Plaque variant trichoblastoma—An unusually aggressive neoplasm: Presentation of 11 cases in 4 individuals and a review of the literature

Alexander D. Woods, MD,[a] Solomiya Grushchak, MD,[b] Uros Rakita, MD,[c] Wenhua Liu, MD,[a] Vesna Petronic-Rosic, MD, MSc, MBA,[b] and Aleksandar L. Krunic, MD, PhD[b]

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INTRODUCTION

Trichoblastoma is a rare, benign adnexal neoplasm of the hair germ composed of follicular germinative cells surrounded by a dense stroma. These tumors originate from the deep dermis/subcutis, and are usually small, solitary, and do not display aggressive features. However, they may be multiple, bigger than 1 cm, and/or may invade deeply in the subcutis, or rarely into the skeletal muscle.[1,2] An uncommon, poorly defined, plaque variant was initially described in 1995, and termed 'plaque variant trichoblastic fibroma'.[3] More recently in 2019, Requena et al[4] described a case series of 8 patients who presented with multiple facial plaque variant trichoblastomas and emphasized the variant's infiltrative nature.

Herein, we describe additional 4 patients, who over the course of 11 years presented with plaque variant trichoblastomas on the head and neck. Furthermore, we discuss the biologic and clinical significance of the tumor's proposed aggressive features, as well as its suitability for treatment with Mohs micrographic surgery (MMS).

Abbreviations used:

BCC:	basal cell carcinoma
Bcl-2:	B-cell lymphoma 2
CD10:	cluster of differentiation 10
CD34:	cluster of differentiation 34
CYLD:	CYLD Lysine 63 Deubiquitinase
F:	female
H&E:	hematoxylin and eosin
L:	left
M:	male
MMS:	Mohs micrographic surgery
NL:	nasolabial
PTCH:	Protein patched homolog
R:	right

MATERIALS AND METHODS

We identified 4 patients from our dermatology clinic spanning 11 years (2011-2022) that were diagnosed with plaque variant trichoblastoma. Patient sex, age, location of tumor, treatment modality, defect size, number of stages, and closure were collated and summarized in Table I. Frozen tissue specimens were saved for permanent processing and hematoxylin and eosin (H&E) staining. Paraffin embedded and H&E-stained sections were reviewed by board certified dermatopathologists (W.L. and V.P-R.). At least one trichoblastoma from each patient underwent immunohistochemical analysis that included CD10, CD34, Bcl-2, and Ber-EP4 staining. We compared our results with the

From the Department of Dermatology, University of Illinois Chicago College of Medicine, Chicago, Illinois[a]; Department of Dermatology, Cook County Health, Chicago, Illinois[b]; and Department of Internal Medicine, Montgomery Campus of the University of Alabama Heersink School of Medicine, Montgomery, Alabama.[c]

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Correspondence to: Alexander D. Woods, MD, Department of Dermatology, University of Illinois Chicago College of Medicine, 808 S. Wood St, Chicago, IL 60612. E-mail: awoodsfive@gmail.com.

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Table I. Case details

Patient	Sex/age	Tumor	Location	Treatment	Defect (mm)	Stages number/closure
1	M/17	TB	L posterior scalp	Mohs	40 × 35	3/triple rotational flap
		TB	R posterior scalp	Mohs	17 × 12	1/triple rotational flap
		TB	Mid vertex	Mohs	26 × 24	2/rotational flap
		TB	Posterior neck	Mohs	20 × 15	1/CLC
2	F/59	TB	L brow	Mohs	52 × 45	3/plastic surgery referral
		TB	L preauricular cheek	Mohs	49 × 30	2/rhombic flap
		TB	L NL fold	Mohs	13 × 12	1/rotational flap
		TB	R forehead	Mohs	14 × 13	1/H plasty
		TB	R upper lip	Mohs	16 × 13	1/rotational flap
3	F/35	TB	R nasal dorsum	Mohs	11 × 8	2/bilobed flap
4	F/66	TB	L medial cheek	Mohs	31 × 13	3/CLC

CLC, Complex layer closure; *F*, female; *L*, left; *M*, male; *NL*, nasolabial; *R*, right.

immunohistochemical patterns that have been previously described in the literature.

