CASE REPORT

Sinonasal melanoma arising from conjunctival primary acquired melanosis

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SUMMARY

A 66-year-old woman was treated with excision and cryotherapy for recurrent primary acquired melanosis (PAM) with atypia of the right conjunctiva. Four years later, she developed a melanoma of the ipsilateral inferior turbinate and nasolacrimal duct. She was treated with right medial maxillectomy and postoperative radiation therapy. This is the first reported case of conjunctival PAM resulting in delayed progression to melanoma in the nasolacrimal duct and sinonasal cavity.

BACKGROUND

Primary acquired melanosis (PAM) is any acquired flat, non-cystic pigmented lesion of the conjunctiva, cornea or caruncle that lacks the typical features of localised nevus or racial melanosis.¹ PAM is unilateral, as opposed to racial melanosis, which is generally bilateral.² PAM is primarily a condition of Caucasian adults, with 96% of cases occurring in Caucasians and a mean age of presentation of 56.¹ It is classified as PAM with or without mild, moderate or severe atypia based on the histological appearance of the melanocytes. It is typically a benign condition, but it carries the risk of progression to invasive conjunctival melanoma depending on degree of atypia. Shields *et al*¹ reports that there is no risk of progression without atypia or with mild atypia; a very small risk with moderate atypia; and a 13% risk for progression to invasive melanoma with severe atypia. Other risk factors for progression of PAM to invasive melanoma include size above 3 clock hours; palpebral conjunctiva, fornix, caruncle or plica location; and corneal involvement. Since benign and potentially malignant lesions cannot be distinguished clinically, excisional biopsy is recommended for any conjunctival melanotic lesion over 6 mm.³ Excision is typically followed by cryotherapy to destroy residual atypical melanocytes.² Once removed, PAM with atypia has a rate of local recurrence of 30%.¹

In the event that PAM with atypia progresses to invasive melanoma, there is risk of locoregional spread and of distant metastases. Paridaens *et al*⁴ reported that 5% of invasive conjunctival melanomas arising from areas of PAM with atypia spread locally to the ipsilateral nasal cavity and paranasal sinus. Distant metastasis occurs through lymphatic spread through channels in the conjunctival substantia propria or through haematogenous spread.⁵ Rate of distant metastasis for conjunctival melanoma arising from PAM was reported by Shields *et al*⁶ to be 5% at 5 years and 26% at 10 years. This case is unique in that it represents a sinonasal

melanoma arising from conjunctival PAM in the absence of evidence of invasive conjunctival melanoma.

CASE PRESENTATION

A 66-year-old woman presented in 2006 with a flat melanotic lesion of the bulbar conjunctiva of the right eye (figure 1), measuring 10×5×2 mm. This was treated with excision and cryotherapy. Examination of the sections together with immunohistochemical studies with antibodies for melan-A revealed a diagnosis of PAM with mild-to-moderate atypia (figure 2A, B). Examination of multiple tissue levels failed to demonstrate invasive features. Conjunctival PAM recurred in 2007 and again in 2009. The lesion was treated with excision and cryotherapy on both occasions. The latter was followed with 9 months of topical adjuvant mitomycin C drops. The patient remained asymptomatic until December 2013, when she presented with a 3-month history of recurrent right epistaxis, right bloody epiphora and haemoptysis.

INVESTIGATIONS

CT sinus imaging revealed a 2.5 cm mass associated with the right inferior meatus (figure 3). The patient underwent incisional biopsy of the mass, with pathology revealing invasive melanoma. Multiple right conjunctival mapping biopsies were performed, but there was no evidence of invasive conjunctival melanoma or PAM. A positron emission tomography scan after incisional biopsy revealed faint metabolic activity in the right nasolacrimal duct, but no other evidence of disease.

