ACCSCIENCE PUBLISHING

Tumor Discovery

CASE REPORT

Malignant proliferating trichilemmal tumor post-chemotherapy: A case report

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Abstract

The malignant proliferating trichilemmal tumor (MPTT) is an exceptional adnexal neoplasm of the skin, primarily observed in the scalp of elderly women, often precipitated by local trauma or chronic inflammation. Notably, MPTT exhibits a propensity for local aggressiveness, frequently leading to diagnostic challenges reminiscent of squamous cell carcinoma. The primary treatment modality entails surgical excision with adequate margins, yielding a relatively low local recurrence rate. Herein, we present the case of a 50-year-old woman diagnosed with MPTT of the scalp several years subsequent to undergoing chemotherapy for breast cancer, initially misdiagnosed as squamous cell carcinoma upon biopsy. This case marks only the third reported instance associating MPTT with chemotherapy following breast cancer treatment. We aim to draw attention to this particularly aggressive tumor and its potential origination from benign trichilemmal cysts due to chemotherapy.

Keywords: Malignant proliferating trichilemmal tumor; Trichilemmal cyst; Breast cancer; Chemotherapy

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1. Background

Proliferating trichilemmal tumors (PTTs) are a rare entity of adnexal tumors arising from the isthmic portion of the outer root sheet of the hair follicle.[1,2] They represent only 0.1% of skin tumors.[1,3] Malignant proliferating trichilemmal tumors (MPTTs), on the other hand, are even rarer. Their exact incidence is undetermined due to the rarity of reported cases in the literature, the absence of case series, and the lack of clinical and histological features differentiating them from squamous cell carcinoma. MPTTs appear to occur mostly in the scalp region of elderly women. They are locally aggressive tumors associated with recurrence and even nodal or distant metastatic spread. Herein, we report a case of an MPTT of the scalp in a female patient. It marks only the third reported case of MPTT associated with a history of breast cancer treated by chemotherapy.[4,5] Through this case report, we aim to attract the attention of specialists to investigate a potential causal link between chemotherapy and MPTT.

2. Case presentation

A 50-year-old woman was referred to the Maxillofacial Department of our hospital by her oncologist due to a scalp mass. The patient reported that the lesion had been present

for 20 years but started growing rapidly over the past 10 months, becoming painful, itchy, and spontaneously bleeding. Thirteen years ago, the patient was diagnosed with breast carcinoma, for which she underwent radical mastectomy with lymph node dissection, followed by radiotherapy, chemotherapy, and hormonotherapy. Unfortunately, access to the patient's medical records was not possible. The patient also reported a family history of multiple pilar cysts and disclosed having four of them removed 3 years ago. There was no history of trauma or chronic irritation. During the clinical examination, a firm, nodular mass was identified on the parietal region of the scalp, measuring 4 × 3 cm, with irregular borders, a hairless and ulcerated surface, and telangiectasia (Figure 1). In addition, seven subcutaneous cysts were discovered in the different areas of the scalp, ranging in size between 0.5 cm and 2 cm (Figure 2). Notably, no palpable neck lymph nodes were detected.

A biopsy of the mass revealed histological features compatible with squamous cell carcinoma. Subsequent craniofacial and cervical-thoracic computed tomography scans revealed no evidence of bone invasion, lymph node involvement, or distant metastasis. Following these findings, the patient underwent surgical excision of the parietal lesion with macroscopical margins of 1 cm, along with the removal of the largest cyst. The final histological examination depicted a malignant tumor proliferation with lobulated architecture, coupled with focal stromal invasion demonstrating increasing nuclear and cytoplasmic pleomorphism, accompanied by numerous and often atypical mitotic figures (Figure 3A, B and C). In addition, lymphovascular invasion was observed. The definitive diagnosis rendered was a parietal MPTT associated with multiple trichilemmal cysts. Remarkably, no recurrence or metastasis was detected during the 18-month follow-up period.



Figure 1. Nodular mass of the parietal scalp with irregular ulcerated borders, hairless surface, and telangiectasia.

