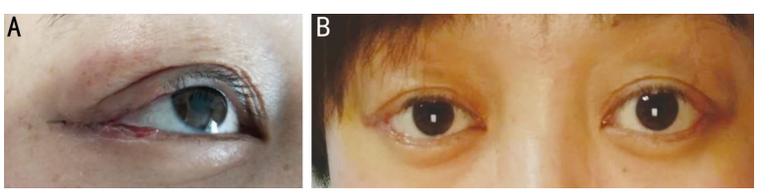

Figure 3 Seven days after the operation, before (A) and after (B) the removal of the stiches.

to recurrent attacks of blepharochalasis. In addition, the elongation/dehiscence of the lateral canthal tendon explained the reduced distance from the lateral canthus to the mid-pupillary area and the pseudoappearance of the overaction of the lateral rectus in this patient. Also, the wrinkles and bronze discoloration at the junction of eyelids could be observed because of the atrophic skin in the lateral canthal region. In summary, the patient had a secondary blepharophimosis due to blepharochalasis. A corrective surgical intervention is currently the primary treatment for blepharochalasis and blephrophimosis and is recommended at least 6mo after the most recent exacerbation[4-5].

Blepharochalasis may also present as ptosis, pseudoepicanthal folds, conjunctival redness, lower eyelid involvement, *etc.* It should be distinguished from other lax eyelid conditions, such as floppy eyelids, herniated orbital fat, and dermatochalasis. For example, both of blepharochalasis and floppy eyelid may display eyelid laxity associated with dry eye, conjunctivitis and/or ocular surface abnormalities (ptosis, upper or lower eyelid entropion). However, floppy eyelids are more often observed in obese middle-aged men associated with obstructive sleep apnea[6], while blepharochalasis occurs in puberty without distinctive distribution between sexes[2].

The double lip is indispensable for the diagnosis of Ascher syndrome. The deformity consists of a redundant mucosa, often bilateral, with a midline constriction because of the attachment of the frenulum[7]. Ascher syndrome usually affects the upper lip and is particularly obvious when smiling. Recurrent swelling causes duplication between the inner and outer parts of the upper lip[8]. The treatment for double lip is corrective surgical intervention, which is indicated mostly for aesthetic reasons or when having difficulty in chewing or speaking. Non-toxic enlargement of the thyroid is present in only 10%-50% cases of Ascher syndrome[8], but it is not usually associated with Grave's disease. In our case, the five times high titer of blood serum TGAb and TPOAb implicate Hashimoto's thyroiditis, because increased antithyroid antibodies are currently considered the most specific markers to establish the diagnosis[9]. The high plasma IgE level is a non-specific indicator of over-reactive adaptive immune responses. The cause of Hashimoto's thyroiditis in the patient is unknown but may be related to an autoimmune disorder.

Most cases of Ascher syndrome are sporadic, but familial cases suggestive of autosomal dominant inheritance have also been reported[10]. Genes related to blepharochalasis, such as *GSN*, *OSMR*, *ADAMTS2*, *MMP3*, and *MMP9*, have been reported previously[11-13]. In our case, none of the known mutations were detected in above genes.

This syndrome is often undiagnosed because of its rarity. The acquired blepharophimosis in our case is a rare form of blepharochalasis. The pathological findings of the eyelid and buccal mucosa confirm the diagnosis of Ascher syndrome. To the best of our knowledge, Hashimoto's thyroiditis has never been reported in patients with Ascher syndrome.

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