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Case report

Enemy in disguise: A case report of solitary trichoepithelioma initially diagnosed as BCC

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ABSTRACT

Introduction: Solitary trichoepitheliomas (TE) are benign tumors that are strikingly similar to their malignant counterpart, basal cell carcinoma (BCC).

Presentation of case: An 83-year-old man presented with a 10-year history of a right lower lid skin mass initially diagnosed as BCC. Intraoperatively, an excisional biopsy was performed with primary reconstruction of the skin defect and the specimen was submitted for histopathology processing. Eventually, histopathology findings suggested the diagnosis of benign hair follicle tumor. The postoperative results were aesthetically pleasing and the integrity of the lower lid was preserved.

Discussion: Despite being rare, benign solitary TE are frequently misdiagnosed as malignant BCC, and vice versa. Oculoplastic surgeons face considerable difficulty distinguishing the two pathologies due to their similar clinical and histological pictures. Hence, excisional biopsy should be considered whenever such discrepancy is confronted to avoid the possibility of recurrence or malignant transformation. Furthermore, immunohistochemical staining could increase the accuracy of diagnosis in such unequivocal findings.

Conclusion: Correlation of clinical, dermoscopic and histopathological findings are essential to establish an accurate diagnosis and select the appropriate management. In-depth understanding of eyelid reconstruction principles is mandatory to achieve desirable goals.

1. Introduction

Clinical distinction between malignant neoplasms and other benign tumors of the eyelid can pose a real challenge for ophthalmologists. Solitary TE of the eyelid is a rare benign follicular tumor that can be difficult to distinguish from BCC, both clinically and histologically. The distinction between these two tumors is important to determine the treatment course and prognosis. This case aims to minimize clinical misdiagnosis of solitary TE lesions with BCC and subjecting patients to unwarranted surgical excision. This work has been reported in line with the SCARE criteria [1].

2. Case presentation

An 83-year-old Middle Eastern male, lives in a sunny country presented to the outpatient department complaining of a slow growing skin tumor involving the right lower eyelid and lateral canthus in the past 10 years. The patient is a known case of hypertension and suffered an episode of stroke 3 years back. Past surgical and family history was insignificant.

Ocular examination revealed worsened visual acuity, especially in the right eye (counting finger at 1 m distance), owing to cataract. Examination of the extraocular muscles showed full range of motion in all directions. Intra-ocular pressure (IOP) was within normal range in both eyes. The lower lid mass measured $2 \times 1.5 \times 0.5$ cm^3 in dimension, was skin-colored, multilobulated with telangiectatic vessels without surface ulceration. Encroaching on the lid margin, the lesion spanned the lateral half of the right lower lid and was associated with satellite lesions confined to the anterior lamella without involvement of the tarsus, the meibomian gland structures nor the palpebral conjunctiva and without a corresponding loss of eyelashes (Fig. 1). Due to the limited extent of the lamellar defect along with increased surrounding tissue mobility as a result of old age, a decision was taken to perform an excisional biopsy of the mass with a 2 mm safety margin (Fig. 2). Sufficient laxity of the lower lid skin permitted approximating the excision margins without placing tension on the eyelid (Fig. 3). *Histopathology* report documented

