Malignant proliferating trichilemmal tumors arising in patients with multiple trichilemmal cysts: A case series

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Key words: malignant proliferating trichilemmal tumor; pilar cyst; proliferating trichilemmal tumor; squamous cell carcinoma; trichilemmal cyst.

INTRODUCTION

Proliferating trichilemmal tumors (PTTs) are rare tumors that arise from the outer root sheath of the hair follicle. They typically occur on the scalp of elderly women and commonly correspond to transformation of a simple trichilemmal cyst (TC).[1-4] PTTs can reach sizes up to 25 cm and are most often benign, but malignant transformation is possible with the presence of local invasion, atypia, and necrosis. Clinically, malignant proliferating trichilemmal tumors (MPTTs) present as rapidly growing exophytic ulcerated tumors.[1,2] Here, we report 4 cases of MPTTs and multiple TCs in middle-aged men and women with typical and atypical localizations, along with 3 different simultaneous transformation stages in one patient, and concomitant leukonychia in another.

Abbreviations used:

CT:	computed tomography
MPTT(s):	malignant proliferating trichilemmal tumor(s)
PET:	positron emission tomography
PTT(s):	proliferating trichilemmal tumor(s)
TC(s):	trichilemmal cyst(s)

CASE SERIES

Case 1

A 66-year-old Caucasian man presented to the dermatology clinic with multiple skin nodules on his scalp and trunk that had developed over the past 20 years. The size of 3 of these nodules (2 on the posterior aspect of the scalp and 1 on the back) had rapidly increased over the previous months. The patient reported an occurrence of cutaneous trauma at the site of the back tumor suffered several years earlier from a blunt object. Family history was positive for multiple cysts on the scalps of both his mother and daughter. Physical examination revealed 2 bulky ulcerated tumors, each measuring 10 cm on the posterior aspect of his scalp (one in the right side of the occipital region and the other one in the nape region) together with multiple adjacent subcutaneous nodules ranging from 1 to 5 cm (Fig 1, *A* and *B*). Another 8-cm exophytic purplish-red tumor was identified on the left side of the paravertebral region along with an adjacent subcutaneous nodule on the central back (Fig 1, *C*). The initial punch biopsies revealed invasive, moderately differentiated squamous cell carcinoma in the right side of the occipital tumor and PTT in the left paravertebral tumor. Computed tomography (CT) showed bilateral cervical lymphadenopathies but no local bone invasion. Positron emission tomography (PET) showed intense hypermetabolism for the right side of the occiput, nape, and left paravertebral tumors, with slight metabolic activity of the cervical lymphadenopathies. Wide local excision with 2 cm and deep margins was performed by the otorhinolaryngologist. The occipital and nape tumors were excised in a single resection, as were

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Funding sources: None.
IRB approval status: Not applicable.

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JAAD Case Reports 2022;22:42-6.
2352-5126

https://doi.org/10.1016/j.jdcr.2022.01.033

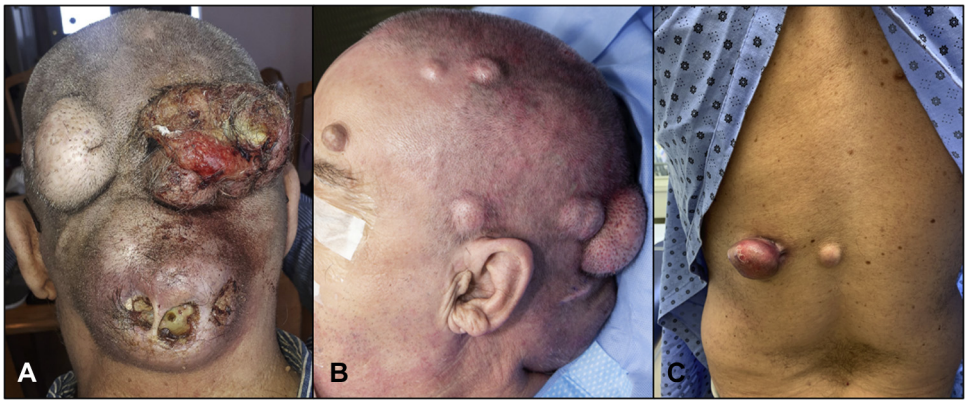

Fig 1. Case 1. **A,** Two bulky ulcerated tumors on the posterior aspect of the scalp (proliferating trichilemmal tumor on the nape region and a malignant proliferating trichilemmal tumor on the right side of the occiput). **B,** Multiple subcutaneous nodules (trichilemmal cysts) on the scalp. **C,** Purplish-red exophytic tumor on the left paravertebral region (MPTT) and subcutaneous nodule on the central portion of the back (TC).

