

Brief Communication

The clinicopathological features, treatment patterns, and prognosis of trichilemmal carcinoma: a retrospective case-series study

Chuyan Shi^{1,2*}, Bing Liu^{3*}, Bo Wei¹, Wei Zhang³, Huawei Liu¹, Peng Chen¹

¹Department of Stomatology, The First Medical Center, Chinese PLA General Hospital, No. 28 Fuxing Road, Haidian District, Beijing 100853, China; ²Medical School of Chinese PLA, Beijing 100853, China; ³Department of Stomatology, Air Force Medical Center, Beijing 100853, China. *Co-first authors.

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Abstract: Trichilemmal carcinoma (TC) is a rare malignant cutaneous appendage neoplasm originating from the epithelium of the outer root sheath of hair follicles. TC is generally non-invasive, causing only localized damage, and can be successfully managed with wide excision. Although recurrence and metastasis are rare, such cases often exhibit high malignancy, necessitating regular follow-up. Here, a retrospective study was conducted to review the clinical and histopathological features, diagnosis, and treatment of TC. Seven TC patients were enrolled in this study with 3 female and 4 male patients. The average age was 56.14 ± 20.72 years old and the average year of lesion onset to clinic visit was 3.91 ± 5.07 years. All patients received enlarged excision therapy. Six of Seven patients were followed for at least two years. Only one reported lesion relapse one year after surgery with 0.5 cm enlarged margin. In conclusion, surgery is a great method for TC treatment with at least 1 cm margin. Long-term post operative follow-up is necessary to screening recurrence.

Keywords: Trichilemmal carcinoma, skin accessory tumor, surgical resection, oral and maxillofacial surgery

Introduction

Trichilemmal carcinoma (TC) is a rare cutaneous adnexal malignancy that originates from the epithelium of the outer root sheath of hair follicles [1]. The term “hair sheath carcinoma” was first proposed in 1976, clearly defining it as an aggressive lesion that originates from the outer root sheath of the hair follicle and exhibits features of transparent cell differentiation [2]. It typically occurs on sun-exposed skin, particularly on the face, scalp, neck, torso, and upper limbs [3]. These tumors are commonly observed in middle-aged and elderly patients, typically between the ages of 40 and 80, but they can develop at any age [4]. The pathologies of TC remained a poorly understood entity due to its extreme rarity [5]. TC The pathogenesis of TC is not fully understood but may be associated with ultraviolet light, x-ray radiation (from more than 50-60 diagnostic chest radiographs), trauma, genetic disorders, immunosuppression following organ transplantation,

and other factors. To date, fewer than 500 cases have been reported globally, with a striking predilection for populations in high-ultraviolet (UV) exposure regions (e.g., Australia, Southern Europe), underscoring the role of environmental factors in its pathogenesis [6].

Therapeutic strategies for TC have evolved with accumulating evidence. Early reports [7] highlighted high recurrence rates (up to 20%) with wide local excision, prompting adoption of Mohs micrographic surgery (MMS), which achieves superior margin control - retrospective analyses [8] show MMS reduces recurrence to 3.2% vs. 14.5% with conventional surgery. Prognostically, TC is generally indolent: a meta-analysis [9] of 103 cases found 5-year local recurrence and distant metastasis rates of 5.2% and 0.9%, respectively, supporting long-term follow-up (≥ 5 years) post-resection.

TC is a low-grade malignant tumor with slow progression. Patients often have a history of

Table 1. Clinical details of the seven enrolled patients

No.	Gender	Age	Year of onset	Location	Lesion size	symptom	Margins of excision	Follow up
1	F	67	3	Scalp	2 × 1 cm	-	0.5 cm	Recurrence after one year. No recurrence after enlarged excision with 1 cm margin
2	M	87	4	Scalp	8 × 3 cm	Eroded exudate	1 cm	No recurrence
3	M	66	0.8	Right ear lobe	0.5 × 0.5 cm	scales	1 cm	No recurrence
4	F	54	0.5	Scalp	1 × 1.4 cm	-	1 cm	No recurrence
5	F	24	3	Scalp	0.8 × 0.9 cm	-	1 cm	No recurrence
6	M	37	1	Scalp	1 × 1 cm	pruritis	1 cm	No recurrence
7	M	58	15	Face	4 × 3 cm	-	1 cm	No recurrence

