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Case Report

Conjunctival Intraepithelial Neoplasia in a Patient Presenting with Pigmented Conjunctival Lesion

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Keywords
Conjunctival intraepithelial neoplasia · Pigmented conjunctival lesion · Conjunctival melanoma

Abstract
We report a case of conjunctival intraepithelial neoplasia (CIN) in a patient presenting with the pigmented conjunctival lesion. This study involved a 56-year-old woman that presented with right eye irritation for 1 month. She noticed brownish pigmentation arising from her right nasal conjunctiva and growing slowly over time. Biomicroscopic examination showed a gelatinous pigmented conjunctival mass with feeder vessels. Conjunctival impression cytology (CIC) was done and reported as CIN. Treatment was started with 0.02% mitomycin-C eye drops. The conjunctival lesion responded well to medication. This report shows that CIN can manifest as a pigmented tumor, resembling melanoma. CIC plays a role in the diagnosis of this condition. This tumor responded well with 0.02% mitomycin-C eye drops.

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Introduction

Ocular surface squamous neoplasia (OSSN) are common malignancies of the conjunctiva and encompass a wide and varied spectrum of disease from dysplastic lesion to invasive squamous cell carcinoma. Conjunctival intraepithelial neoplasia (CIN) is non-invasive by definition. The basement membrane remains intact, and the substantia propria is spared. The etiology appears to be a multifactorial, involving a variety of environmental factors in a susceptible host. Exposure to ultraviolet [1], aging [2], and smoking [3] have been implicated in the pathogenesis of CIN. Some studies have shown the association of CIN with human immunodeficiency virus (HIV) infection [4–7]. This malignancy classically manifests as a non-pigmented, gelatinous conjunctival mass with feeder vessels and intrinsic papillary vascular pattern [8, 9]. This can mimic pinguecula, pterygium, papilloma, and conjunctival melanoma, which is a more fatal malignancy due to a higher rate of metastasis compared with squamous cell carcinoma. The clinical differentiation of these two malignancies is based on several features, and the presence of pigment is a strong indicator for melanoma [8]. Despite this accepted dictum, we report a patient who displayed prominent intrinsic brown pigmentation within CIN. Clinical features, management, and results of treatment are discussed.

Case Report

A 56-year-old woman with no underlying disease presented with right eye irritation for 1 month prior to being seen. She noticed a brownish mass arising from her right nasal conjunctiva and growing slowly over time. She went to a primary hospital with no history of smoking. Primary acquired melanosis was suspected, and she was referred to the Department of Ophthalmology, Chiang Mai University Hospital.

At initial examination, she had a dark brown skin; best-corrected visual acuity (BCVA) was 6/9 in the right eye and 6/6 in the left eye. Biomicroscopic examination demonstrated an elevated gelatinous mass with brownish pigment and feeder vessels located at the nasal side of conjunctiva in her right eye (2.0 × 4.0 mm in diameter) (Fig. 1a, b, 3a). Intraocular pressure was 16 mm Hg, OU by Goldmann applanation tonometry and fundus examination was normal.

Conjunctival impression cytology (CIC) was performed and reported as CIN with mild dysplasia (grade 1/3). No melanocytic cells were found (Fig. 2a, b). The serological test of the patient for HIV was negative by the ELISA method. The patient was treated as an outpatient with 0.02% mitomycin-C eye drops 4 times daily for 1 week. Non-preservative lubricants were given to the patient as adjunctive treatment. The treatment with 0.02% mitomycin-C was well tolerated by the patient, without the need for anti-inflammatory eye drops.

After treatment with 0.02% mitomycin-C, BCVA was 6/9 in the right eye, the pigment from the conjunctival lesion was slightly alleviated, and the feeding vessels started to regress (Fig. 3b). The conjunctival lesion had nearly no pigment and the feeding vessels markedly decreased after 2 cycles of treatment (Fig. 3c). One cycle of treatment was defined as 1 week using medication followed by 1 week without medication. The lesion responded well with 0.02% mitomycin-C treatment for 3 cycles. No recurrence of the conjunctival lesion was seen at 6 months' follow-up which was confirmed by CIC (Fig. 3d).

Discussion

CIN is one spectrum of the OSSN which has good prognosis, with little tendency to metastasize and a low mortality rate [10]. Typically, it presents as a non-pigmented tumor which is usually a fleshy mass on the conjunctiva and may occasionally invade the cornea [11]. However, CIN may manifest as melanotic mass signaling a potentially more serious type of tumor such as malignant melanoma [8]. Conjunctival melanoma has a higher percentage of metastasis than CIN; therefore, the clinical differentiation of these 2 malignancies is crucial [8]. Brown pigment is a clinical clue to differentiate the pigmented CIN from melanotic melanoma [8]. Misdiagnosis of this condition can lead to loss of vision, which is preventable, and the need for more aggressive treatments.

