Surgical Treatment for Adult-Onset Limbal Xanthogranuloma: A Case Report with 4-Year Follow-Up

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Abstract
Xanthogranuloma is a benign histiocytic disorder that generally appears in infants and children and often called juvenile xanthogranuloma (JXG). Typical reddish-yellow cutaneous papules or nodules are the most common presentation of JXG. Extracutaneous JXG affects eyes, brain, lungs, liver, spleen, and other sites. Isolated ocular manifestation without skin lesion is rare, especially in adult patients. Here, we report a case of a 27-year-old man who presented with gradually growing yellowish mass at the corneoscleral area of the left eye for 5 months. The patient had worn soft contact lenses for more than 10 years. With atypical age of onset and the absence of skin lesion, total mass excision with lamellar corneoscleral graft and amniotic membrane transplantation was done, and the diagnosis of adult-onset limbal xanthogranuloma was made by histopathological and immunohistochemical examinations. Postoperatively, the patient had good vision with corrected distant visual acuity of 20/30, and the graft was clear. There was no evidence of recurrence at 4-year follow-up. We found that excision with lamellar corneoscleral graft in limbal xanthogranuloma shows good result with no recurrence. The same result occurred to other previous cases reported, so complete excision with graft could be an effective treatment of choice in patient with limbal xanthogranuloma.
Introduction

Xanthogranuloma is a benign histiocytic disorder characterized by typical reddish-yellow cutaneous lesions that generally appear in infants and children [1]. Because the disease typically occurs during young age, it is often called juvenile xanthogranuloma (JXG). Adult-onset xanthogranuloma is less typical but shares many clinical and histological characteristics of the juvenile form [2]. However, children with JXG had an increased risk of developed systemic disease such as neurofibromatosis type 1 and juvenile myelomonocytic leukemia more than adults [3]. Extracutaneous JXG affects eyes, brain, lungs, liver, spleen, and other sites [4]. Approximately 0.3–10% of children with JXG have been reported with eye involvement [5]. Ocular xanthogranuloma mainly involves the iris with some reports of the orbit, optic nerve, retina, and choroid involvement [6, 7]. Limbal xanthogranuloma is rare, and very few cases have been reported [2]. Therefore, limbal JXG in adult is extremely rare with only 11 cases reported to date [8–18]. Here, we present a case of isolated limbal xanthogranuloma in a 27-year-old man with a history of soft contact lenses use for more than 10 years. After treatment, no recurrence was seen at 4-year follow-up. We believe complete excision with graft could be an effective treatment for limbal xanthogranuloma, as a few previous cases showed recurrence with different treatment modalities [11, 14, 18–20].

Case Report/Case Presentation

A 27-year-old man presented with irritation and yellowish mass in the left eye. The patient was a long-term contact lens wearer (more than 10 years) with no other remarkable medical and family history. He used soft contact lenses made from polymacron and replaced them monthly. He usually forgot to remove the contact lenses and wore them overnight. The patient reported that he usually felt itching on his left eye and therefore rubbed the left eye regularly. At first, the patient noticed the mass while he placed the contact lens and felt a tiny mass at his limbal area; then, the mass gradually grew and became easily visible in 2 months (shown in Fig. 1).

Fig. 1. External photographs of the eyes. A yellowish mass at the superior limbus of the left eye was visible while looking upward and downward.
He went to visit a primary hospital in his neighborhood, and fluorometholone acetate eye drops were prescribed for him. He continued to use his contact lenses in both eyes until the mass became larger and obstructed contact lens placement on the left eye. After 3 months of using topical fluorometholone acetate, no improvement in shape or size was noticed. On the contrary, the mass continued to grow until it affected his contact lens placement. The patient decided to visit our hospital. At our hospital, his uncorrected visual acuity was 20/200 in both eyes, and his best corrected visual acuity was improved to 20/32 in the right eye and 20/80 in the left eye with −2.50 D contact lenses. Slit-lamp examination revealed a 6.5 × 10.0 × 2.0 mm, well-circumscribed yellowish mass extending 2 mm on to the cornea with vascularization located at the superior limbus of the left eye (shown in Fig. 2). The anterior segment ocular coherent tomography showed hyporeflective mass at 12 o’clock of the cornea (shown in Fig. 3). Iris and posterior segment examinations were unremarkable. Complete blood cell counts, serum lipid levels, creatinine clearance, plasma viscosity, liver function test results, and chest X-ray were within normal limits. The lesion was completely excised under general anesthesia, and lamellar corneoscleral graft with amniotic membrane transplantation was done subsequently. Excised mass was sent for histopathological examination. Histological examination showed dense infiltrate of lymphocytes, plasma cells, eosinophils, and neutrophils. Numerous foamy histiocytes and Touton giant cells were observed (shown in Fig. 4). These cells contained a ring of nuclei surrounding a central homogeneous eosinophilic cytoplasm, while the cytoplasm near the periphery of the cells was foamy and pale. Surgical margin was negative for neoplasm. Immunohistochemical studies were positive for CD68 and negative for CD1a and S-100 (shown in Fig. 5), which confirmed the diagnosis of xanthogranuloma and excluded Langerhans cell histiocytosis (LCH). No cutaneous lesion and systemic involvement frequently seen in JXG were found. Examination of cardiorespiratory and abdominal systems...
disclosed normal results. Postoperatively, the graft was clear. There was no complication after surgery. The patient discontinued contact lenses after surgery and used glasses instead. There was no recurrence of the lesion seen during 4 years of follow-up (shown in Fig. 6). His latest refraction was $-2.50, -0.50 \times 15$ in the right eye and $-2.50, -3.00 \times 5$ in the left eye which corrected his vision to 20/20 and 20/30, respectively, and the patient maintained good vision using glasses.

