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Single Case

Don't Judge a Tumor by Its Biopsy!

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Trichoblastoma · Basal cell carcinoma · Clinical assessment · Punch biopsy

Abstract
Trichoblastomas (TBs) are extremely rare, benign hair germ tumors that can mimic basal cell carcinoma (BCC). They usually arise on the head or neck and have a potential for malignant transformation, albeit it is rare. We report a case of giant TB on the forehead of a 75-year-old otherwise healthy woman. Since the age of 20 she reported a bulge on her forehead, in which a superficial-looking wound had now developed. Initially a dermatologist biopsied the tumor suspecting a BCC, which the histological analyses confirmed. The patient was then referred to the Department of Plastic Surgery for complete excision of the carcinoma, including the large frontal bulge. Surprisingly, the concluding pathology report changed the diagnosis from a BCC to a TB. Current management of most skin lesions relies on the histopathological subtype of a single punch biopsy. Many benign and malignant dermatological entities may mimic BCC, and therefore misdiagnosis can lead to either unnecessary excision or delayed treatment of metastatic disease. Mimics may include various types of nonneoplastic processes, benign adnexal tumors, including TB, or cutaneous carcinomas with basaloid features. A single punch biopsy is not always adequate in making the correct diagnosis. Although it is considered the gold

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standard, the clinical assessment is just as important. Due to its potential for malignant transformation, it is recommended to excise TB with negative margins.

Introduction

Cutaneous adnexal tumors cover a large group of mostly benign neoplasms. Trichoblastoma (TB) is a rare, mesenchymal-epithelial tumor arising from rudimentary hair follicles, usually on the head or neck. Macroscopically, TB appears typically as a skin-colored, exo- and endophytic nodule without ulceration, may range up to 8 cm in diameter, and is defined as "giant TB" when >2 cm. Microscopically, TB typically lacks epidermal connection and presents as a symmetrical neoplasm composed of monomorphous basaloid cells with follicular germs, fibrillary stroma, and papillae.

Another nonadnexal tumor of the skin is basal cell carcinoma (BCC), which is the most common malignant neoplasm with an estimated overall lifetime risk of 30%; it is also the most frequently encountered diagnosis in dermatopathology [1]. Clinically, dermoscopically, and histopathologically, the differentiation between TB and BCC can be challenging.

With this case report we want to emphasize the importance of taking all the above aspects into consideration in the assessment of skin tumors and delineate the similarities and differences between TBs and BCCs.

Case Presentation

A 75-year-old woman went to the doctor because she had noted a persistent lump on her central forehead that had grown considerably in size during the last couple of years (Fig. 1, 2). The lump had supposedly been present following a bicycle trauma with forehead involvement at the age of 20. Superiorly on the lump, an erythematous swelling with central ulceration had developed, and she was referred to a dermatologist, suspecting a BCC. The dermatologist assessed the underlying tumor as being completely benign with an obvious nodular BCC on top. Punch biopsy from the ulcerated area revealed a BCC of nodular type, made up of basaloid cells, palisading along the edge, and a surrounding desmoplastic reaction (Fig. 3). No vascular or nerve invasion was present. She was then referred to the Department of Plastic Surgery for excision of both the BCC and the underlying probably benign tumor. The underlying tumor was macroscopically assumed to be a lipoma of 30 × 20 × 15 mm with a BCC on top that amounted to 13 mm in diameter. Fusiform excision of both elements including a 5-mm surgical margin was performed.

Surprisingly, the final pathology report described a tumor solely compatible with giant TB, and not enough convincing evidence of the previously mentioned BCC could be seen. Due to the remaining TB cells present in all of the outer edges, the pathologist recommended an additional small excision to ensure radicality, which was performed accordingly and which revealed clear surgical margins. Six months following surgery, the patient was still well with no clinical signs of relapse.

Discussion

Headington [2] introduced the name "trichoblastoma" in 1970 and divided neoplasms of the hair germ into TBs, trichogenic TBs, trichogenic myxomas, and trichoblastic fibromas, based on their degree of stromal induction. In 1993, Ackerman et al. [3] published a new classification of the neoplasms of the hair germ. They described TBs as benign tumors with a sharp circumscription, vertical orientation, smooth borders, and symmetrical growth, and trichoepitheliomas as a superficial type of TBs with a cribriform growth pattern. As formerly mentioned, giant TBs are rare, and the previously reported cases are listed in Table 1 [4–16].