TREATMENT

The patient was definitively treated in February 2014 with right medial maxillectomy including en bloc resection of the right inferior turbinate, nasolacrimal duct and lacrimal sac. A darkly pigmented 1 cm mass (figure 4) was identified on the inferior aspect of the inferior turbinate at the exit of the nasolacrimal duct and involving the inferior nasolacrimal duct. No gross abnormality was found in the superior nasolacrimal duct or lacrimal sac. The mucosa around the darkly pigmented tumour was grossly normal and margins were negative for disease. Pathology confirmed melanoma involving bone and mucosa with CTNNB1T41A and CKITL576P missense mutations (figure 2C, D). The patient was treated with 60 Gy postoperative intensity-modulated radiation therapy to the nasolacrimal apparatus and sinonasal cavity.

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Figure 1 Primary acquired melanosis of the right bulbar conjunctiva, measuring 10×5×2 mm.

Figure 3 CT sinus coronal imaging revealing a 2.5 cm mass associated with the right inferior turbinate.

OUTCOME AND FOLLOW-UP

The patient had no complications or sequelae of treatment other than very mild right lower eyelid ectropion. Follow-up at 9 months suggested no evidence of residual or recurrent disease of the sinonasal cavity or conjunctiva.

DISCUSSION

In this patient, the size of the lesion, areas of moderate atypia, and involvement of the plica and palpebral conjunctiva

increased the risk for progression to invasive melanoma. Paridaens *et al*⁴ reported that 5% of invasive conjunctival melanomas arising from areas of PAM with atypia spread locally to the ipsilateral nasal cavity and paranasal sinus. Yet, the patient reported here was never found to have invasive melanoma of the conjunctiva. It is possible that this patient may have had an invasive component associated with one of her previous lesions, which was not appreciated on pathology review. However, even with re-review of the pathology slides at a tertiary care

Figure 2 (A) Conjunctival biopsy revealing a disorganised intraepithelial proliferation of single and nested intraepithelial melanocytes along the basilar epithelium (H&E, ×4; inset: ×20). (B) This proliferation is highlighted with an immunohistochemical study with antibodies for melan-A (×4; inset: ×20). (C) Subsequent maxillectomy specimen revealing invasive melanoma involving mucosa and extending into bone (H&E, ×4). (D) High power examination revealing a proliferation of malignant epithelioid cells with pigmented cytoplasm and enlarged oval nuclei with conspicuous nucleoli (H&E, ×20).

Figure 4 Darkly pigmented inferior turbinate lesion measuring approximately 1 cm at the exit of the nasolacrimal duct.

institution, the original PAM lesions and both recurrences were not consistent with invasive melanoma. Additionally, after the ipsilateral inferior turbinate mass was diagnosed as melanoma, a map biopsy of the right conjunctiva was performed, which found no evidence of any amelanotic melanoma lesion.

Primary mucosal sinonasal melanoma is rare, comprising less than 1% of melanomas.⁷ A metachronous primary sinonasal mucosal melanoma was considered but thought to be highly unlikely in this case. An inferior turbinate melanoma on the ipsilateral side of a PAM lesion within 4 years suggests local spread of disease through the nasolacrimal duct. A previous case report demonstrated that a patient with multifocal conjunctival melanoma exfoliated melanocytes into tears, indicating that sloughing of melanoma cells into tear drainage and thus seeding of the nasolacrimal duct and nasal cavity may be possible.⁸ In the current patient, the inferior turbinate melanoma was found

to extend into the nasolacrimal duct on pathology, suggesting that the disease very likely spread through tear drainage into the nasolacrimal duct. This case illustrates the importance of follow-up and astute examination of unusual findings in a patient treated for PAM with atypia, especially with multiple recurrences. To our knowledge, this is the first case in the literature to present an occurrence of melanoma of the nasal cavity in a patient with history of PAM with moderate atypia in the absence of invasive melanoma of the conjunctiva.

Learning points

- ▶ Long-term follow-up is important in a patient with history of conjunctival primary acquired melanosis (PAM) with atypia due to risk of recurrence and progression to invasive melanoma.
- ▶ An ipsilateral inferior turbinate mass should be approached with a high degree of suspicion of melanoma in a patient with history of conjunctival PAM with atypia.
- ▶ Sinonasal melanoma can arise in a patient with a history of conjunctival PAM in the absence of evidence of invasive melanoma of the conjunctiva.

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