lesions spanning several years to decades, but the condition can progress rapidly after stimulation. The prognosis is generally good, with rare recurrence and metastasis following early diagnosis and wide excision. However, if untreated or misdiagnosed, the metastasis rate may exceed 10%. This is not uncommon, as TC is often asymptomatic and atypical, resembling many other skin lesions. It can also be accompanied by primary cutaneous anaplastic large cell lymphoma, ductal eccrine glands, sebaceous nevus, or proliferative outer hair cyst. Consequently, TC is frequently overlooked, and most patients only seek medical attention if the lesion grows rapidly.

Due to the rarity of metastatic and recurrent TC, there is no consensus on the best treatment for this kind of TC. However, the collection of a small number of cases shows that patients with this kind of TC have a poor prognosis and a high mortality rate. In this article, we retrospectively analysis seven patients who presented in our clinic and received surgery treatment. All patients were followed for at least two years post operatively.

Methods

We conducted a retrospective study to review the prognosis of patients who presented to our clinic in the past thirty years and received surgery treatment of TC. This study was approved by Ethics Committee of the Chinese PLA General Hospital (S2025-018-01).

Patients with TC were finally diagnosed based on pathology and immunochemistry stains by two certified derma-pathologists in our institution. The criteria of diagnose included (1) PAS-positive glycogen within neoplastic cells; (2) folliculocentricity; (3) peripheral palisading of

clear cells; (4) a prominent Periodic Acid Schiff Diastase (D-PAS)-positive basement membrane; (5) trichilemmal keratinization (loss or mini-mization of granular layer, sudden unicellular keratosis and dense non-lamellar keratin formation); (6) lobular architecture; (7) the presence of pre-existing trichilemmoma. Patients with obscure diagnosis were excluded from this study.

The basic information of patients was retrieved from the electronic health records in our hospital. All patients were pictured before and after operation treatment. Patients with incomplete photo records were also excluded from this study.

This study used SPSS 23.0 for statistical analysis.

Results

In this study, we finally enrolled 7 TC patients including three female and four male. Their average age was 56.14±20.72 years old. The average year of lesion onset to clinic visit was 3.91±5.07 years. Six out of seven patients were followed at least two years after excision with no recurrence. Clinical details of the seven enrolled patients were summarized in **Table 1**. The clinical presentation of enrolled patients with TC was presented as hard enlarging soy-bean macule. One presented with locally erosion with extrude and one was found a little scale on the lesion on his first visit. The average lesion area was 5.91±8.97 cm². Six of them reported no symptoms like pruritus and pain while only one complained increasingly itching.

Typical case presentation: A 58-year-old male patient was admitted to the Department of Oral and Maxillofacial surgery in our hospital on