BCCs are composed of cells with large, elongated nuclei that display palisading at the edge of tumor nodules. Usually mitoses and single-cell apoptoses are present, and their cytoplasms can be pale, lightly eosinophilic, or inconspicuous. They display characteristic clefting between the stroma and the tumor edge and are associated with a myxoinflammatory stroma that contains different degrees of mucin and lymphocytic inflammation [1]. BCCs exhibit several patterns of growth and can be broadly divided into aggressive (including micronodular, infiltrative, morpheaform, and metatypical) and indolent (nodular and superficial) types. Combinations of growth patterns are present in 40–75% of all BCC specimens [16, 17]. Moreover, when comparing punch biopsies to complete excisions, an intrinsic error rate of approximately 20% in determining the correct BCC subtype classification exists. BCCs express a profile of cytokeratin similar to that of follicular germinative cells characterized by CK5/6, CK14, and the absence of CK20 [16].

In challenging cases, immunohistochemical stains can be helpful in differentiating between TBs and BCCs. CK20 is seen on benign Merkel cells, which often colonize TBs, and the androgen receptor is often seen on BCCs, but no single marker appears completely sensitive or specific for this distinction [1]. In Table 2 we have listed certain similarities and differences between TBs and BCCs [1, 18].

In the present case, the final pathology report described a neoplasia built up of multinodular units separated by thin collagen strokes. The neoplastic cells were basaloid with a follicular germinal imprint and some palisading and occasional mitoses. Central factors that pointed towards a giant TB were its well-defined and dermal location without relation to the epidermis and the lack of desmoplastic stroma, together with the immune profile with CK20 (Fig. 4).

Conclusion

Both the clinical appearance and the histopathological analysis must be taken into account in clinical assessment. A single punch biopsy might not always be adequate in making the correct diagnosis. Although it is considered the gold standard and a powerful tool, the clinical assessment can be just as important. Therefore, we suggest taking several biopsies from larger indefinite tumors prior to surgery for accuracy. With this case report, we wish to strengthen the reader's attention to TBs, and despite their rarity, it is important to be able to distinguish them from BCCs. Due to their potential for malignant transformation, it is recommended to excise benign TBs with negative margins.

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Statement of Ethics

This research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The patient gave written informed consent for publication of her case (including publication of images).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

M. Demant: study consent, design, data collection, interpretation, writing of the paper. I. Saltvig, H. Trøstrup, V.J. Schmidt, and J. Hesselfeldt: design, interpretation, writing of the paper.

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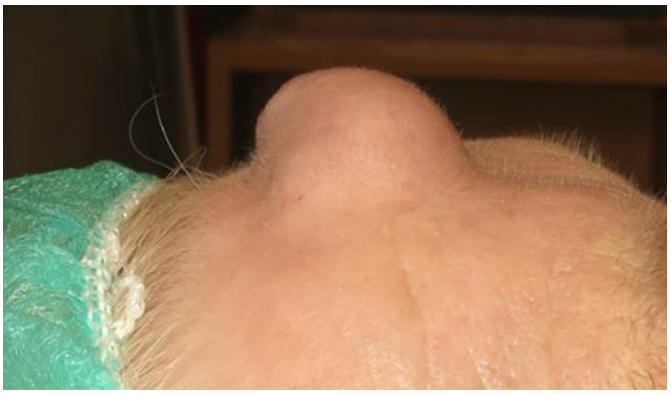

Fig. 1. Lateral view of the trichoblastoma.

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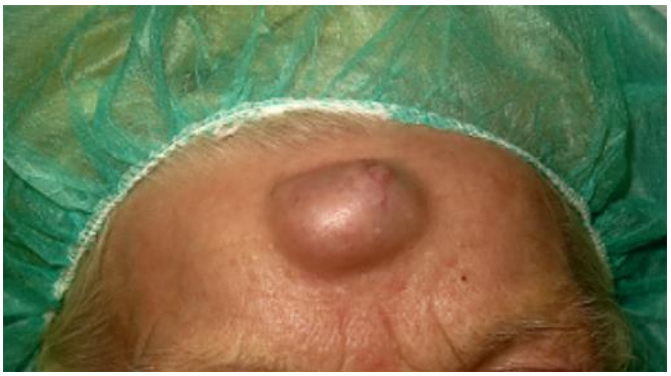

Fig. 2. Anterior view of the trichoblastoma.