RESULTS

Four patients with solitary or multiple head and neck plaque-variant trichoblastomas were identified from our clinic records and included in the current study. In total, 11 trichoblastomas are presented in Table I.

Patient 1 is a 17-year-old male who developed 4 trichoblastomas on the forehead, scalp, and neck over the course of 3 years. His tumors presented as large, slow-growing plaques with surface telangiectasia (Fig 1, *A*). Family history was unremarkable for skin cancer or other malignancies. Genetic testing did not disclose the presence of CYLD or PTCH gene mutation.

Patient 2 is a 59-year-old female with a history of radiation exposure during the 1986 Chernobyl nuclear disaster. Over the course of 6 years, she developed 5 facial trichoblastomas. The tumors were indolent and presented as well-demarcated, pink-red plaques (Fig 2, *A*). She had 4 subsequent tumors identified 3 years after her initial presentation.

Patient 3 is a 47-year-old Hispanic female who developed a centrofacial, pink red plaque on the right nasal bridge (Fig 3, *A*).

Patient 4 is a 66-year-old Caucasian female who developed a centrofacial plaque on the left medial cheek (Fig 4, *A*).

Histopathologic features were similar for all tumors. Nests of dermal basaloid cells without clear peripheral palisading and infrequent mitoses were present (Fig 2, *B*), mucinous stroma was absent (Fig 3, *B*) and follicular germinative centers were seen inside the tumor islands (Figs 1, *B* and 2, *C*). The neoplastic islands were surrounded with compact eosinophilic stroma (Fig 4, *C*). Tumor cells were negative or patchy positive for Ber-EP4 and Bcl-2 staining was primarily localized at the periphery of tumor islands (Fig 1, *C*). CD10 and CD34 staining revealed a diffuse stromal pattern (Fig 3, *C*) without labeling tumor parenchyma. All tumors were treated with MMS. The majority of tumors treated with MMS were removed in one stage; however, the number of stages ranged from 1 to 3. The deepest levels of tumor extensions were seen in the lower subcutis (Fig 4, *B*). The defect sizes ranged from 11 × 8 mm to 40 × 25 mm. There were no tumor recurrences during the postoperative follow-up period, which ranged from 1 to 6 years.

DISCUSSION

Consensus on the terminology of trichogenic tumors, including trichoblastoma, is lacking.[5-7] Many authors consider trichoblastomas as benign cutaneous tumors composed of epithelial follicular germinative cells and dense fibrocellular stromal components with foci of primitive follicular papillae.[5] Clinically, trichoblastomas present as solitary, skin colored, slow-growing papules or nodules on the face and scalp with low risk for deep invasion or recurrence. Altman et al further subdivided these neoplasms into nodular and plaque variants, which are described as being either histologically well-circumscribed and nonencapsulated or poorly circumscribed with a higher mitotic rate and a propensity for deep infiltration, respectively. Recently, a multiple facial plaque variant of trichoblastoma, with deeply infiltrative behavior, was reported in 8 patients.[4]

Our results suggest that plaque variant trichoblastoma may demonstrate locally aggressive behavior