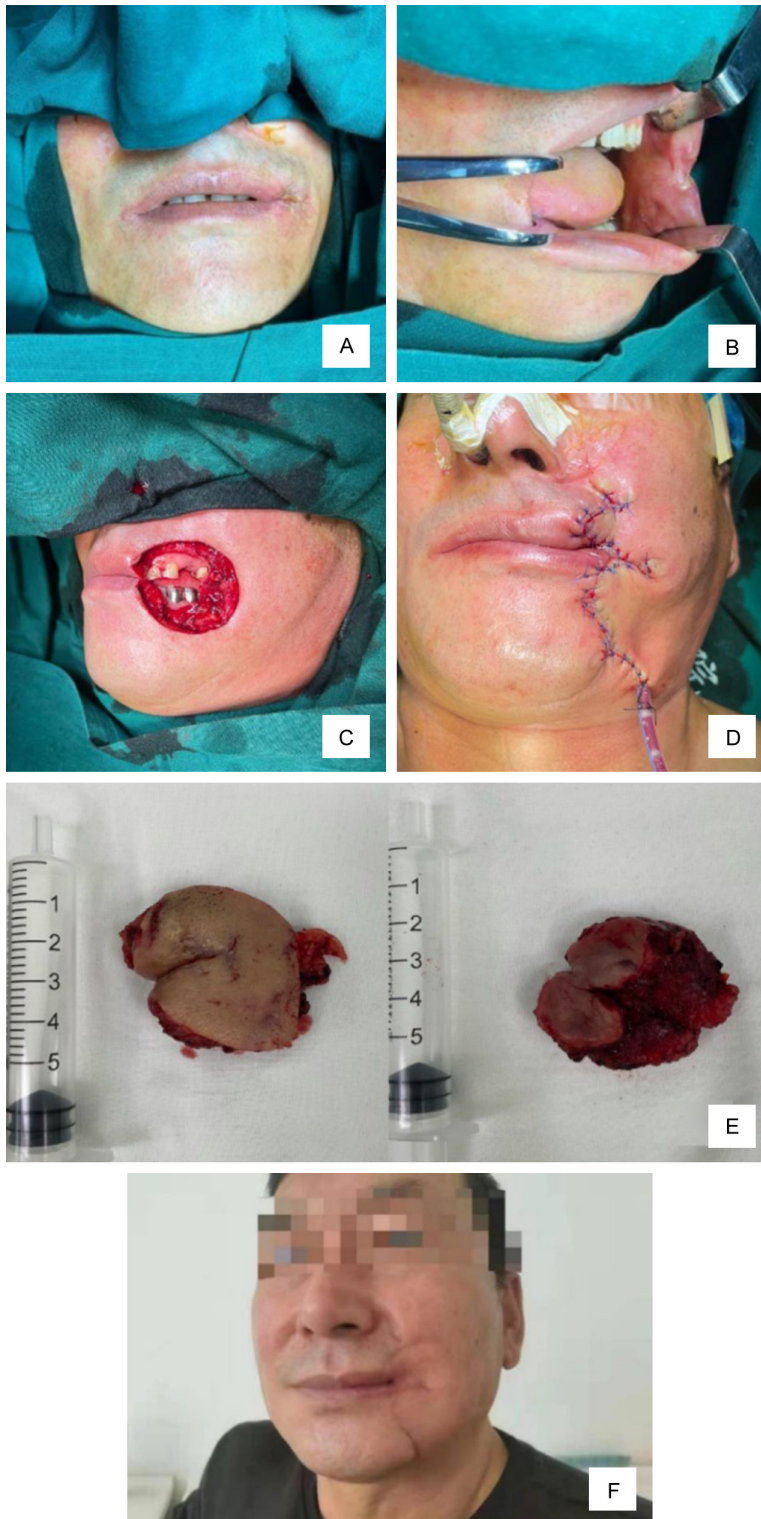


Figure 1. Clinical presentation of a representative TC case at key treatment stages. A. External view of the oral commissure mass; B. Intraoral mucosal side; C. The tumor was completely resected at the enlarged 1 cm, and the deep surface was cut to the mucosal layer; D. One adjacent diamond-shaped tissue flap on the top and bottom was designed, and the flap was transferred to the defect, pulled together, and sutured layer by layer, drainage was placed, repair the wound and restore the facial shape; E. Orofacial swelling;

ings removed through surgery, skin side (Left) and mucosal side (Right); F. Six months follow-up after surgery. Written informed consent was obtained from the patient prior to the collection of clinical data and imaging materials, including permission for the publication of this case report and accompanying figures.

January 8, 2021. The patient reported that there was a hard soybean-sized mass at the left oral junction. The lesion appeared 15 years ago and grew slowly without any symptoms until two months ago, when it began to grow rapidly. The tumor has invaded the patient's left corner of the mouth and surrounding tissues. A hard, well-demarcated, approximately 4 cm × 4 cm swelling was present at the left corner of mouth. It is non-tender to palpation. The skin-colored swelling showed a central depression with an elevated rim and visible capillary dilatation. Palpation reveals a distinct hard nodule at the base of the swelling. This lesion significantly impairs left commissure mobility and restricts mouth opening (**Figure 1A**). Examination of the corresponding oral mucosa reveals firmness and irregular thickening, resembling mucosal fibrosis (**Figure 1B**). Given the pathological changes of the oral mucosa invaded patient, in this case, an enlarged resection of the left orofacial mass and repair of the adjacent tissue flap transfer was performed under general anesthesia. The complete enlarged resection of the mass was performed approximately 1 cm outside the left oral commissure, and the deep surface was cut to the mucosal layer. After exci-

