

Case Report

Anal malignant proliferative trichilemmoma: report of a rare case with review of literature

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Abstract: Trichilemmoma is a rare type of benign cutaneous neoplasm, which derives from outer sheath of hair follicle. It barely develops malignant progression and has rarely been reported in anal cancer. In this article, we report a case of a 73-year-old woman who presented to the outer-patient department with complaints of a ruptured and longstanding anal phyma. All the appearances were atypical. Blood routine examination showed that neutrophilic granulocyte percentage was elevated and suggest it was a simple inflammation response. No evidence of malignancy was detected upon the laboratory examinations. Then we performed an abscess incision drainage for the patient. A few days later, the biopsy pathological report suggested the specimen is a malignant proliferative trichilemmoma. We decided to perform a wide local excision instead of an extended radical operation in order to preserve anus. After the surgery, we chose not to give chemoradio-treatment for fear of side effects and complications. Careful follow-up indicates that peri-anal malignant proliferative trichilemmoma may have a good prognosis and our treatment is a good choice for the patients with this tumor. Because of the low occurrence rate of anal cancer, especially malignant trichilemmoma, any clinical manifestation and experience are valuable. On one hand, our case may help to take the consideration of the diagnosis of malignant trichilemmoma in case of longtime-suffered peri-anal mass, on the other hand it propose a different treatment method from other anal cancers for clinical doctors.

Keywords: Malignant trichilemmoma, anal cancer, pathology, local excision, prognosis

Introduction

Carcinoma of the anus is not a commonly-reported malignant tumor. It only comprises about 4% of all anorectal malignancies and 1.5% of gastrointestinal malignancies. Broadly, anal cancer can be classified into anal canal cancer and anal margin cancer, which presents 75% and 25% respectively. The anal canal cancers (ACC) are more common, and 75% of these cancers are squamous cell carcinoma (SCC). The anal margin cancers (AMC) behave like skin lesions occurring in any other cutaneous site and are staged accordingly. SCC is also the commonest type of AMC, it accounts for almost one-fourth to one-third of all SCC of the anus [1]. Other types of anal margin cancers are extremely rare, including perianal Paget's disease, basal cell carcinoma, malignant melanoma, giant condyloma acuminatum and perianal malignant proliferative trichilemmoma.

Trichilemmoma is a rare benign cutaneous neoplasm which derived from the outer sheath of hair follicle, and 90% occurs on the scalp and the back, lesion occurs around anus is extraordinary uncommonly reported. In addition, trichilemmoma is usually a solitary lesion, multifocal appearance of trichilemmoma is very infrequent which is more likely associated with Cowden syndrome resulted by loss-of-function mutations in PTEN [2]. The first manifestation of trichilemmoma is always nonspecific. There are evidences showing that indistinct facial nodular masses presented for years without any uncomfortableness may possibly be considered as trichilemmoma.

It was also because of its asymptomatic appearance, only histological and pathological findings are specific of this tumor. Here we report a case of a 73-year-old female who had a peri-anal phyma for more than ten years. She was diagnosed as peri-anal abscess previously. But

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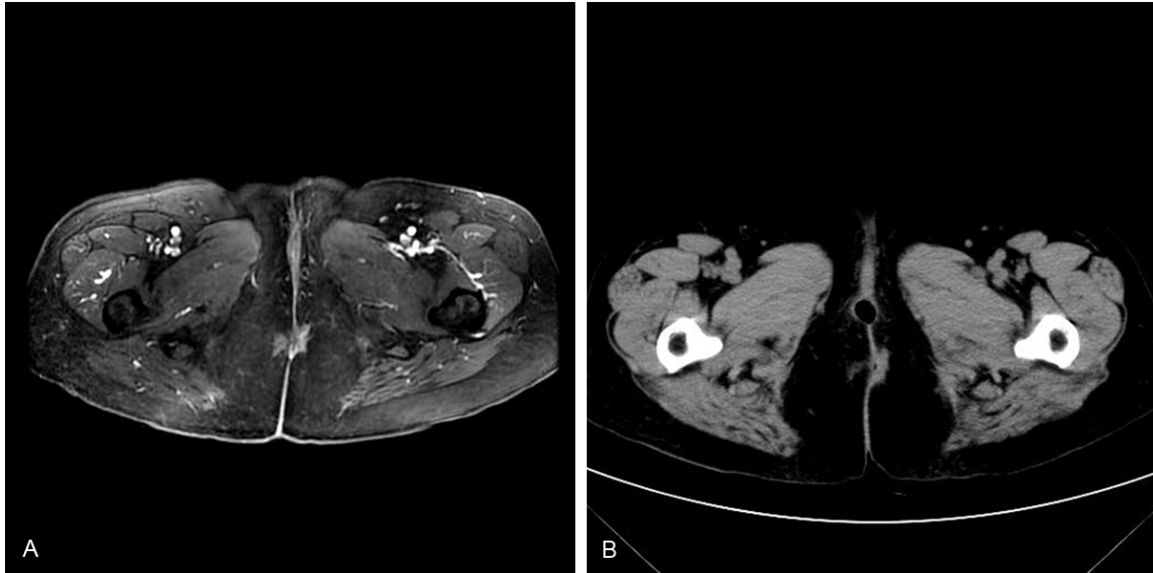