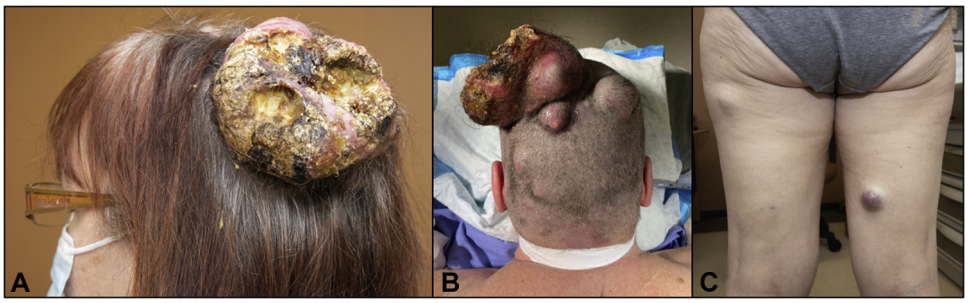

Fig 2. *Case 2.* **A,** A 14-cm ulcerated tumor on the left side of the parietal region (malignant proliferating trichilemmal tumor). **B,** Posterior view of the tumor before surgery with multiple adjacent subcutaneous nodules (trichilemmal cysts) on the scalp. **C,** Subcutaneous nodules on the legs.

the left paravertebral tumor and the adjacent subcutaneous nodule. Reconstructions with flaps and skin grafts as well as cervical lymph node dissection were subsequently performed. The final histopathology report revealed MPTTs for the right side of the occipital and the left paravertebral tumors, a benign PTT for the nape tumor, and a TC for the middle back subcutaneous nodule. The margins were negative, and there was no lymph node metastasis. At the 10-month follow up, there was no evidence of local recurrence.

Case 2

A 58-year-old Caucasian woman presented to the dermatology clinic with a complaint of multiple long-standing 2-to 3-cm skin nodules on the scalp and extremities. Over the past 6 months, one of the nodules on the left side of the parietal region had begun to grow disproportionately, with abundant discharge. Family history was positive for multiple cysts in her paternal grandmother, her father, and her 2 brothers. Physical examination revealed a 14-cm ulcerated tumor on the left side of the parietal region (Fig 2, *A*), with multiple subcutaneous nodules on the scalp and extremities (Fig 2, *B* and *C*). A CT scan revealed bilateral cervical lymphadenopathies without bone invasion, and a PET scan showed a hypermetabolic left parietal tumor, multiple scalp nodules, and lymphadenopathies without metabolic activity. Histology of the large tumor revealed a MPTT (Fig 3). Lymph node biopsies showed reactional changes without lymph node metastasis. A wide excision with 2 cm and deep margins was performed in plastic surgery followed by reconstruction with a free flap and skin graft. The margins were free from tumor. Concurrently, 6 adjacent subcutaneous nodules on the scalp were removed, and histologic findings were consistent with TCs. At the 5-month follow up, there was no evidence of recurrence.

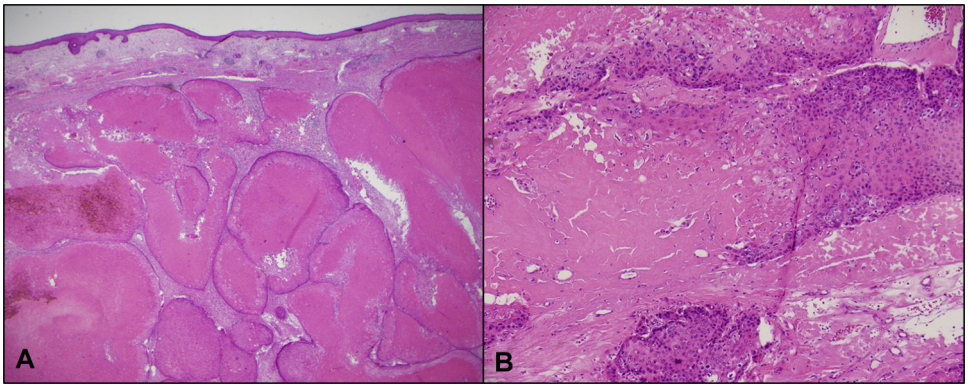

Fig 3. Histopathologic features of the malignant proliferating trichilemmal tumor from Case 2. **A,** Abrupt trichilemmal keratinization and lobular proliferation of squamous epithelium (Hematoxylin-eosin stain; original magnification, ×100) **(B)** High-power view showing nuclear and cytoplasmic atypia, high mitotic index, and necrosis (Hematoxylin-eosin stain; original magnification, ×200).