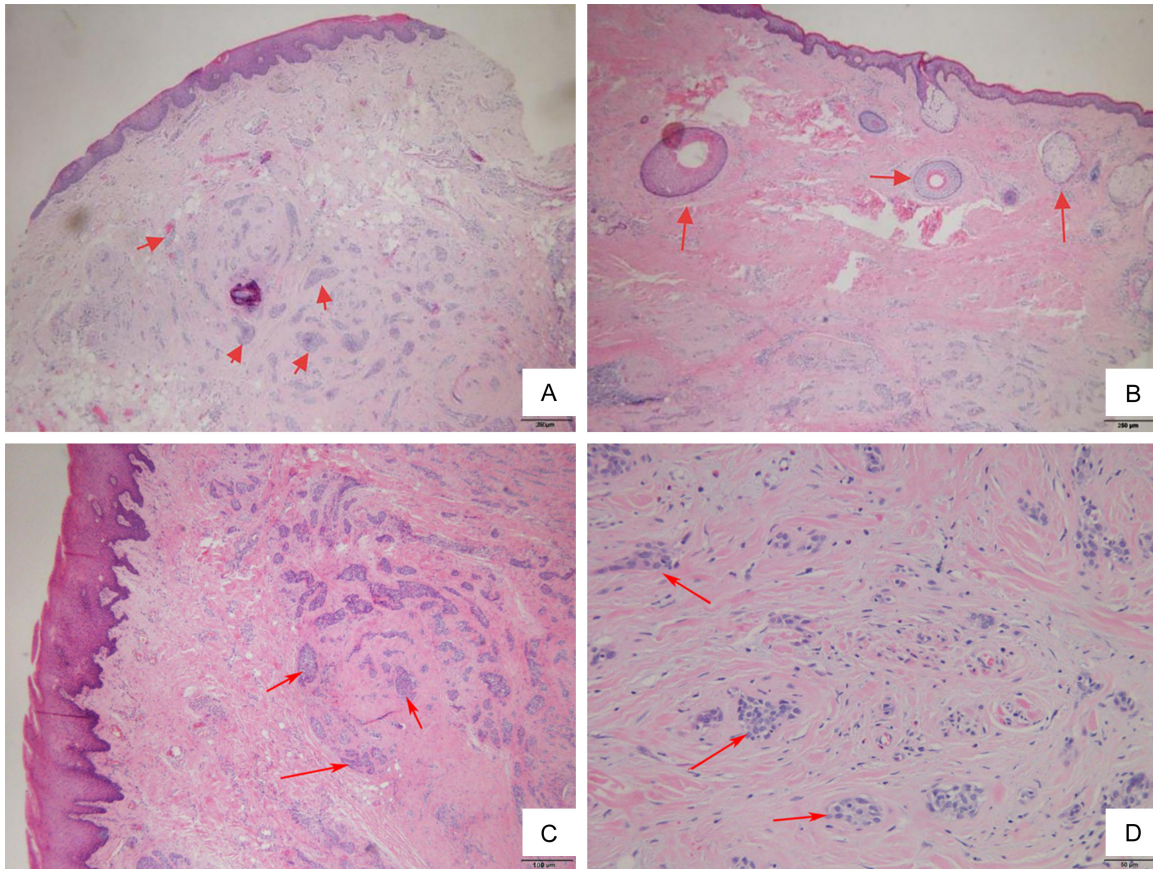


Figure 2. Representative histopathological features of the biopsy specimen from the patient's lesion (Hematoxylin and Eosin staining). A. The tumor is composed of epithelioid cells with numerous vacuolated cells ($\times 4$, scale bar = 250 μm); B. Tumor cells exhibit clear cytoplasm, prominent nuclei, and form lobular lesions attached to the epidermis; they are polygonal with increased mitotic activity ($\times 4$, scale bar = 250 μm); C. Infiltrative growth pattern of the tumor, with fenestrated arrangement of cells around the nests ($\times 10$, scale bar = 100 μm); D. Tumor cells and the surrounding basement membrane show positive purplish-red staining ($\times 20$, scale bar = 50 μm).

sion of the lesion, two adjacent diamond-shaped tissue flaps were designed and transferred to the defect, and the buccal mucosa was closed with sliding flaps, pulled together layer by layer, and indwelled drainage tube (**Figure 1C, 1D**). What was seen on examination: (left orofacial swelling) skin on one side and mucosal tissue on the other side, size 4 \times 3 \times 1.8 cm, cut surface grayish white and brittle (**Figure 1E**).