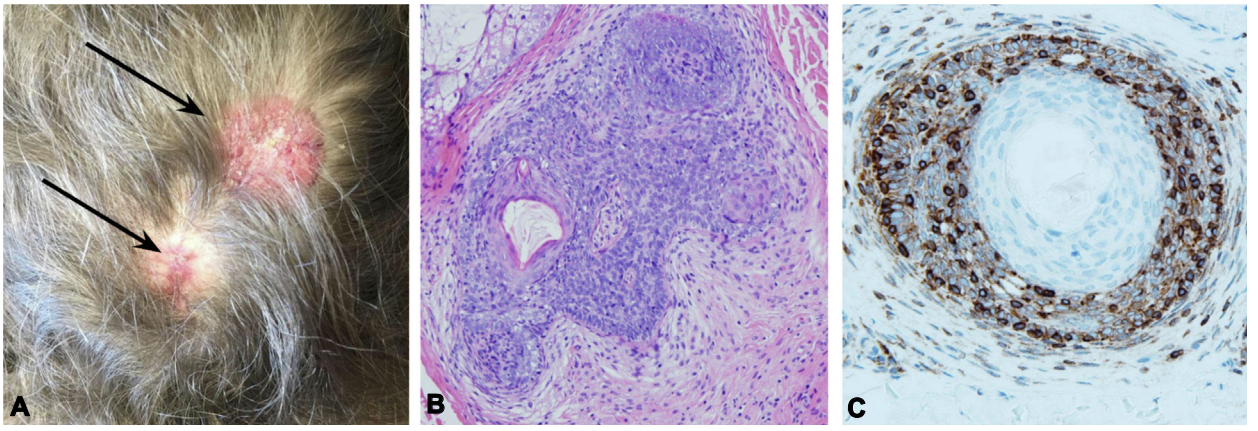

Fig 1. Plaque variant trichoblastoma. **A,** *Pink* plaques on the vertex (*arrows*); (**B**) basaloid proliferation with germinative center and compact eosinophilic stroma; and (**C**) Bcl-2 staining expressed on the periphery of the lobules. (**B** and **C,** Hematoxylin-eosin stain; original magnifications: **B,** 400×; **C,** 400×.)

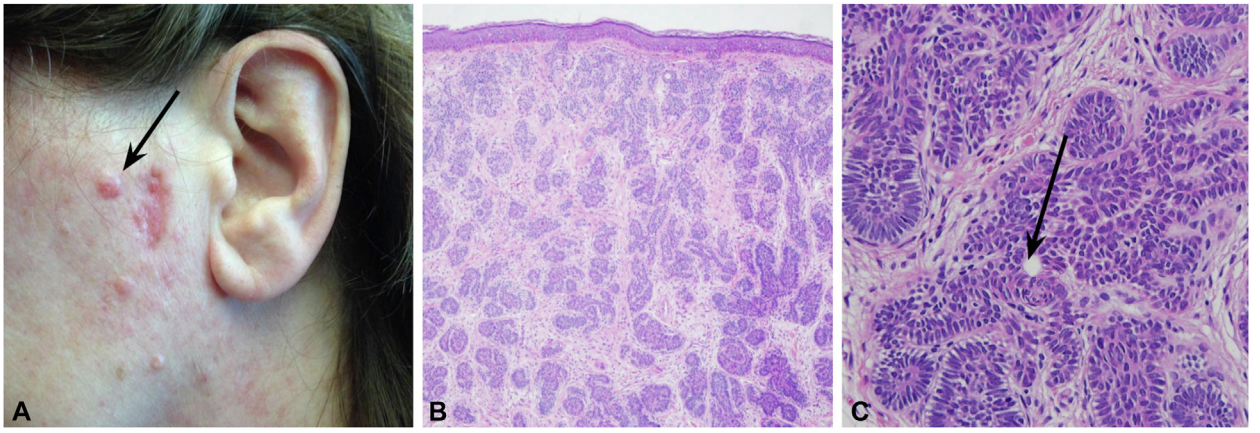

Fig 2. Plaque variant trichoblastoma. **A,** *Pink* plaque L preauricular area (*arrow*); (**B**) basaloid proliferation of tumor nodules; and (**C**) germinative centers (*arrow*). (**B** and **C,** Hematoxylin-eosin stain; original magnifications: **B,** 400×; **C,** 400×.)