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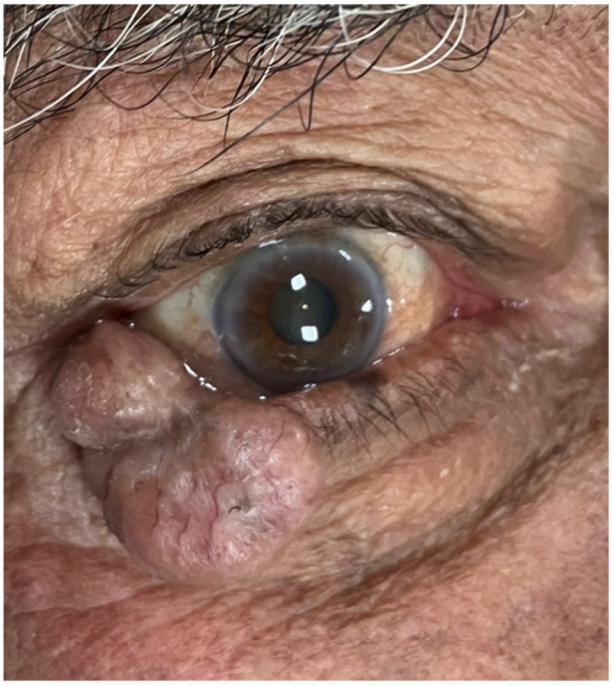

Fig. 1. Trichoepithelioma. Pre-operative photo of the right lower lid tumor lesion originally considered to be basal-cell carcinoma.

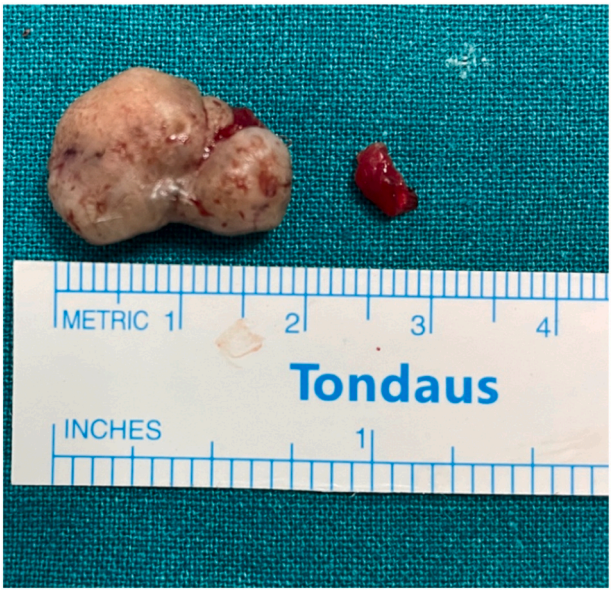

Fig. 2. Post-operative photo of the excised tumor sample measuring 2 × 1.5 × 0.7cm^3 (left) and 0.6 × 0.3 × 0.3cm^3 (right).

a soft to firm nodular eyelid lesion measuring 2 × 1.5 × 0.7 cm^3. On the cut section being greyish in color with the absence of hemorrhage and necrotic tissue. Microscopic examination showed unremarkable epidermis, with benign tumorous growth in the underlying tissue corresponding to TE (Fig. 4).

3. Discussion

Benign and malignant eyelid neoplasms originate from a variety of eye and supportive adnexal structures. Table 1 lists major eyelid skin tumors according to their origin. Hair follicle tumors are classified

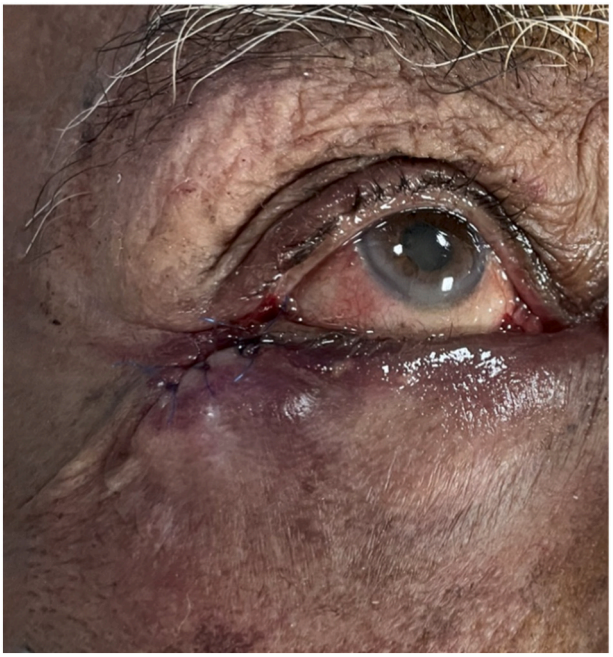

Fig. 3. Postoperative primary closure of the lower lid skin defect.

according to their tissue of origin into: bulb matrix tumors (pilomatrixoma, melanocytic matricoma) and tumors of the follicular germinative/papillary mesenchymal interface cells (trichoepithelioma, trichoblastoma). [2,3].