Figure 1. A. The MRI scanning performed before the second operation showed an abnormal high intensity on T2-weighted imaging around the anal canal. B. The Pelvis contrast-enhanced computed tomography (CT) showed high density lesion around the anal canal before the second operation.

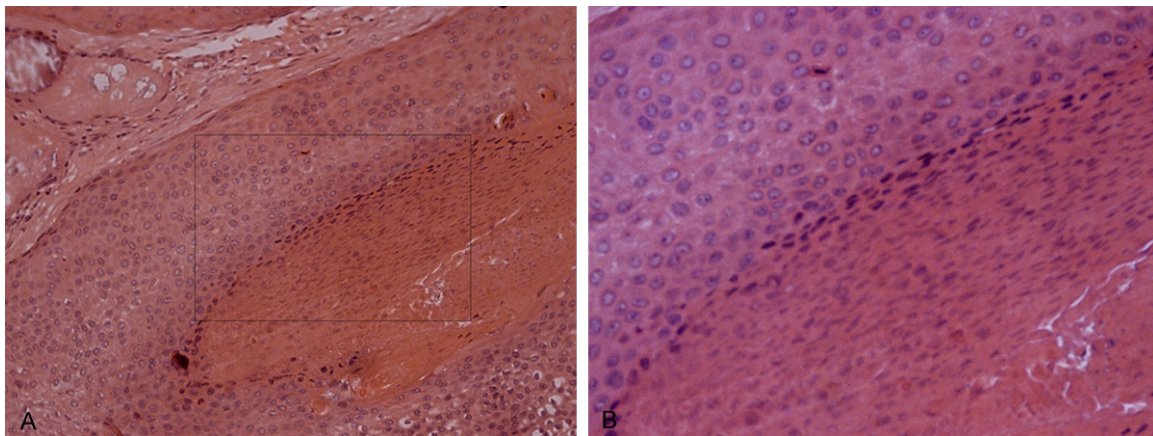


Figure 2. A. A photomicrograph of H&E staining (20 ×) showed the mass is surrounded by lobules of epithelial cells. It resembles the outer root sheath of a hair follicle including glycogen-rich, clear cytoplasm. There are heteromorphic cells palisading around it and indicated that the phyma was a malignant proliferative trichilemmoma. B. Enlarge the framed image (40 ×).

biopsy exam after the surgery reminded a malignant proliferative trichilemmoma.

Case presentation

A 73-year-old female visited Xinhua Hospital of Shanghai Jiaotong University with a complaint of an aching ruptured perianal phyma. According to this patient, she had had this phyma for more than ten years and never felt any uncomfortable. The 3 cm-in-diameter phyma was round, and seemed like subcutaneous. It was

smooth on the surface and no crusting. There was no chromatinosis or hair growth near the phyma. During the decades, she had got no pruritus and pain, and never has been to a doctor for the phyma. One week before the patient came to the outpatient department, the phyma ruptured and began to ooze with pyogenic fluids. This continued for several days and the wound had not close up. The patient had no history of diabetes mellitus, infectious diseases, smoking, alcoholism, toxin exposure, nutrition deficiency or medication use. She had no sig-

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nificant family history of gastrointestinal tumor, and other hereditary diseases.

Upon the physical examination, the only notable finding was a 3 cm × 2 cm painful mass at the direction of two o'clock in lithotomy position. Skin around the anal was red and swollen. Laboratory studies showed that neutrophilic granulocyte percentage elevated to 75% and leukocyte count was normal. The levels of cancer-antigens 125, 19-9, 15-3, CEA were all in the normal range. All these symptom simply indicated a peri-anal abscess.