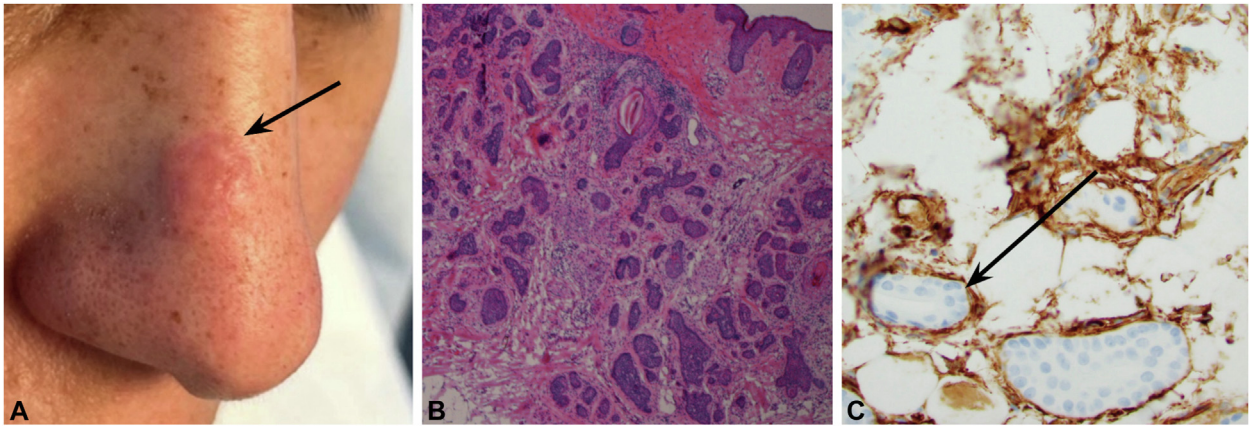

Fig 3. Plaque variant trichoblastoma. **A,** *Pink* plaque R nasal dorsum (*arrow*); (**B**) basaloid proliferation of tumor nodules; and (**C**) CD34 positive periphery of the tumor lobules centers (*arrow*). (**B** and **C,** Hematoxylin-eosin stain; original magnifications: **B,** 40×; **C,** 400×.)

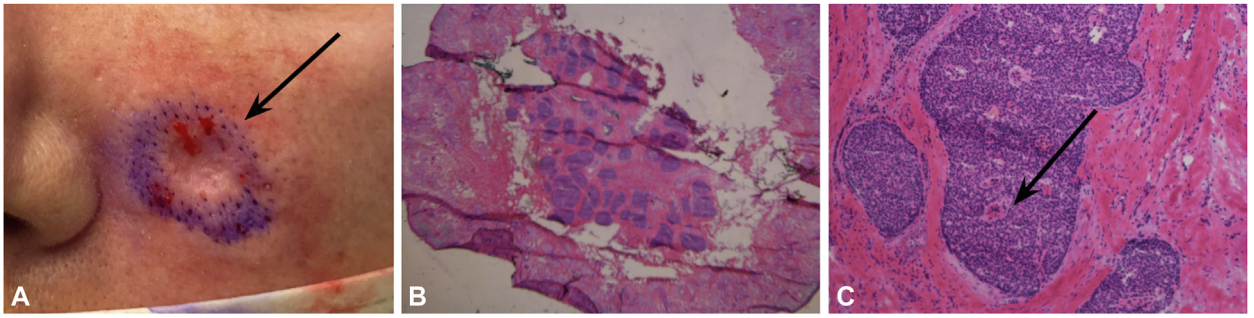

Fig 4. Plaque variant trichoblastoma. **A,** *Pink* plaque L medial cheek (*arrow*); (**B**) basaloid proliferation of tumor nodules on the first Mohs section in the subcutis (H&E 20×); and (**C**) higher power reveals basophilic lobules with compact eosinophilic stroma and germinative centers (H&E 200×) (*arrow*). (**B** and **C,** Hematoxylin-eosin stain; original magnifications: **B,** 20×; **C,** 200×.)

and deep infiltration as it has been reported previously.[1] All tumors were successfully managed with MMS which can successfully trace the neoplastic proliferation and obtain clear margin with minimal sacrifice of the healthy tissue, which is of utmost importance in cosmetic areas like the central face. In the only other published report on multiple facial plaque trichoblastoma, a majority of reported tumors required 3 MMS stages due to the fact that some of their tumors extended down to the striated muscle,[4] while in our group they were mostly limited to suprafascial subcutaneous fat. While small nodular trichoblastomas are typically treated using simple excision,[8] MMS may be a more effective approach for plaque variant trichoblastomas, especially lesions larger than 1 cm, given their propensity for infiltrative growth.