**Discussion/Conclusion**

The differential diagnosis of yellowish limbal mass includes dermoid, lipoderma, pyogenic granuloma, lymphoproliferative disorders, histiocytic disorders, benign and malignant neoplasm [21]. Some of them have typical features and can be diagnosed by history taking and ocular examination. However, tissue diagnosis remains necessary in a few cases. Excision was done in our case to make a definite diagnosis, and histopathological examination revealed characteristics of xanthogranuloma. Although ocular JXG is not common, it is crucial to have early diagnosis to prevent extension to the cornea, hyphema, and secondary glaucoma as complications [22]. Typical histological findings of JXG contain foamy histiocytes and Touton giant cells as well as lymphocytes and eosinophils [23]. Histiocytic disorders were broadly divided into LCH and non-LCH. JXG is one of the most common non-LCH disorders. Immunohistochemical studies help differentiate JXG from LCH such as positive CD68, HAM56, and factor XIIIa, which are markers for tissue macrophages together with negative S-100 and CD1a, which are Langerhans cell markers [24]. Histopathological and immunohistochemical examinations of our case showed foamy histiocytes and Touton giant cells with positive CD68 and did not show immunoreactivity for S-100 and CD1a, which were consistent with xanthogranuloma.

The etiology of JXG remains unknown. The pathogenesis is thought to be of reactive origin. Local tissue injury and irritation-induced inflammatory reaction that evoke a histioxanthomatous
Fig. 5. Immunohistochemical study of the lesion. a Positive CD68 staining for confirmation of the histiocytic phenotype. b Negative S100 staining. c Negative CD1a staining.
reaction are considered possible causes due to the presence of inflammation that characterizes the lesion [5, 18]. The patient had a history of itching and rubbing the affected eye together with inappropriate long-term contact lens use. Local injury from regular eye rubbing and inappropriate contact lens use could be one of many factors that contributes to local irritation. The association between contact lenses and xanthogranuloma may be possible, considering the reactive origin of the disease. Nevertheless, it should be remarked that contact lenses were worn bilaterally, but xanthogranuloma occurred only in one eye. Therefore, the use of contact lenses and xanthogranuloma could be more a coincidence than a causality.

Majority of limbal xanthogranuloma cases in the literature were treated by excision or keratectomy with lamellar graft or both to ensure complete eradication of the mass because the differential diagnosis of JXG includes malignancy [24]. According to previous case reports, a few cases underwent simple excision had recurrence [6, 14, 18, 19, 24–26], while all the cases underwent keratectomy with graft showed no recurrence [19, 25, 27]. Collum and Mullaney suggested keratectomy and lamellar graft to eradicate the mass completely and to give a good cosmetic result because complete removal of the lesion did leave a defect [18]. Topical corticosteroids seem to be ineffective in treating limbal JXG [20], while combining surgical treatment and postoperative intralesional corticosteroids seems to show good result [24]. Hermel et al. [11] reported a case of limbal JXG treating with intralesional triamcinolone acetonide alone, and the mass regressed, but lipid deposit was still visible. Also, the risk of inadvertent corneal perforation during procedure and increase in intraocular pressure from corticosteroids administration should be aware. Our patient was treated by complete excision with lamellar corneoscleral graft, and no recurrence was seen during 4 years of follow-up which is the longest follow-up period previously had been reported of recurrence [18]. This result is consistent with previous cases underwent excision together with graft. We believed that mass excision with graft could prevent recurrent disease and results in a good visual outcome.

In conclusion, adult-onset limbal xanthogranuloma is considerably rare that histopathological and immunohistochemical examinations are essential for the diagnosis. The association of limbal xanthogranuloma and contact lens is still unclear; more evidence is needed to support the causality. Because adult-onset limbal xanthogranuloma is an extremely rare disease, recommendation for treatment is limited to evidence from existing case reports. Surgical excision with lamellar corneoscleral graft shows great result with no evidence of any recurrence of the disease in our patient. Thus, it may be a preferable choice of treatment for xanthogranuloma involving the limbal area.
Statement of Ethics

This study protocol was reviewed and approved by the Institutional Review Board, Royal Thai Army Medical Department, on November 11, 2021. The approval number is S088h/64. Written informed consent was obtained from the patient for education and publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Pichaya Chuephanich contributed to conceptualization, data validation, manuscript editing, and supervision on the project. Warissara Kitsirilarp worked on manuscript drafting and visualization. Nutthaporn Laoharojvongsa worked on manuscript reviewing, editing, and visualization. Theeratep Tantayakom examined the patient and reviewed and edited the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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