Soon we performed an abscess incision drainage and biopsy specimen, then let the patient go home. Several days later, pathological exam showed that the mass is surrounded by lobules of epithelial cells microscopically. These features resemble the outer root sheath of a hair follicle including glycogen-rich, clear cytoplasm. There are heteromorphic cells palisading around the root sheath and indicated that the phyma was a malignant proliferative trichilemmoma (**Figure 2**). Thus we asked the patient to return to our hospital for further treatment.

In order to realize the current status of the tumor, we performed imaging studies for next step operation. The magnetic resonance imaging (MRI) showed an abnormal high intensity on T2-weighted imaging around the anal canal (**Figure 1A**). Pelvis contrast-enhanced computed tomography (CT) showed high density lesion near the previous injuries (**Figure 1B**).

Based on the imaging and pathological studies, a wide local excision was performed. The new surgical margin was 3.5 cm in depth, and 1.5 cm outside the original incision. Biopsy specimen reported that our patient was with a negative circumferential resection margin. After post-operative discussion, we decide not to give the patient chemoradiotherapy. We provided a routine treatment and the wound surface was covered with asepsis gauze. Finally, we ask the patient to follow up every 3 months in order to take care of her closely. We perform a chest X-ray, abdomen B-ultrasound examination and blood tumor marker test every three months, electronic colonoscopy and MRI scan every six months. After one-year's follow-up, the patient is recovering well and no signs indicate recurrence.

Discussion

All anal cancer can be broadly classified into anal canal cancer and anal margin cancer, which account for about 75% and 25% respectively. In both of them, the overwhelming majority is squamous cell carcinomas [1]. In these years, due to the new identifiable risk factors, such as increasing risk of HIV, HPV infection from promiscuous sexual activities, the incident of anal cancer has shown a stable increasing trend in HIV/HPV-positive patients worldwide [3]. On the other hand, mutations of tumor suppressor genes inside our body, such as p53, APC, may contribute to the tumorigenesis of anal cancer in HIV/HPV-negative patients. In epidemiology, the other risk factors of anal cancer includes smoking, race, Crohn disease [1]. These antecedent events are all closely related to the mechanism of anal cancer. Pathological diagnosis of anal cancer depends on cytology. According to a worldwide survey, 53% of clinics require abnormal anal cytology prior to performing high-resolution anoscopy (HRA) in asymptomatic patients in order to confirm pathological type [4]. The perianal malignant proliferative trichilemmal tumor belongs to anal margin cancer. It looks like a skin lesion and is rarely-reported. Actually, trichilemmal tumor is a kind of adnexal neoplasms. The proliferative trichilemmal tumor is an uncommon benign neoplasm derived from outer sheath of hair follicle [5]. It seems to present a gender-related and pathogenic site-limited manner. There have been several lines of evidence that suggest trichilemmoma should be considered in the differential diagnosis of any indistinct facial papule [6]. 84% of the 50 patients reported by Brownstein and Arluk were women, 90% of the lesions were located on the scalp, with the rest on the back, forehead, wrist, and chest [7]. Even if in worldwide, the case reported were most women. The lesion was almost invariably solitary, multiple lesions occurred on one person were more infrequent [8]. The clinical manifestations are also atypical and asymptomatic. Patient's chief complaint may be a subcutaneous cystic nodule or a slowly growing nodular mass that have been presented for years. Thus, cytological exam is very important to diagnose and stage this disease. Saida and her colleagues classified the oncological development of the trichilemmal type of tumor into three stages: 1) trichilemmal cyst, adenomatous

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stage; 2) proliferating trichilemmal cyst, epitheliomatous stage; and 3) malignant proliferating trichilemmal cyst, carcinomatous stage [9].

In order to clarify the diagnosis, histopathological examination is the only specific method to this tumor. Due to the presence of heteromorphism and mitotic figures, trichilemmoma may be confused with squamous cell carcinoma. Other differential diagnosis of this rare tumor include basal cell carcinoma, desmoplastic trichoepithelioma and desmoplastic trichoblastoma, clear cell hidradenoma, other follicular tumors such as inverted follicular keratosis and tumor of follicular infundibulum [10].