All patients received enlarged excision therapy. Six out of Seven patients received enlargement excision with 1 cm margin while only one received surgery with 0.5 cm margin. We performed pathology and immunochemistry examination for every patient. All of the enrolled patients presented with trichilemmal keratinization, a peripheral palisading pattern and focal necrosis on under microscopy and EMA

(-), Calponin (-), CK7 (-), p53 (-), AR (-), p16 (+), GCDFP-15 (-), CK18 (partial +), Ki-67 (+ about 20%), CK19 (+), p63 (+), CK5 (+) which confirmed the TC diagnosis. In the representative mucosa involved case, the lesion in the left corner of the patient's mouth was seen as fibrous tissue hyperplasia in the dermis and subcutaneous tissue of the skin, during which striated and small nest-like tumor cells were seen, and some of the nests were keratinized in the center and infiltrated in the transverse muscle tissue (**Figures 2, 3**).

Patients with TC after surgical treatment usually have a good prognosis, but they need regular follow-up and early detection of recurrence and metastasis [6]. Six months after operation, the patient recovered well, had a small scar, no functional damage or recurrence, and the patient was satisfied with the appearance of

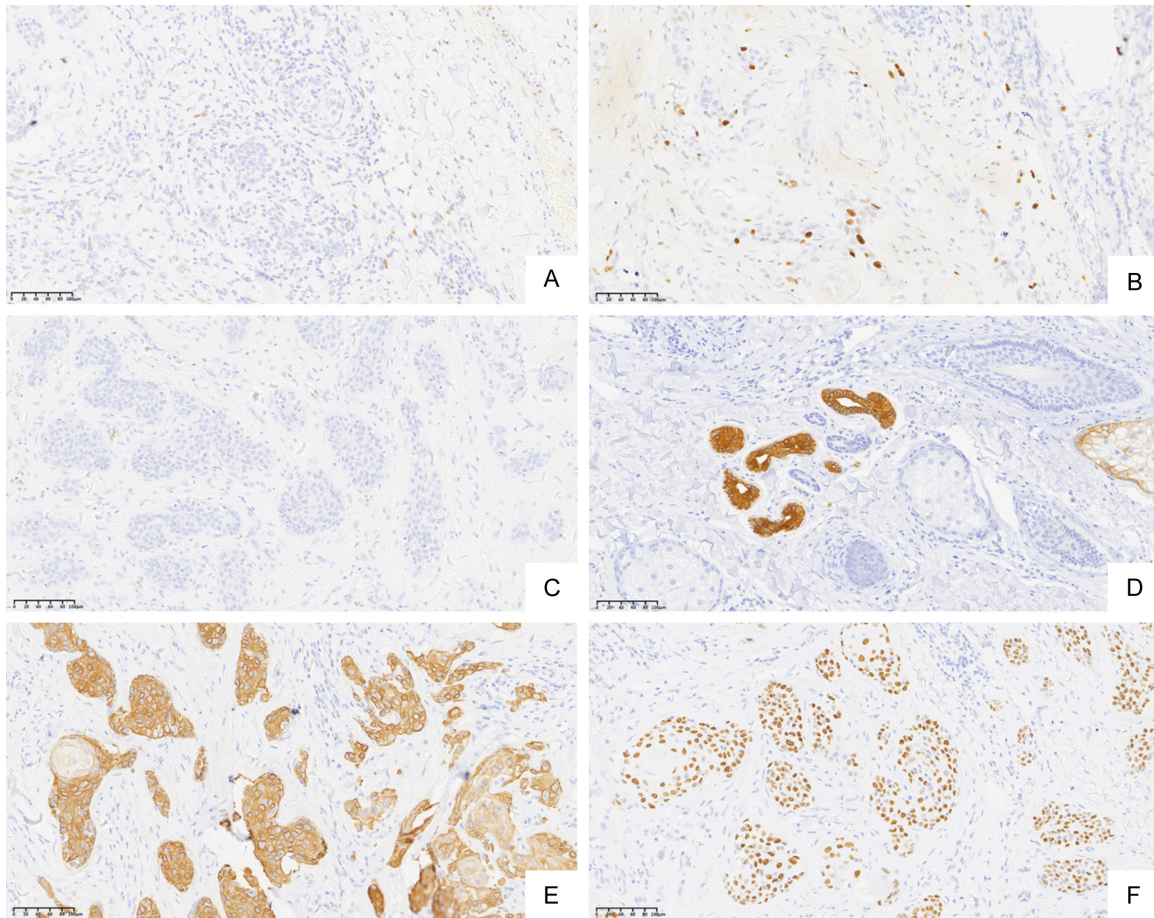


Figure 3. The patient's lesion was detected via immunohistochemistry (IHC) staining. A. AR ($\times 20$, scale bar = 100 μm); B. Ki-67 ($\times 20$, scale bar = 100 μm); C. EMA ($\times 20$, scale bar = 100 μm); D. CK7 ($\times 20$, scale bar = 100 μm); E. CK5 ($\times 20$, scale bar = 100 μm); F. P63 ($\times 20$, scale bar = 100 μm).

the prognosis (**Figure 1F**). Six of Seven patients were followed for at least two years. Only one reported lesion relapse one year after surgery with 0.5 cm enlarged margin. We repeated the surgery with 1 cm margin, and further followed up two more years, the patient was fully recovering with no recurrence. Other patients with 1 cm enlarged margin were clear in the two-year follow up.

Discussion

Based on 7 clinical cases, we conducted a research analysis on TC in this report, which will be beneficial for our diagnosis and treatment of TC. TC is challenging to distinguish from other skin tumors based solely on clinical examination, often leading to misdiagnoses such as basal cell carcinoma (BCC), squamous cell carcinoma (SCC), malignant proliferating trichilemmal tumor (MPTT), nodular melanoma,