In this study, we demonstrate a patient who had CIN with a pigmented conjunctival mass which is not usually present in a typical case of an immunocompetent patient. The elevated gelatinous conjunctival lesion is located at nasal conjunctiva which is typically found in CIN [8]. CIC was performed to confirm the diagnosis, which revealed a CIN without melanocytic cells. The result can distinguish the CIN from conjunctival melanoma. A limitation of this investigation is that it may not differentiate CIN from squamous cell carcinoma, because only superficial cells are obtained with the CIC method [12]. 0.02% mitomycin-C eye drops were given for the treatment. The patient was treated in the outpatient department and followed up to evaluate the clinical outcomes and to monitor any possible side effects. The patient responded well to 0.02% mitomycin-C eye drops as the lesion became smaller and decreased in size at each following visit. Without the need of surgery, the pigmented conjunctival lesion of this patient has totally improved and was replaced by normal conjunctiva after 3 cycles of treatment. No side effect was found during the treatment with 0.02% mitomycin-C eye drops in this patient. After 6 months' follow-up, CIC showed no dysplastic squamous cells with a complete regression of the conjunctival mass. As medical therapy has been increasingly popular in the treatment of OSSN, mitomycin-C is considered to be superior to invasive approaches such as surgery which has some undeniable complications such as scarring, symblepharon, and limbal stem cell deficiency [13]. This study showed that mitomycin-C was effective as the primary treatment [14]. Despite the effectiveness of mitomycin-C, the mitomycin-C-related side effects including limbal stem cell deficiency, photophobia, dry eye, and persistent epithelial defect need to be taken into account.

Conclusion

This report shows that CIN can manifest as a pigmented tumor resembling melanoma. CIC plays a role in the diagnosis of this condition. This tumor responded well to 0.02% mitomycin-C eye drops.

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Statement of Ethics

The patient has given written informed consent, and the study protocol was approved by the Ethics Committee of Faculty of Medicine Chiang Mai University (approval No. 6409/2019).

Conflict of Interest Statement

There are no conflicts of interest to report for all authors.

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Author Contributions

Study concept and design: Winai Chaidaroon, Chutikarn Dejkriengkraikul. Acquisition, specimen analysis, and interpretation of data: all authors. Drafting of the manuscript: Winai Chaidaroon, Chutikarn Dejkriengkraikul. Critical revision of the manuscript for important intellectual content: Winai Chaidaroon. Study supervision: Winai Chaidaroon. All authors approved the final version of the manuscript.

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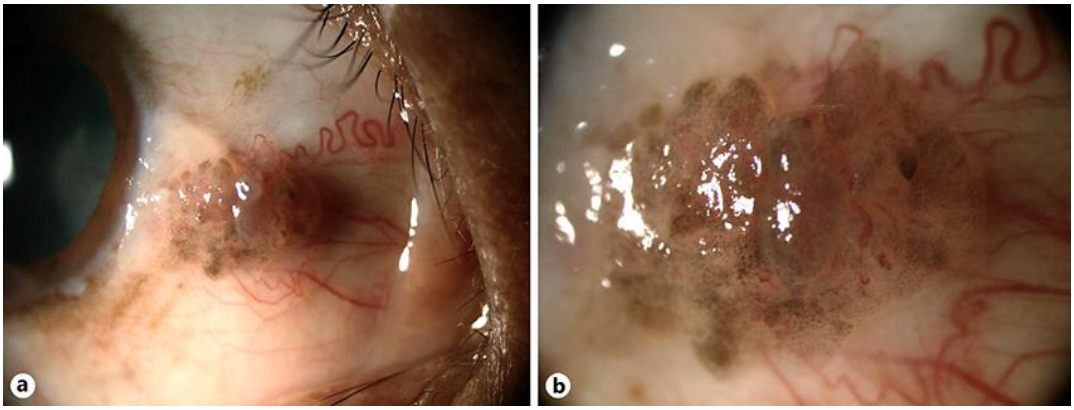

Fig. 1. **a** Slit lamp photographs of the right eye showed an elevated gelatinous pigmented mass with feeder vessels at the nasal side of the conjunctiva. **b** Magnification ×25.

