Multiple Proliferating Trichilemmal Tumor with Positive Family History: A Case Report and Review of the Literature

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Abstract: Objective: Proliferating trichilemmal tumor is uncommon tumors that develop from the hair follicle's outer root sheath. They frequently correspond to the transition of a simple trichilemmal cyst, and they typically occur on the scalp of elderly women. However, multiple proliferating trichilemmal tumor are more rare and difficult to diagnose. Therefore, the diagnosis and treatment of this disease were discussed based on the relevant literature and the clinical data of multiple proliferating trichilemmal tumor in our hospital. Methods: The clinical data of a 74 year old female patient with multiple proliferating trichilemmal tumor and positive family history admitted to department of dermatology were retrospectively analyzed, combined with relevant literature review and discussion. Results: After surgical radical treatment, it is suggested to be multiple proliferating trichilemmal tumor based on the pathological result and immunohistochemical results. Conclusion: Proliferating trichilemmal tumors a rare but morphologically distinctive tumor. The diagnosis is mainly based on pathological results. Based on the histopathologic findings of tumor, this case was diagnosed as proliferating trichilemmal tumor. Surgery is the first choice for treatment. The patient's condition was successfully treated with total excision. Regular postoperative review is required. Proliferating trichilemmal tumor need to be diagnosed and treated using a multidisciplinary strategy. Close clinical follow-up is the most efficient method of early metastasis and recurrence detection.

Keywords: Multiple Proliferating Trichilemmal Tumor; Pathology; Immunohistochemistry; Surgery; Diagnosis and Treatment

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1 Preface

Proliferating trichilemmal tumor (PTT) is a rare lesion, which develops in the hair follicles' exterior root sheath and is characterized by the lobulation of many squamous epithelial cells. It is mainly located on the head and neck, where there are the most hair follicles [1]. 90% of cases occur as solitary lesions on the scalp in elderly women above the age of sixty years old, where it is often more prevalent. The occurrence of PPT is infrequent, and its biological activity is characterized by unpredictability. Histologically, there is a frequent confusion between pilomatricoma (PTT) and malignant proliferating trichilemmal tumor (MPTT), as well as metastatic or invasive squamous cell carcinoma (SCC) [2]. This particular case exhibits a unique instance of multiple proliferating trichilemmal tumors accompanied by a positive family history, hence posing a diagnostic challenge. Distinguishing between a benign or malignant process in these lesions can sometimes be difficult. A necessary condition for an accurate diagnosis is careful clinical and

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histological assessment.

2 Clinical Information

A female patient, aged 74, sought medical attention at the dermatology department of our hospital. She reported the presence of several skin nodules measuring between 3 and 6 centimeters on her scalp and face, which had been present for a significant period of time.. Over the past 10 years, The patient has scattered nodules on the forehead, which are the size of peanuts and are hemispherical in shape. After scratching, they are locally ruptured, gradually increasing to a chestnut sized lump, with central ulceration and a small amount of yellow secretion, accompanied by itching. Recently, skin lesions have gradually increased, with skin nodules ranging in size from mung beans to fava beans appearing in the temporal, nasal, and cheek regions. Some of the nodules have a central depression and are covered with white secretions (Figure 1①②③). The disorder exhibits a prolonged duration. The patient's family history revealed the presence of multiple nodules in her mother, three sisters, and nephew (Figure 2).