The incidence of different eyelid tumors, expresses a wide variation that is believed to be influenced by racial and possibly geographical factors. Fortunately, 82–98 % of all eyelid tumors are benign neoplasms. Among malignant eyelid tumors, BCC expresses the highest prevalence towards Caucasians (86–91 %) while sebaceous gland carcinoma (SGC) reached up to 77 % among Asians. [4]. TE can be classified into: multiple, desmoplastic and solitary TE, the latter being the least common type with extremely rare eyelid involvement [5]. However, the scientific literature is lacking enough epidemiological data regarding the incidence and prevalence of TE. Simpson et al., conducted the largest study of eyelid trichoepitheliomas, which demonstrated a prevalence among middle-aged male patients [6]. Mutation of the tumor suppressor human patched (PTCH) gene has been suggested in the pathogenesis of solitary TE [7].

The literature reports numerous dermoscopic, histological and even molecular features to aid the distinction of those entities, yet no single feature can be solely reliable. On clinical examination, BCC and solitary TE tumors are strikingly similar. Even though most authors agree that TE and BCC probably share a common origin from pluripotential cells developing towards hair follicle differentiation, the literature suggests that they represent two different stages of differentiation. This might explain the high level of overlap in dermoscopic resemblance of the two entities [8]. The lack of characteristic dermoscopic features makes differentiating these two entities practically impossible. Hence, clinical examination alone is insufficient to make a diagnosis. Table 2 includes key dermoscopic and histopathological features to differentiate between TE and BCC. Fig. 5 illustrates the common dermoscopic features of BCC.

Histological features including nests of basaloid epithelial cells with peripheral palisading cells is the hallmark for both BCC and TE, making the histological diagnosis challenging. In TE however, the fibroblast-rich stroma is more pronounced and is limited to the dermis. Another histological feature that supports the diagnosis of TE is the presence of clusters of undifferentiated fibroblastic cells known as papillary mesenchymal bodies (PMBs). According to a review of 30 similar pathologies, the prevalence of PMBs was confirmed in 93 % of all TEs and