Detail distinctions still rely on the examination of pathology. The trichilemmal tumor mass is surrounded by lobules of epithelial cells microscopically. These features resemble the outer root sheath of a hair follicle including glycogen-rich, clear cytoplasm and peripheral palisading. Malignant proliferating trichilemmal tumors and proliferating trichilemmal tumors are histopathologically similar, but the former may have obvious superficial ulcer and necrotic tissues and the partial tumor cells may have an increase of cell heteromorphism, mitotic activities and the amount of clear cell.

Trichilemmoma may differentiate mainly towards two directions: infundibular keratinization and proliferation of the outer root sheath with undifferentiated and pluripotent characteristics [11]. Desmoplastic trichilemmoma (DT) is a variant of trichilemmoma, characterized by a densely sclerotic stroma, surrounded by lobules of epithelial cells with features of outer root sheath differentiation, including glycogen-rich, clear cytoplasm and peripheral palisading. In the central part of the tumor, irregular cords of epithelial cells entrapped in the desmoplastic stroma were found. In DT, the tumor epithelium shows CD34 immunostaining [12] and stains with anti-cytokeratin antibodies while the stromal cells were positive with vimentin. The centro-tumoral extracellular matrix showed a diffuse and intense positivity for type I collagen and tenascin, whereas stains for laminin and type IV collagen were uniformly negative [13]. All of these may be of great value in the differential diagnosis with other anal cancer.

The imaging studies are also essential for the diagnosis of malignant proliferating trichilemmoma

including endoanal ultrasound, CT scan, MRI scan and PET/CT scan etc. Most practice guidelines, including those from the NCCN, suggest a DRE, anoscopy chest imaging, and a CT or MRI of the abdomen and pelvis to stage and assess anal cancer. It was reported that MRI was more sensitive than CT in detecting primary anal canal lesions [14]. MRI can diagnose rectal wall laminar structure and show the details of the relationship of the tumor with the meso-rectal fascia and surrounding organs. MRI was also superior to CT and PET/CT in detecting lymph node involvement and bowel wall invasion of the tumor [15]. MRI scan is also a powerful means for differentiating trichilemmal tumor from other tumor.

The primary treatment modalities for anal cancer include surgical excision, immunotherapy, chemotherapy and radiotherapy. A worldwide survey of anal cancer shows that internal high-grade anal intraepithelial neoplasia (AIN) is most often treated with infrared coagulation (61%), whereas external high-grade AIN is most commonly treated with imiquimod (49%), a kind of immuno-regulator [4]. There are also evidences indicate that the use of radiotherapy with concurrent 5-FU and MMC as standard treatment for anal cancer can decrease colostomy and local failure rate [16]. But to malignant proliferative anal trichilemmoma, due to the small number of published cases, the efficacy of either treatment is not evaluated. In order to preserve organ, researchers globally have established non-surgical treatment with combined chemo radio therapy as the standard method of managing anal cancer. However, toxicity from combined radiotherapy and chemotherapy for anal carcinoma is significant. The side effects include dermatitis, gastrointestinal toxicity, sexual dysfunction, proctitis, tenesmus, anal stenosis and bladder dysfunction. As such, a large amount of patients still seek for surgical management in the end. Broadly, surgical treatments divide into three main management: salvage operations, local excision and miscellaneous surgical interventions [1]. A salvage abdominoperineal resection is proved to achieve long term survival. Even in today, salvage abdominoperineal resection is required in almost 30% anal cancer. Wide local excision can be used on well differentiated T0 and early T1 tumors. The advantage of local excision is noticeable, the wound is small and the peripheral damage is mild, but residual tumor may

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probably cause recurrence. Thus, a reliable follow-up must be taken. In this case, we demand our patient to schedule a follow-up every three months. We perform a chest X-ray, abdomen B-ultrasound examination and blood tumor marker test every three months, electronic colon scope and MRI scan every six months. After one-year's follow-up, the patient is recovering well and no signs indicate recurrence.

In conclusion, the diagnosis of malignant proliferating trichilemmal tumor should be considered in cases of longstanding cystic and nodular lesions and histopathological examination. Our case may suggest that peri-anal malignant proliferative trichilemmal tumors can be treated by simple wide local excision. After the operation, chemoradiotherapy may not be necessary for these patient for fear of a series of side effects and complications. Our careful follow-up provides detail data of our treatment's effect and indicates that this tumor seems to have a relatively good prognosis. Simple wide local excision is a good choice for the patient both to achieve organ preservation and functional recovery.

Disclosure of conflict of interest

None.

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