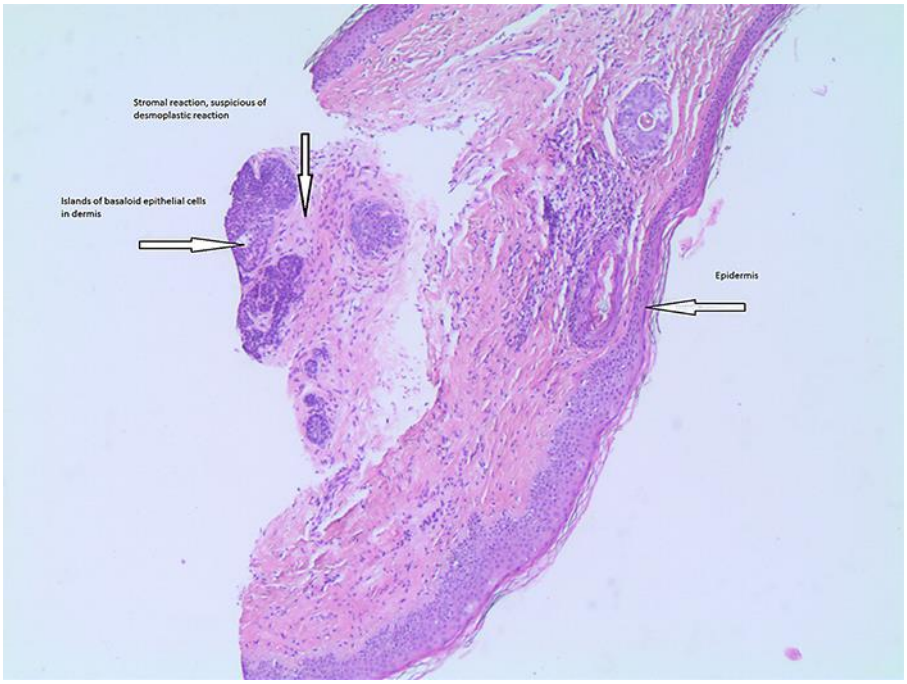

Fig. 3. Initial punch biopsy. Basaloid epithelial cells in the dermis and stromal reaction. Hematoxylin-eosin, ×5.

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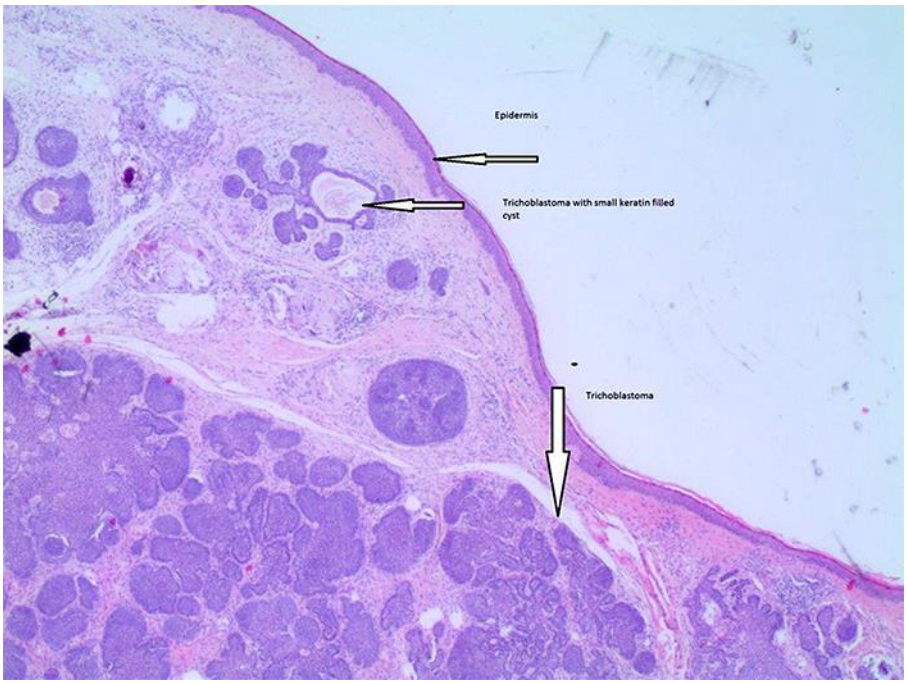

Fig. 4. Excision of a well-circumscribed tumor with islands of basaloid epithelial cells, no connection to the epidermis, and dermis with minimal stromal reaction. Hematoxylin-eosin, ×2.5.