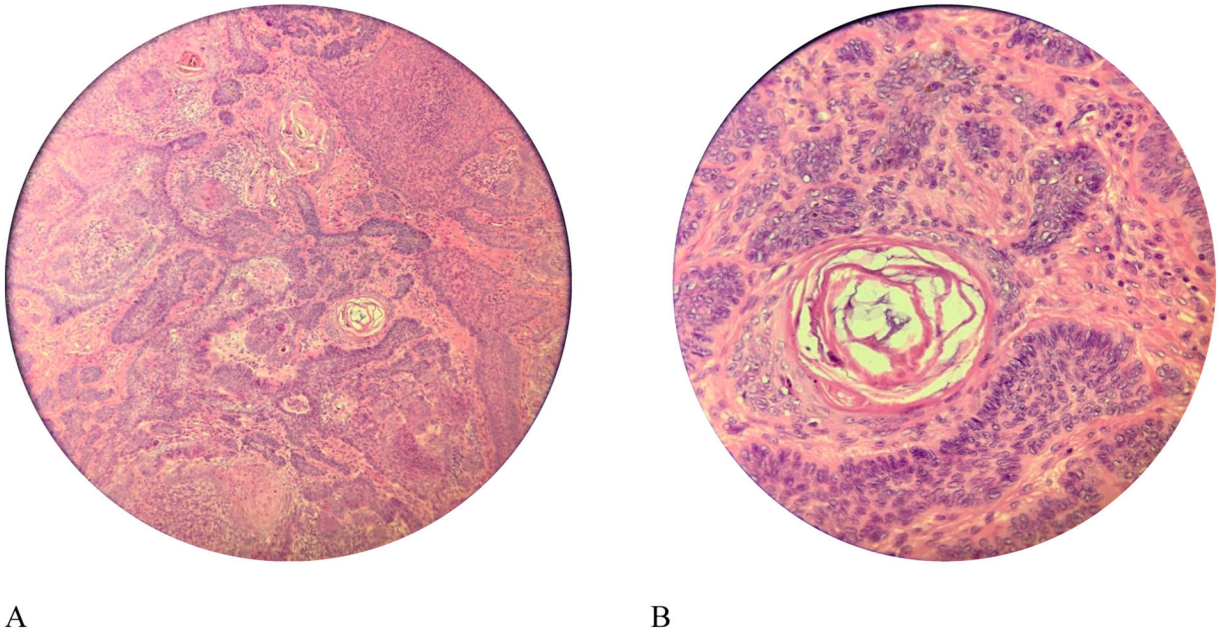

Fig. 4. Trichoepithelioma. (A) H&E staining showing superficial nests of basaloid cells with keratin horn cysts formations. (H&E, at 100× magnification). (B) Prominent keratin cyst with surrounding basaloid cell aggregates. (At 200× magnification).

Table 1
summary of major differential diagnoses of eyelid skin tumors.

Tumors of the eyelids					
Differential diagnosis	Benign tumor	Epidermal	Epithelial	Squamous papilloma	
				Cutaneous horn	
				Epidermoid/dermoid cyst	
			Melanocytic	Ephelis “freckles”	
				lentigo simplex	
				Solar lentigo	
				Eyelid nevi	
		Adnexal	Cystic lesion	Meibomian gland “chalazion”	
				Epidermal inclusion “epidermoid” cyst	
				Hydrocystoma “sweat gland ductal cyst”	
			Sweat gland lesion	Apocrine “at the lid margin”	Apocrine hydrocystoma
				Eccrine “across eyelid skin”	Syringoma
					Spiradenoma “hydradenoma”
			Hair follicle lesion	Trichoepithelioma	
				Trichofolliculoma	
				Trichelemmoma	
				Pilomatrixoma	
			Sebaceous gland adenoma		
		Miscellaneous lesions	Xanthelesma		
			Molluscum contagiosum		
	Vascular tumor	Capillary hemangioma			
		Nevus flammeus “port-wine stain”			
		Eyelid varix			
	Neural tumor	Neurofibroma			
	Malignant tumor	Basal cell carcinoma -BCC (90 %)			
		Squamous cell carcinoma -SqCC (5 %)			
		Sebaceous gland carcinoma -SGC			
		Malignant melanoma (<1 %)			
		Markel cell carcinoma (MCC) “cutaneous neuroendocrine carcinoma”			
		Kaposi's sarcoma			
		Sweat gland adenocarcinoma			

0 % of all routine BCC cases. The authors argue that the recognition of this highly specific hard to miss histological criterion is more reliable that other histological features [9–11]. Moreover, the presence of PMBs in TE supports the hypothesis of its advanced stage of follicular differentiation in contrast to their rarity in BCC.

The surgical aim of eyelid lesions follows the same oncological principles of other skin lesions, namely complete excision with adequate clearance margin to minimize recurrence, metastasis and preserve the structural integrity of the eyelid. Unlike the upper lid where full mobility is required, reconstruction of the lower lid should preserve its static position allowing proper contact during lids closure. In general, adequate eyelid closure, tear film preservation, clear visual field maintenance and aesthetically appealing reconstruction should be the surgeon's goal for eyelid reconstruction. The choice of the surgical approach of eyelid reconstruction depends primarily on the type of tumor, the defect's thickness, size and location. [12] Eyelid

Table 2
Summary of key differentiating clinical and histopathological features of TE and BCC.