In comparison to basal cell carcinoma (BCC), trichoblastoma histologically has both stromal and epithelial components, while BCC classically only shows the latter.[8] Immunohistochemical staining adds additional diagnostic confidence. Trichoblastoma typically demonstrates CD10 and CD34 positive staining in an exclusively stromal pattern, differentiating it from the tumoral cell staining pattern in BCCs, which is negative for CD34 and positive for CD10.[8,9] Conversely, BCCs stain diffusely with Bcl-2, while trichoblastoma tumoral cells are moderately highlighted with Bcl-2 at the periphery of the tumoral islands.[9] Although both tumors usually stain positively with Ber-EP4,[10] trichoblastoma tends to demonstrate patchy staining, unlike BCC, which shows a diffuse Ber-EP4 staining pattern.[11] The histopathological and immunohistochemical differences between BCC and trichoblastoma are summarized in Table II.

Although genetic analysis was only performed in patient 1, given the multiplicity, aggressive nature, and early age of onset in some patients, a genetic component is plausible. CYLD and PTCH are genes implicated in syndromes characterized by multiple cutaneous neoplasms with follicular differentiation[4]—however, these were both negative in patient 1, who developed trichoblastomas in his late teens. Requena et al, as well as other authors investigating such syndromes also did not identify CYLD or PTCH gene mutations in their cohorts.[4,12] Conceivably, other currently unknown genetic mutations may be responsible for the pathogenesis of the aggressive trichoblastoma plaque presented in this report. Importantly, one of our patients was exposed to ionizing radiation from the Chernobyl nuclear disaster and subsequently presented with her first trichoblastoma about 30 years later. Ionizing radiation is a documented risk factor for both BCC and trichoblastoma tumors (although to a lesser degree).[13] Our report suggests that environmental carcinogens can also contribute to the development of this rare aggressive trichoblastoma variant.

CONCLUSION

In conclusion, we highlight the deeply infiltrative growth, poorly defined margins, histologic similarity to BCC, and larger defects after surgical removal that exist with multi facial plaque variant trichoblastomas. Dermatologic surgeons should be aware of the deeply infiltrative nature of this benign tumor, especially given the possibility of misdiagnosis as BCC. Lastly, we put forth MMS as a suitable surgical intervention for this rare tumor. A greater understanding of the biological behavior and histopathologic features of trichoblastoma variants is necessary to definitively determine appropriate treatment recommendations. Further research may focus on the aggressive behavior of plaque variant trichoblastoma, the genetic stimulus responsible for its growth,

Table II. Histopathological and immunohistochemical differences between trichoblastoma and basal cell carcinoma

	Trichoblastoma	BCC
Origination	Mid-lower dermis, adnexal	Epidermis
Connection with epidermis	−	+
Components	Stromal and epithelial	Epithelial
Peripheral palisading of basaloid cell nests	−	+
Cleft between neoplasm and stroma	−	+
Stromal condensation and pilar differentiation	+	−
Inflammatory infiltrate	−	+
Bcl-2	+ Peripheral tumor island staining	+ Diffuse staining
Ber-EP4	+/− Patchy staining	+ Diffuse
CD10	+ Diffuse stroma	− Stroma, + epithelium
CD34	+ Stroma	− Stroma, − epithelium

BCC, Basal cell carcinoma.

and the mutations that may result in a more infiltrative and indolent growth pattern.

Conflicts of interest

None disclosed.

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