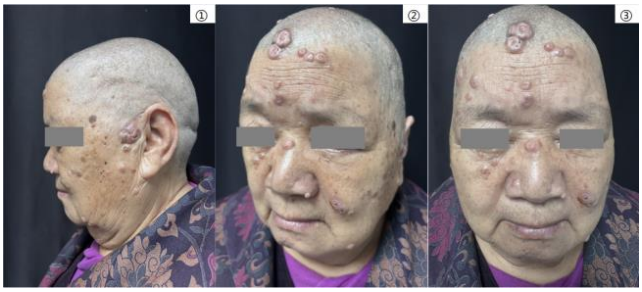

Figure 1 ①-③ multiple nodules on the forehead and face

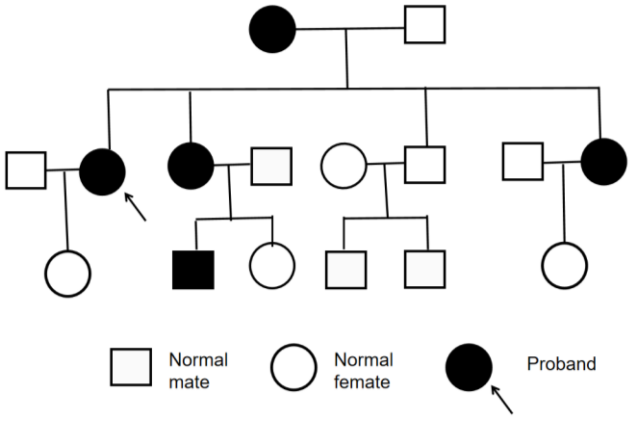

Figure 2 Pedigree of the family showing an autosomal dominant inheritance

2.1 Physical Examination

Generally in good condition, no palpable enlargement of superficial lymph nodes, no abnormalities in all system examinations.

2.2 Assistant Examination

Liver and kidney function, ECG, blood, urine, stool routine examination with no abnormal changes. Skull radiographs showed normal skull.

2.3 Histopathological Examination

The tumor was located in the dermis, composed of squamous epithelial cell clumps in lobular shape. There were characteristic squeezed, clearly bounded, and regular non-infiltrating zones between the lobules of the tumor clumps (Figure 3 ①). The basal-like cells around the tumor clumps were arranged in palisade shape (Figure 3 ②), and extensive hair sheath keratosis and necrosis could be seen (Figure 3 ③). A large number of clear cells were seen in the tumor clumps (Figure 3 ④), and keratosis and squamous vortex formation of individual cells could be seen (Figure 3 ⑤). No pathological mitosis was observed (Figure 3 ⑥).

According to clinical and histopathological examination, the patient was diagnosed as PTT.

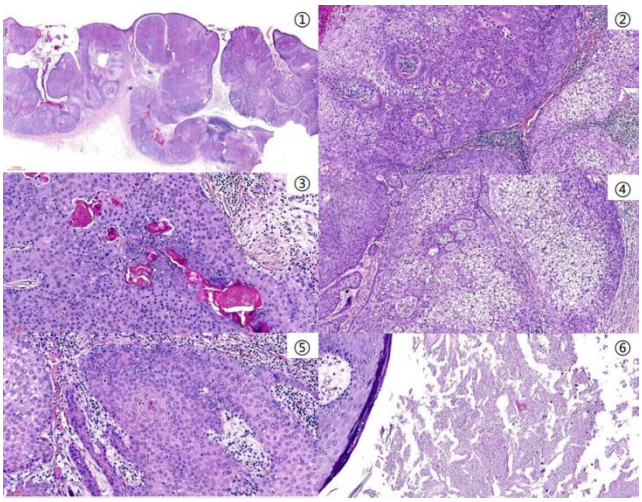

Figure 3 ①-⑥ Pathology of multiple nodulesr (100×)

2.4 Immunohistochemical Indicators

Ki-67 (+, 5-10%) (Figure 4①②), CK14 (+), P53 (+, 30%, wild type) (Figure 4③), P63 (+) (Figure 4④), CK5/6 (+) (Figure 4⑤⑥), CD34(-), BerEp4 (-), CD10 (-), Bcl-2 (-), CEA (-). HPV16(+).

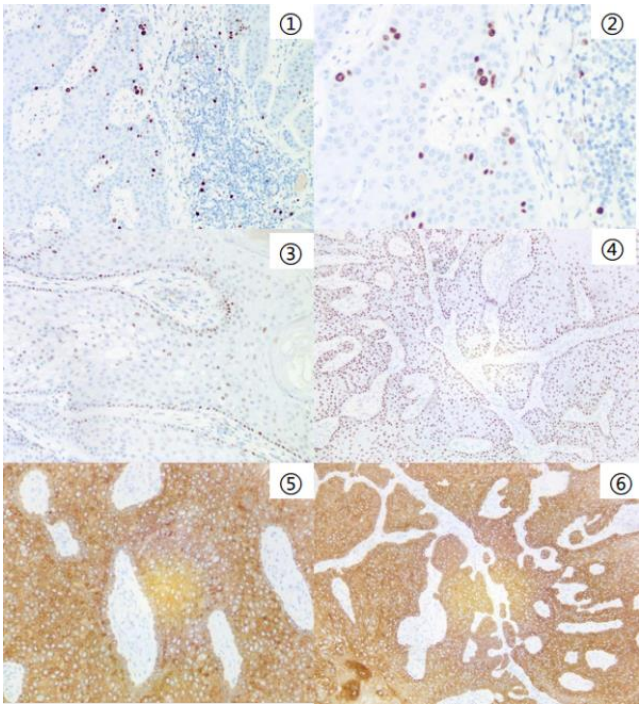

Figure 4 ①-⑥ Immunohistochemical results of postoperative pathology: ①Ki-67(+)(100×); ②Ki-67(+,5-10%)(100×); ③P53(+, 30%, wild type) (100×); ④P63(+)(100×); ⑤ CK5/6(+)(200×); ⑥CK5/6(+)(100×)

3 Treatment

Head mass resection and free flap repair under local anesthesia.