	Trichoepithelioma (TE)	Basal cell carcinoma (BCC)
Incidence	Rare benign adnexal neoplasm in young to middle-aged adults with a female predilection.	Most common cancer in fair-skinned populations Predilection to sun-exposed areas Increasing incidence >1000/10,000/year in Australia 93.9–935.9/100,000/year in USA
Dermoscopic features	Arborizing blood vessels Multiple milia-like cysts and rosettes over a whitish background Focal "shiny white" areas Ivory-white colored lesions Lack of blue-grey ovoid nests and leaf-like areas (negative sign)	Arborizing blood vessels Short fine annular telangiectasias Focal "shiny white" areas Leaf-like areas Spoke-wheel areas Large blue-grey ovoid nests Multiple blue-grey globules Chrysalis structures (shiny, bright white, orthogonally oriented linear streaks) Annular hypopigmentation Multiple erosions/ulcerations Translucency – Approx. 95–100 % of BCC in large studies.
Histopathologic features	Islands of basaloid cells that do not interact with the epidermis Papillary mesenchymal bodies Horn cysts Fibroblastic stroma No high-grade Atypia Few to no mitoses	Basaloid islands that may connect with the epidermis Clefting between tumor and stroma Peripheral palisading of basaloid cells Central cell necrosis Myxoid stroma Mitotic figures

reconstruction options in anterior lamellar defects include primary closure, laissez fair (healing by secondary intention), skin grafts and flaps. Due to its unique function and lack of tissue substitutes, eyelid defects involving the tarsal and conjunctival aspects of the posterior lamella remain much more challenging. For large and complex defects, histological confirmation of tumor-free margins occasionally delays reconstruction. Major disadvantages of anterior lamellar reconstruction involve tissue contraction complications (i.e., entropion) in small (<25 %) lid defects and compromised flap blood supply in large (>50 %) lid defects. Reconstruction complications of posterior lamellar and full-thickness defect are mainly seen in large (>50 %) defects and are related to graft and flap contracture, blood supply compromise, corneal irritation, lower lid ectropion and post-upper lid related laxity visual impairment. [13,14] Since BCC and TE share a wide range of clinical and histopathological features, misdiagnosing TE as BCC is not uncommon. Hence, in such localized lid margin-preserving suspicious lesions, a wide excisional biopsy with 2–4 mm margin under frozen section control with primary reconstruction is considered superior to punch biopsy, since the former allows the evaluation of the entire mass and prevents malignant recurrence of the pathology.

The dependance on H&E stain alone can be challenging to differentiate the two tumors with similar histopathological findings. Hence the limitation of this study case is the unavailability of special staining techniques which distinguish TE from BCC through immunohistochemical stains positive for peripheral epithelial Bcl-2, peritumoral CD34, and PHLDA1 marker [15–17]. Although a statistical analysis study shows contrasting findings in immune marker panels [18].

Prognosis for TE is usually very satisfactory in the majority of cases, with post-excisional recurrence in solitary nodules being very unlikely. Despite being rare, the possibility of sporadic transformation of TE into BCC should not be underestimated. In fact, multiple familial TEs have been reported of occasional high-grade carcinoma transformation [19].

4. Conclusion

In conclusion, three clinical considerations of great importance need to be emphasized. Firstly, given the possibility of misdiagnosing TE with BCC, a multidisciplinary approach between ophthalmologists and histopathologists ensures a correct diagnosis is more likely to occur. Secondly, excisional biopsy combined with immunohistochemical staining (e.g., CD10, Bcl-2) are prognostically superior to punch biopsy of suspicious anterior lamellar tumors. Finally, adequate knowledge of eyelid anatomy, following a reconstructive ladder principle which follows the defect characteristics is paramount to achieve desirable functional and aesthetic reconstruction results.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Ethical approval

The authors together with the Standing Committee for the Coordination of Medical Research at the Ministry of Health in Kuwait directed the research, assessed its design, and reviewed the feasibility and the validity of the data.