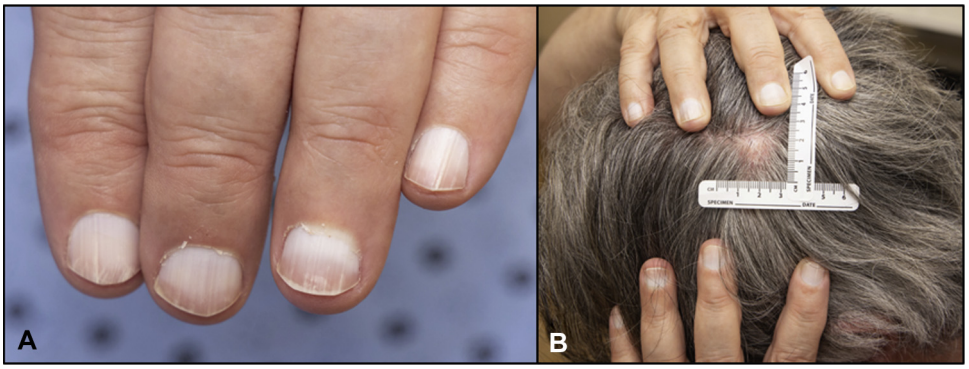

Fig 4. Case 3. **A,** True leukonychia totalis. **B,** Subcutaneous nodule on the scalp.

Case 3

A 63-year-old Caucasian man presented to the plastic surgery department for a 4-cm nodule on the central portion of the back that was excised with an initial suspicion of lipoma. The nodule was present for several years but had recently grown and become painful. Histologic findings were consistent with MPTT. He was then referred to the dermatologic clinic for further evaluation. The medical questionnaire revealed a history of multiple long-standing cysts in the scalp and congenital porcelain white nails (Fig 4). Family history was positive for porcelain white nails in his brother and sister as well as multiple cysts in his sister. Physical examination showed a linear scar on the central portion of the back and 20 nails true leukonychia totalis. There was no lymphadenopathy. Mohs micrographic surgery was performed, followed by plastic surgery for additional deep margins and reconstruction with a rotation flap. No additional imaging was performed. At 3-year follow up, there was no evidence of local recurrence.

Case 4

A 42-year-old Caucasian woman presented to the emergency department with a large ulcerated draining tumor on the vertex. The tumor had been growing slowly over the past 30 years. She also had multiple long-standing scalp nodules. She was referred to the dermatology clinic for management. Family history was unknown. The physical examination revealed a 7 × 6-cm exophytic ulcerated tumor on the vertex with a purulent discharge as well as a dozen of subcutaneous nodules on the scalp and one on the right shoulder (Fig 5) A punch biopsy of the main scalp tumor initially showed histologic changes consistent with keratinizing squamous cell carcinoma. A CT scan of the head and neck was negative for bone extension and lymphadenopathy. A wide local excision with 2 cm margins of the large tumor and peripheral nodules was performed by the otorhinolaryngologist followed by reconstruction with rotation flap. The final histopathology report revealed a MPTT with several peripheral TCs on the excision specimen.

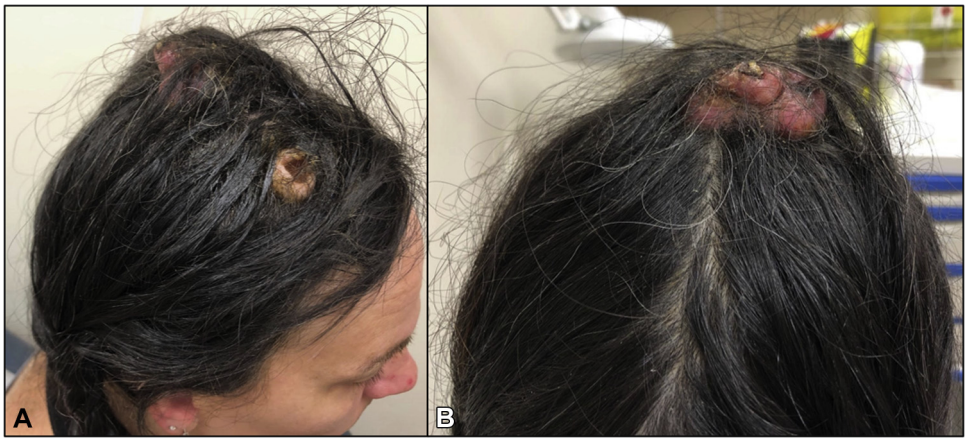

Fig 5. Case 4. **A,** Exophytic tumor on the vertex (malignant proliferating trichilemmal tumor) covered by hair and one visible nodule with central opening on the frontal area (trichilemmal cyst). **B,** Posterior view of the exophytic multinodular ulcerated tumor on the vertex.