and keratoacanthoma [10]. Therefore, differential diagnosis is essential [11]. The diagnosis of TC is primarily established through histopathological examination using hematoxylin-eosin (HE) staining, with immunohistochemical (IHC) examination being utilized as needed [12]. The typical pathological changes of TC are infiltrative growth of tumors with various growth patterns, lobular, parenchymal, and trabecular. Centered on a pilosebaceous unit, TC generally presents a typical histopathology of trichilemmal keratinization, a peripheral palisading pattern and focal necrosis. The growth of TC always presents lobular and invasive, characterized by classical large, polygonal, transparent tumor cells with eccentric nuclei but without hair follicle differentiation, nuclear heterogeneity, and abnormal mitotic signs [13-15]. In some cases, TC was found attached to the epidermis and infiltrating the hair follicle within the dermis, with the infiltrative lobules of clear cells where

trichilemmal keratinization can be found [16]. In our case, HE analyses were also conducted on the biopsy specimens of the patient's lesion, which was helpful to determine that the TC patient might have a primary tumor with malignant transformation. Immunohistochemical (IHC) staining for TC is usually negative for CEA (carcinoembryonic antigen) and EMA (epithelial cell membrane antigen) [17]. Studies have shown that positivity for CK1, CK10, CK14, CK-17, CK19, Ki-67, p63, and p53, and negativity for S-100, CK-L, CEA, HMB-45, CK7, CK8, CK15 and CK16 can serve as diagnostic indicators for TC [14, 18-21]. TC is positively correlated with the mutation rate of p53 [22]. Our IHC results also showed positive expression of ki-67 and p63, negative expression of CK7 and EMA, further confirming that the patients were suffering from TC.

There are many treatment options for TC, including Mohs micrographic surgery (MMS), surgical resection, radiotherapy, chemotherapy and application of 5% imiquimod ointment [23, 24]. MMS has been proven to be an effective treatment for TC. Although this method preserves normal tissue as much as possible, it is still necessary to ensure that the surgical margins are free of tumor cells for it is not foolproof [25]. Although the histological features of TC are moderate to highly malignant, the clinical presentation is generally benign and can be cured by extended local excision. Numerous scholars have also concluded that surgical resection of a 1 cm tumor-free margin is the safe, economical and effective treatment of choice for TC [26, 27]. In our report of seven TC patients, all underwent primary excision with a 1 cm clinical margin; six remained disease-free at ≥ 2 years. One patient initially resected with a 0.5 cm margin developed local recurrence at 12 months and was cured by re-excision to 1 cm. These data indicate that a ≥ 1 cm safety margin at first surgery minimizes the risk of the rare but problematic recurrence or metastasis observed in TC.