3. Discussion

The first case of trichilemmal cysts was reported by Wilson Jones in 1966. Trichilemmal cysts occur in 5% to 10% of the population, with barely 2% progressing into PTTs.[3,6] The term MPTT was first proposed by Headington[7] in 1976 and later adopted by Saida *et al.*[8] in 1983 to define a PTT exhibiting malignant features such as infiltrative growth pattern, cytological atypia, atypical mitosis, and lymph node metastasis. Despite being rare, MPTTs predominantly arise in the scalp region (90%), with 84% of cases reported in mainly women aged between 40 and 80 years.[9,10] Other implicated locations include the face, breast, back, chest, abdomen, buttocks, pubis, vulva, back of hand, and wrist.[9,11]

MPTTs are usually characterized as slowly enlarging, firm, painless nodular lesions ranging in size from 1 to 30 cm, often with unremarkable cutaneous covering. These nodules persist for a significant duration before undergoing abrupt and rapid tumor evolution, marked by pain, ulceration, bleeding, or purulent discharge, indicative of malignant metamorphosis.[1,9,10,12-14] Cases of regional lymph node metastasis have also been reported.[8,13-15]

Although malignant degeneration is rare, MPTTs commonly arise from preexisting trichilemmal cysts. Alternatively, several authors have reported cases of MPTTs originating *de novo*, from organoid nevi[16] or seborrheic keratosis.[9] Many researchers have suggested a hypothetical malignant transformation pathway between trichilemmal cysts and MPTTs progressing from the adenomatous stage of trichilemmal cysts to the epitheliomatous stage of PTTs and eventually to the carcinomatous stage of MPTTs.[3,4,9,10,12,17] As in our case, the commonly found accompaniment of MPTTs with simple trichilemmal cysts may support this theory, as does the coexistence of benign and malignant areas within the same neoplasm.[9] Trauma and chronic inflammation are the most incriminated factors in this degeneration. Only two cases of MPTT associated with chemotherapy have been reported in the literature;[4,5] further research and reports are necessary to establish a solid causality link between each of these factors and MPTTs.

MPTTs may be easily confused with squamous cell carcinoma since they share many clinical similitudes and are both rare cases. Similarly, MPTTs must be distinguished from PTTs or trichilemmal carcinoma because they affect prognosis and treatment approach. Histologically, MPTT is described as a tumor that invades neighboring tissues accompanied by anaplasia,

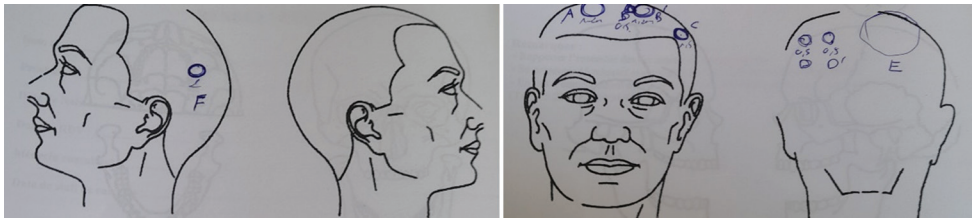


Figure 2. Mapping of the patient's nodular scalp lesions.

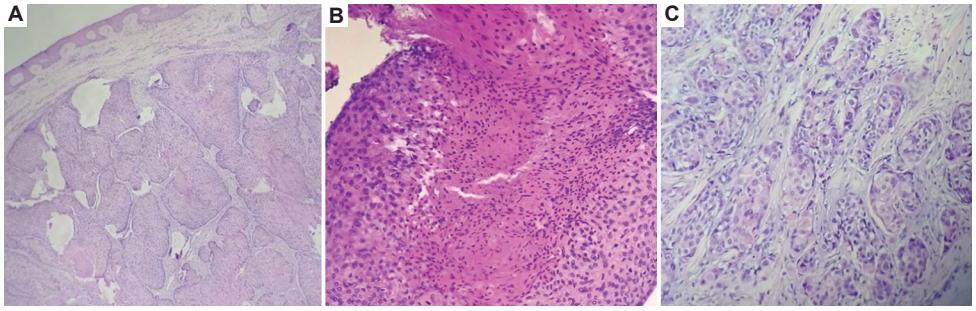


Figure 3. Malignant proliferating trichilemmal tumor. (A) A mid-dermal lobulated proliferation with (B) trichilemmal keratinization, (C) marked cytonuclear atypia and numerous mitosis.