Table I. Histopathologic features of trichilemmal cysts, proliferating trichilemmal tumors, and malignant proliferating trichilemmal tumors

Tumor type	Trichilemmal cysts	Proliferating trichilemmal tumors	Malignant proliferating trichilemmal tumors
Histologic features	■ Cystic cavity with abrupt trichilemmal keratinization without a granular layer	■ Abrupt trichilemmal keratinization without a granular layer	■ Abrupt trichilemmal keratinization without a granular layer
		■ Lobular proliferation of squamous epithelium	■ Lobular proliferation of squamous epithelium
		■ Low mitotic index	■ High mitotic index
		■ No nuclear and cytoplasmic atypia	■ Significant nuclear and cytoplasmic atypia
Histologic stage	■ Adenomatous	■ Epitheliomatous	■ Carcinomatous

The margins were free of tumor. There was no metastasis in the lymph node dissection. At the 1-year follow up, there was no evidence of local recurrence.

DISCUSSION

MPTTs most often represent a malignant transformation of TCs but in rare cases may arise *de novo*.[2,4,5] About 2% of TCs can transform into PTTs, with trauma and local inflammation reported as triggering factors.[2,3,4] As illustrated by our 4 cases, the classic clinical scenario is that of a long-standing nodule that begins to rapidly grow in size, becoming exophytic and ulcerated over a period of a few months. There is often presence of multiple TCs and a positive family history for multiple cysts.[1] Hörer et al[6] stated that familial TCs are inherited in an autosomal dominant manner, with a predisposing variant in the PLCD1 gene. Rare families with this variant present with multiple TCs in combination with porcelain white nails (leukonychia).[6] This association was present in *Case 3*.

PTTs have most frequently been described on the scalp of elderly women.[1-3] In the present series, the 4 patients are middle-aged (between 43 and 66) and of both sexes. In 2 cases, MPTTs were located on the back, outside the usual scalp area. Folpe et al[7] mentioned that a PTT in a nonscalp location could be indicative of malignancy. Other clinical criteria consistent with MPTTs include recent rapid growth and a size greater than 5 cm.[6]

Histologic findings of MPTTs include abrupt trichilemmal keratinization without a granular layer, as well as lobular proliferation of squamous epithelium with significant nuclear and cytoplasmic atypia, high mitotic index, and necrosis.[1,3,7] Histology can sometimes mimic squamous cell carcinoma, especially on incisional biopsy samples,

as seen in *Cases 1* and *4*. Helpful histologic features to distinguish between these 2 entities include trichilemmal proliferation and cystic formation in MPTTs.[1,3,6,7] The different histopathologic features of TCs, PTTs, and MPTTs are presented in Table I. Three stages of transformation have been described in the literature for trichilemmal tumors. The common TC represents the first adenomatous stage, the PTT is the epitheliomatous stage, and finally, the MPTT is the carcinomatous stage.[1,2] This hypothesis further supports the presence of concomitant TCs, a benign PTT, and MPTTs in *Case 1*. This is apparently the second reported case, in which the 3 stages are simultaneously present.

Suggested management of PTTs include total excision with adequate margins because of the malignant transformation potential and to rule out the possibility of a carcinomatous component that would not be visible in an incisional biopsy. MPTTs require wide surgical excision with margin analysis.[1,4,5,8] Imaging such as CT scan and PET scan can assess the degree of locoregional extension and rule out metastatic involvement. There is currently no clear guideline, since only a few cases have been reported in the literature; however, radiation therapy for local recurrence or chemotherapy for metastatic disease have been described as treatment options.[1] In a clinicopathologic analysis of 59 cases of PTTs, 1 patient (1.7%) had a local recurrence 8 months after the excision,[5] and in a review of 30 cases of MPTTs, 5 patients had nodal metastasis, and 3 patients had distant metastasis.[8]

The present case series describe PTTs and MPTTs arising in patients with multiple TCs. Therefore, clinicians should be aware of the potential of malignant transformation of TCs and should advise patients with multiple TCs to seek medical attention if rapid growth occurs. Eventually, it would be helpful to specify the genes associated with this clinical entity in order to better characterize these patients and improve their follow up.

Conflicts of interest

None disclosed.

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