As we know, metastatic disease seldom occurs but carries a poor prognosis when it does. TC is generally considered to have an inert course and benign clinical evolution, and is considered to be a low-grade cancer with low metastatic potential. Local recurrence is rare after complete resection, and local lymph node metastasis

and distant metastasis are rare, but still exist [28]. The most common metastatic organ is regional lymph node. It has been reported that cervical lymph node metastasis, axillary groove lymph node, inguinal lymph node metastasis and so on [29]. It is suggested that chemotherapy and radiotherapy can be used for metastatic TC, but sometimes it cannot inhibit metastatic lymph node enlargement [30]. At this time, regional lymph node dissection is more effective [9]. Yi HS et al. have reported that after extensive local resection of the TC of the left thigh, metastasis occurs in the aortic cavity, para-aortic and portal vein areas [15]. Lv W et al. also reported a complex case of right lower abdominal TC with ipsilateral axillary and inguinal lymph node metastasis [11]. However, local recurrent TC is often difficult to be treated by reoperation. Radiotherapy can be considered as a clinical choice to avoid surgical risks and complications. For example, Gao S and others have used radiotherapy to treat an elderly case of recurrent periorbital hair sheath carcinoma [23]. A few chemotherapeutic regimens have been used for metastatic TC. Cisplatin in combination with either cyclophosphamide, 5-FU, or vindesine and bleomycin have slowed the progression of metastatic disease but have not been curative [12, 15, 31, 32]. The seven patients in our report were followed up for at least two years after the surgery. Only one patient had a recurrence of the lesion one year after the operation, with the margin increasing by 0.5 cm. Subsequently, we repeated the operation with a 1 cm margin and followed up for more than two years until the patient fully recovered without recurrence. Therefore, while recurrence is rare, patients should be examined for such sequela with periodic surveillance. And radiotherapy can be reserved for further relapse.

This study reviewed seven TC patients and summarized the postoperative follow up results which might offer experience to medical practitioners in TC treatment. Also, this study has some limitations, due to the rarity of the disease, the sample size was limited, which may affect the generalizability of the findings. Currently, most TC cases still rely on surgical resection, but the high risk of recurrence remains a major challenge. Although radiotherapy can serve as an adjuvant treatment due to the radiosensitivity of tumor cells, and targeted

therapies against aberrant signaling pathways (e.g., EGFR or PI3K/AKT inhibitors) hold promise, there is still a lack of validated clinical applications. Moreover, the local invasiveness of the tumor necessitates careful evaluation to avoid recurrence following incomplete resection. Most existing research remains descriptive, focusing on pathological characteristics and clinical misdiagnosis, with limited breakthroughs in targeted treatment strategies. Future studies should expand the sample size and extend follow-up durations to better assess long-term outcomes. Additionally, potential therapeutic targets identified through genetic profiling and molecular analyses should be validated in preclinical models and clinical trials to advance personalized treatment approaches.

Summary

TC is a rare malignant tumor of the skin adnexa, often delaying treatment due to being mistaken for other skin conditions, making clinical differentiation challenging. Prior to treatment, a definitive diagnosis must be established through a combination of clinical examination, biopsy, and immunohistochemical analysis. Subsequently, an optimal treatment strategy should be selected based on the diagnosis. Wide excision typically yields favorable therapeutic outcomes; however, intraoperative vigilance is crucial to prevent tumor residue and ensure complete excision. Additionally, regular post-surgical follow-ups are essential to monitor for TC recurrence and the development of distant metastases.

Disclosure of conflict of interest

None.

Address correspondence to: Drs. Peng Chen and Huawei Liu, Department of Stomatology, The First Medical Center, Chinese PLA General Hospital, No. 28 Fuxing Road, Haidian District, Beijing 100853, China. Tel: +86-10-6220-8022; Fax: +86-10-6220-8032; E-mail: chenpeng@301hospital.com.cn (PC); liuhuawei840222@126.com (HWL)

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