4 Discussion

The "World Health Organization (WHO) Classification of Skin Tumors" describes PTT as an infrequent benign skin tumor characterized by differentiation of the outer root sheath. It is characterized by a solid-cystic neoplasm that exhibited trichilemmal differentiation similar to the isthmus of the hair follicle [3]. In 1966, this tumor was first recognized by Wilson-Jones as an entity that had the histologic capacity to simulate SCC. The clinical manifestation of PTT is characterized by the presence of a pink to reddish, persistent, subcutaneous, cystic nodule that gradually evolves into a substantial, nodular mass with frequent irregularities in its structure. The majority of cases, around 90% of them are located as isolated lesions in the scalp. The remaining 10% of them are located in other locations. The multiple PTT is very rare [4]. The pathogenesis of this disease is not yet clear, but in some cases, human papilloma virus (HPV), chronic inflammation, or trauma may be associated with the onset of the disease [5]. Multiple studies have documented a potential correlation between the presence of tumors and infection with the HPV [5], which is consistent with the positive detection of HPV type 16 in this case. Histologically, PTT is a well-circumscribed tumor, displaying histological features such as lobulated clusters of squamous cells and keratinization resembling trichilemmal-type. In the absence of a granular layer. it presents as abrupt keratinization. The perimeter of the epithelial bands frequently exhibits the presence of a basement membrane that is thick, hyaline, eosinophilic, and Periodic Acid-Schiff stain (PAS) -positive. Histological examination enables the identification of the presence of inflammatory cells, predominantly consisting of lymphocytes [6]. The tumor occasionally exhibits characteristics reminiscent to the distal portion of the follicular outer root sheath, displaying clusters of cells rich in glycogen. The lesion may sometimes demonstrate necrosis, a foreign-body giant cell response, and calcification In this case, we conducted histopathological biopsies on multiple skin lesions on the patient's face. In the pathology, we found that the basal like cells surround the tumor clusters were arranged in the palese shape, and extended hair sheath keratosis and nearby could be seen. A large number of clear cells were seen in the tumor clusters, and keratosis and square vortex formation of individual cells could be seen [7]. The pathological results are consistent with those of other PTT cases. The disease is rarely malignant. Nevertheless, when they present clinically as rapidly growing exophytic ulcers, accompanied by histological features such as abnormal mitosis, cellular pleomorphism, cytologic or architectural atypia, and infiltrative margins, that is defined as MPTT.. Furthermore, the MPTT have the capacity to metastasis and display a very aggressive biological behavior, with a potential metastatic rate reaching up to 25% [8]. The histological examination of MPTT reveals pronounced nuclear atypia, evident cellular pleomorphism characterized by aberrant mitosis, presence of dyskeratotic cells, and infiltration margins [9]. The frequency of mitoses in PTT ranges from 0 to 4 per 10 high-power fields; however, MPTT should be suspected if there is significant mitotic activity, frequent cytonuclear atypia or aneuploidy, or unusual infiltration patterns in the cystic wall [10]. Some studies reported the coexistence of benign and malignant areas within the same tumor [11]. There has been a proposal suggesting that PTT should be

classified as a low-grade malignant carcinoma or alternatively, that this condition should be designated as proliferating follicular cystic SCC, encompassing both PTT and MPTT. In this particular instance, the presence of p53 (+, 30%, wild type) was detected using immunohistochemical analysis. Takata et al. proposed that the transformation of benign to MPTT might be attributed to the full loss of p53 tumor suppressor gene function. PTT is often confused histologically with metastatic or invasive squamous cell carcinoma, because both of them can isplay keratinocytic nuclear atypia and infiltrative growth. On pathology, the distinction between MPTT and SCC lies in the presence of trichilemmal keratinization, which is characterized by an abrupt transition from nucleated to anucleated keratinized epithelium without the presence of a granular layer.