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Author contribution

Dr. Abdullah Ahmad, M.D., and Dr. Fawaz M. Salman, M.D.: wrote the draft for the case report, carried out the literature search and wrote up the case report.

Dr. Faisal Jeragh, M.D., FRCSC: planned and performed the surgery, edited the draft and helped to analyze the case report results.

Dr. Yusef Dashti, M.D.: contributed to the case discussion, carried out the literature search and analyzed the dermoscopic and histopathological data.

Guarantor

Dr. Faisal Jeragh, M.D, FRCSC.

Research registration number

Not applicable.

Declaration of competing interest

No conflict of interest to declare by authors.

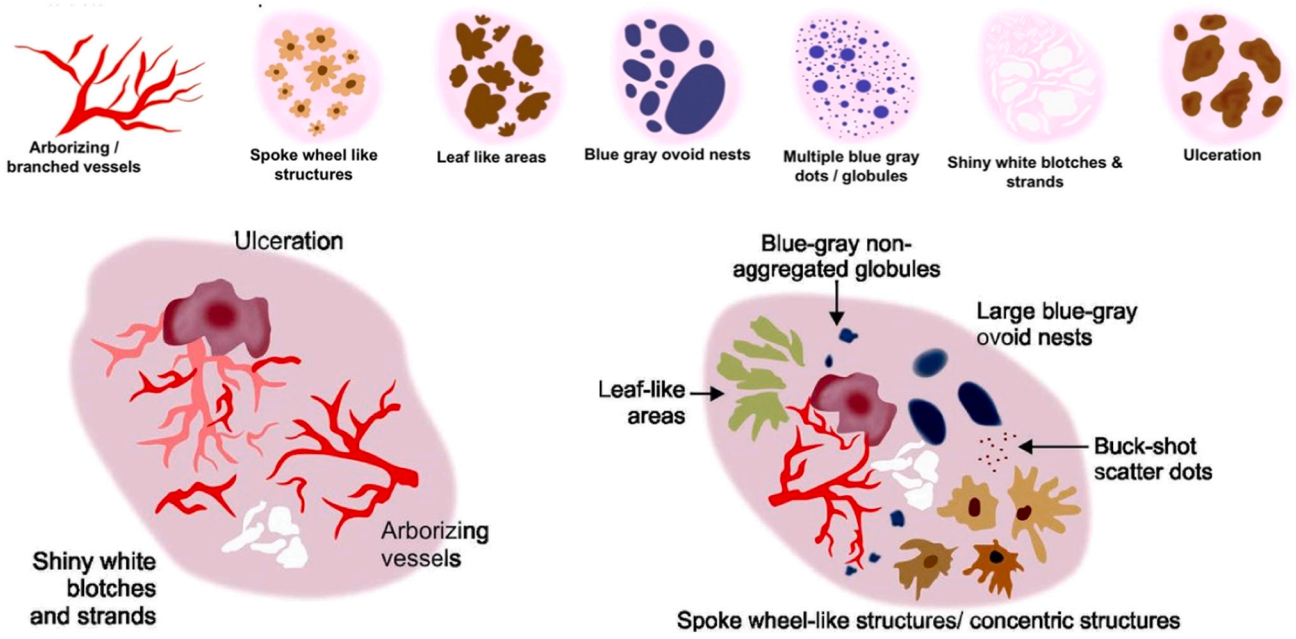

Fig. 5. Dermoscopic features of BCC.
File created by Prof. Natalia James, accessed on 29 Dec. 2022. <*https://dermoscopedia.org/Basal_cell_carcinoma*>.

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