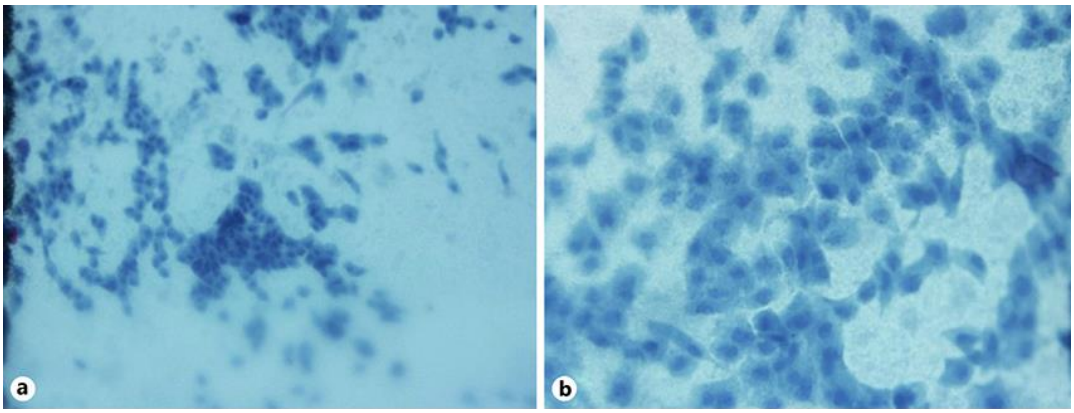

Fig. 2. Conjunctival impression cytology of the patient. **a** Low magnification (10×). The imprints are cellular with sheets and strand of highly dysplastic squamous cells. The background is clean without cellular necrosis. No melanocytic cells are found. **b** High magnification (40×). The dysplastic cells are polygonal with a high nuclear/cytoplasmic ratio. Their nuclei are hyperchromatic with irregular nuclear borders.

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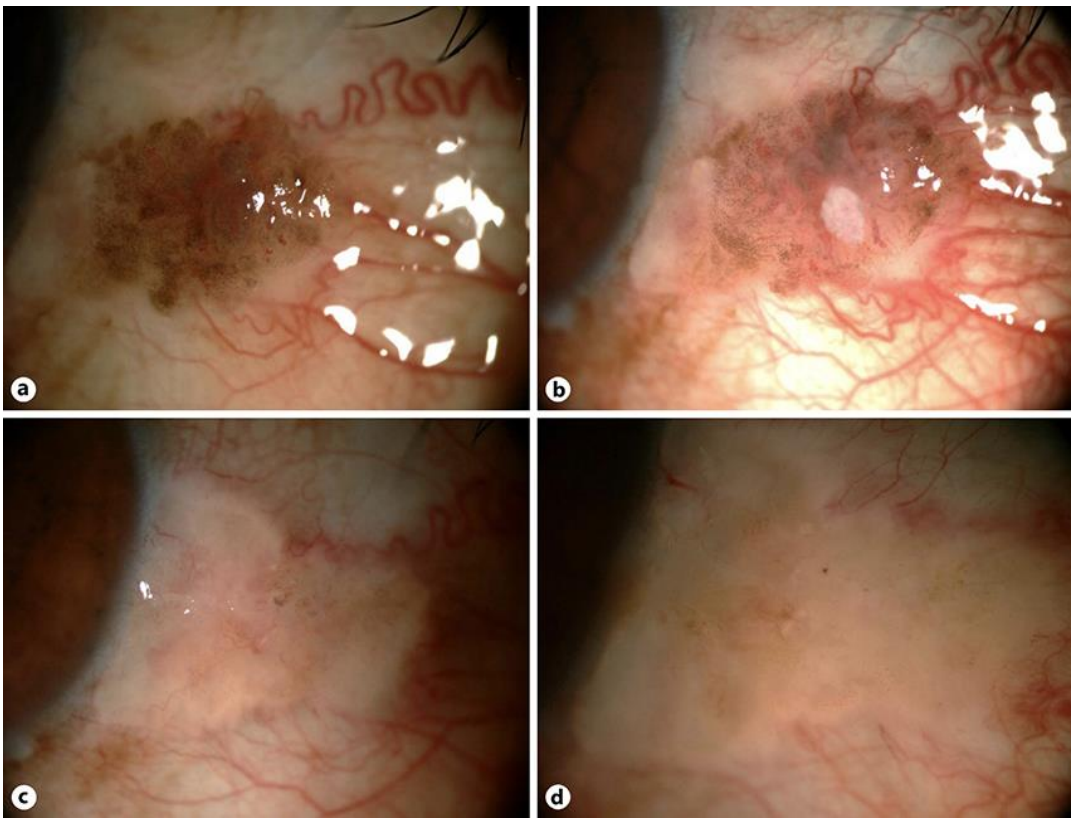

Fig. 3. Photographs of the right eye before and after treatment. **a** At the first visit, an elevated gelatinous pigmented mass with feeder vessels at the nasal side of the conjunctiva. **b** After 1 cycle of treatment with 0.02% mitomycin-C, the pigmentation slightly alleviated with the regression of feeding vessels. **c** After treatment with 0.02% mitomycin-C for 2 cycles, the pigmentation of the conjunctiva and the feeding vessel were markedly decreased. **d** No pigmented conjunctival lesion was found after treatment with 0.02% mitomycin C for 3 cycles.