Immunohistochemical indicators have been given much focus, including P53, Ki-67, and CD34. Several studies, it was found that an observed rise in P53 and Ki-67 staining levels when comparing instances of MPTT with cases of PTT.. In MPTT, Ki-67 expression ranged from 20% to 40%, but in PTT, Ki-67 expression was only 5% or less at the basal layer level. [12]. The expressions of P53 and Ki-67 at 30% and 5-10%, respectively, in our case sesupport the literature findings. CD34 has a crucial role as an immunological determinant in distinguishing between SCC and MPTT. Trichilemmal differentiation is shown by its expression in MPTT. In contrast, SCC do not exhibit the expression of CD34. The observed variation in staining patterns might potentially serve as a significant attribute in the elimination of SCC. Hence, the use of CD34 can enhance our ability to differentiate between MPTT and SCC, particularly in cases when diagnostic challenges arise. PTT is rare case, that may generate confusion due to its morphological similarities with MPTT and SCC. Similarly, it is important to make a clear distinction between PTT, MPTT, and SCC. The precise identification of a medical condition is of utmost importance in determining the appropriate course of therapy and prognosis of the disease.

The utilization of an immunohistochemistry panel consisting of CD34, Ki-67, and P53 has the potential to be beneficial in the process of differential diagnosis and determining morphological features.

Some scholars have classified PTT into groups I, II, and III [13]. Group I PTT are benign, do not re-occur. and histopathology shows regular contours with the surrounding tissues and mild nuclear atypia, but there is no increased mitotic activity, necrosis, or lympho-vascular invasion. The pathological description is similar to this case. Group II PTT is considered low-grade malignant, the irregular and locally invasive contours with elongation to the deep dermis and subcutaneous tissue are apparent. therefore local recurrence may occur. Group III PTT is high-grade malignant, displaying a high recurrence rate, nodal involvement, and metastatic tendency. We can observe nuclear pleomorphism, atypical mitosis, and necrosis may also be observed. Because of their level of differentiation and lack of metastasis [13]. In our case, we presented are classified as Group I PTT.

The presence of dyskeratotic cells and the complicated architecture of PTT can lead that it may simulate a malignancy, specifically squamous cell carcinoma SCC. Therefore, it is crucial to make a meticulous differentiation between PTT, SCC, and other tumours using histology and imaging techniques in order to achieve accurate diagnosis. According to Brownstein and Arluk, the significant cytologic atypia alone in noninfiltrative lesions does not justify classifying them as malignant. [14]. Metastasis to lymph nodes and distant sites has been observed in cases with MPTT. The preferred treatment strategy for both PTT and MPTT involves performing a wide resection of the tumour, ensuring a conservative margin of normal tissue of 1 cm, and implementing diligent follow-up. The treatment modalities of chemotherapy and x-ray therapy have been employed in the management of MPTT [15]. The extent of locoregional expansion can be evaluated, and metastatic involvement can be ruled out, using imaging techniques including CT and PET scans. Since few cases have been documented in the literature, there is currently no definitive recommendation; radiation therapy for local recurrence or chemotherapy for metastatic disease have both been mentioned as potential treatments [16]. However, it is worth noting that adjuvant chemotherapy does not demonstrate superiority over appropriate surgical intervention [15]. In a review of 30 cases of MPTT, 5 patients had nodal metastasis, and 3 patients had distant metastasis. In a clinicopathologic analysis of 59 cases of PTT, 1 patient (1.7%) experienced a local recurrence 8 months after the excision [9].

The use of a qualified and specialized pathologist is occasionally important, and it is recommended that all scalp cysts be forwarded for histological examination. When seeing an increase in size of a persistent scalp nodule, it is important to do an investigation for PPT or

MPPT, since the potential for malignant transformation should not be disregarded. It is important to do regular follow-up examinations on these individuals in order to promptly detect any potential recurrence or degeneration. In this case, we performed head tumor resection and free flap repair on the patient under local anesthesia. After 3 months, we followed up the patient and found no new skin lesions, no increase or metastasis in skin lesions.

5 Conclusion

PTT is uncommon adnexial tumors that need to be diagnosed and treated using a multidisciplinary strategy. Correlating the tumor's histological characteristics with its clinical manifestation is difficult [17]. Increased case reports and comparisons of the long-term outcomes of various treatment methods are required in order to develop treatment algorithms with a suitable degree of evidence. Close clinical follow-up is the most efficient method of early metastasis and recurrence detection, until these happen.

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