aneuploidy, necrosis, and high mitotic activity, especially atypical mitosis. In addition, vascular and neural invasion may also be observed.[2,5,7,18] These histological features, as well as the positivity of proliferation markers such as Ki67 and p53, and the presence of lymph node or distant metastasis, are essential in distinguishing MPTT from PTT.[1,2,4,19] Trichilemmal keratinization is also an important indicator in differentiating PTTs from squamous cell carcinomas;[2] it is characterized by abrupt, compact, amorphous keratinization of epithelial cells enveloping the cyst wall in the absence of a granular cell layer.[1,2,4,9,13] Immunohistochemical studies are also valuable in distinguishing MPTT from squamous cell carcinoma. CD34, an important immune determinant indicating trichilemmal differentiation, is known to be expressed in MPTTs but not in squamous cell carcinomas.[1,2,4,19] Nevertheless, negative staining with CD34 has been detected in several case reports of MPTTs.[2,4,17] Based on clinicopathological findings, Ye *et al.*[20] classified MPTTs into three groups: Group I comprises benign lesions with regular histological contours, modest nuclear atypia, and absence of pathologic mitoses, necrosis, or nerve/vessel invasion, with no reported recurrence. Group II encompasses low-grade malignant tumors with irregular histological contours and local invasion into the deep dermis and subcutis, with potential for local recurrence. Group III consists of high-grade malignant tumors exhibiting invasive growth patterns, remarkable nuclear atypia, atypical mitoses, geographic necrosis, and involvement of nerves or vascular structures, with a high recurrence rate, lymph node involvement, and a tendency for distant metastasis. Our case aligns with the classification of high-grade MPTT. Additional differential diagnoses of MPTT include dermoid cyst, basal cell carcinoma, keratoacanthoma, invasive Bowen's disease, trichoblastoma, cylindroma, spiradenoma, sebaceous carcinoma, clear cell hidradenocarcinoma, and pilomatrix carcinoma.[3,11,14,16]

MPTTs are characterized by aggressiveness, with estimated rates of local recurrence and lymph node metastasis ranging from 3.7 to 6.6% and 1.2 to 2.6%, respectively.[10,13,21] The true metastatic rate of MPTT remains unknown, yet reports indicate figures as high as 25% for grade III lesions.[3,20,21] Metastases have been reported at various stages, ranging from initial presentation to as late as 10 years thereafter.[6] Consequently, a radical approach to treatment is warranted for MPTTs.

Primary treatment typically entails surgical excision with a 1 cm margin of uninvolved tissue.[3,9,11,16] For current lesions, certain authors advocate for a 2 cm margin. Mohs surgery has been proposed as a potentially less invasive and more efficient technique.[22,23] However, the literature lacks conclusive evidence regarding the contiguity of MPTTs. Non-contiguous lesions negate the benefit of Mohs surgery, as skip lesions lead to inaccurate clearance margins.[3] The role of adjuvant chemotherapy or radiotherapy remains debatable, particularly in cases of localized disease, due to the exceptional nature of the condition, requiring further evaluation. Certain authors consider it unnecessary,[3,9] while others have used adjuvant radiotherapy to the treated area and neck to prevent recurrence[7] or to reduce

tumor volume.[3,11,20,21] In one case, it has been used with curative intent.[21] For MPTTs with distant metastasis, palliative chemotherapy with administration of cisplatin, adriamycin, and vindesine or 5-fluorouracil, followed by palliative radiotherapy, is recommended by some authors.[3,8,9,11,14,16] However, standardized recommendations are currently lacking due to the scarcity of literature and the absence of randomized trials.

4. Conclusion

The MPTT is now widely recognized in the literature, yet it still eludes a definitive nosological diagnostic and, therefore, a therapeutic consensus. Indeed, the literature expresses a certain ambiguity, and no epidemiological or physiological data are 100% certain, for several reasons: the scarcity of reported cases and literature reviews, the absence of large case series, the existence of various terminologies, and the clinical and histological similarities between MPTT and other tumors, especially squamous cell carcinoma. Regarding the physio-pathological link between chemotherapy and the transformation of PTT into MPTT, our case marks only the third reported instance in the literature. However, these reports are limited to case studies, offering no conclusive explanations for the potential link between the two. Further specialized research and publications are warranted to establish such a link.

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Conflict of interest

The authors declare no conflict of interest.

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Ethics approval and consent to participate

Our study is exempted from ethical approval. 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.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Availability of data

Data can be obtained from the corresponding author upon reasonable request.

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