Table 1. Previously reported cases of giant TB

Reference (first author)	Age, sex	Duration of history	Tumor size, cm	Location	Histological findings	Immunohistochemical findings	Final diagnosis	Treatment	Outcome
Frings, 2017 [4]	77, M	10 years	5	upper leg, dermis	PP, clefts and dense FS, keratin cysts	Ber-EP4, Ki67, CD10 + EMA –	giant TB	excision	NR
Lee, 2018 [5]	25, M	since birth; excised 3 times before	9	nuchal area, dermis	basaloid proliferation, OM, infiltrative tumor composed of neoplastic cells	cytokeratin, p53, Ki67 +	giant TB differentiated into trichoblastic carcinoma	excision	NR
Nguyen, 2017 [6]	49, M	1 year	5.5	lateral thigh, dermis	BCs, dense FS, OM, clefts	keratin, Ber-EP4, CD10 + EMA, CK7, vimentin –	giant TB	excision	NR
Benaïm, 2014 [7]	62, M	50 years	8	flank, dermis	large epithelial BCs with rare pigmented cells and dendritic melanocytes	S100 protein, MelanA, HMB45, MiTF, pancytokeratin, AE1/AE3, KL1 +	malignant melanoma arising from a giant pigmented TB	excision	died of metastatic disease 8 months after initial diagnosis
Landolsi, 2011 [8]	57, F	28 years	5	scalp, dermis	BCs, PP, OM	ND	giant TB	excision	NR
Krishnamurthy, 2010 [9]	80, M	1 year	3	nose, dermis	uniform BCs, FS	ND	giant solitary TB	excision biopsy	ND
Kim, 2015 [10]	57, M	5 years	6	back, dermis	BCs with scanty cytoplasm, dendritic melanocytes	Bcl-2, CK20, MelanA, S100 protein, HMB45 +	melanotricho-blastoma	excision	ND
Morillo, 2006 [11]	71, F	2 years	6	buttock, dermis	PP, OM, dense FS	ND	giant TB	excision	ND
Takai, 2004 [12]	54, F	ND	3	scalp, subcutis	FGC, mitoses –, keratinous cysts, BCs, FS	ND	giant TB	excision	NR
Takai, 2004 [12]	53, F	6 months	1	left shin, subcutis	FGC, mitoses –, keratinous cysts, BCs, FS	ND	TB	excision	NR
Cheng, 2003 [13]	81, F	5 years	8.5	back, dermis	PP, BCs, papillary mesenchymal bodies, OM	ND	giant TB	excision	ND
Ohnishi, 1999 [14]	34, F	ND	3.5	cheek, dermis	PP, keratinous cysts, dense FS	34βB4, AE3, KL1, 34βE12, LP34, AE1 +	giant TB	ND	ND
Requena, 1993 [15]	69, M	many years	>3	scalp, dermis	PP, FGC	ND	giant TB	excision	ND
Russell, 1999 [16]	73, M	60 years	10	upper arm, deep dermis	BCs, FS, concentric keratinization, abortive hair papilla	ND	giant TB	excision	ND

34βB4, antibody to cytokeratin; 34βE12, antibody to cytokeratin; AE1/AE3, antibody cocktail; BCs, basaloid cells; Ber-EP4, antibody to epithelial cell adhesion molecule; EMA, epithelial membrane antigen; FGC, follicular germinative cells; FS, fibrotic stroma; HMB45, antibody to human melanoma black antigen; KL1, antibody to cytokeratin; LP34, antibody to cytokeratin; MiTF, melanocyte-inducing transcription factor; ND, not described; NR, no recurrence; OM, occasional mitoses; PP, peripheral palisading; TB, trichoblastoma; –, negative for; +, positive for.

Table 2. Similarities and differences between TB and BCC

Feature	TB	BCC
Epidemiology		
Age	younger	older
Site	occurs anywhere	occurs on sun-exposed areas
Location	within deep dermis and subcutaneous fat	within dermis
Histology		
Stroma	sclerotic and minimal amount	sclerotic and normal amount
Peripheral palisading	yes	yes
Keratin cysts	yes	no
Follicular papillae	yes	rarely
Calcification	yes	yes
Immunohistochemistry		
CK20	yes, on colonizing benign Merkel cells	no
Androgen receptor	no	often
CD10	yes	no

BCC, basal cell carcinoma; CK, cytokeratin; TB, trichoblastoma.