

Case report

Pilomatrix carcinoma of the lower extremity: A rare case report and literature review

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ABSTRACT

Introduction: Pilomatrix carcinoma (PC) is a rare skin malignancy of the hair follicles matrix that tends to be locally aggressive with 10–16 % risk of metastasis mostly to the pulmonary and lymphatic system. There are no clear protocols for the management of PCs, however surgical intervention with clear margins has been highly considered in PC management to decrease risk of recurrence.

Case presentation: A 40 year-old male patient presented to our clinic to evaluate an asymptomatic, slow-growing nodule localized on his left thigh. A CT scan revealed a well-defined, enhanced lesion with microcalcification. “En bloc” surgical resection of the lesion was performed and histopathology confirmed the diagnosis of pilomatrix carcinoma.

Clinical discussion: Given its rarity, there are no definitive guidelines regarding PC treatment. However, surgical intervention with clear margins including wide local excision or Mohs micrographic surgery has been highly considered. In our case, wide excision of the lesion with clear margins was performed with no evidence of recurrence one year later.

Conclusion: Given the local aggressive nature of PC, appropriate surgical intervention is essential in decreasing the risk of recurrence. Wide excision with clear margins has been proposed to decrease the risk of recurrence. Additionally, total-body skin examination should be done 2–3 times annually to evaluate for recurrence or metastasis.

1. Introduction

Pilomatrix carcinoma (PC) is an extremely rare, locally aggressive, malignant skin tumor arising from aberrant proliferation of the hair follicles matrix [1]. PC arises de novo or through malignant transformation of a pre-existing pilomatricoma [2]. It most predominantly affects male with a male-to-female ratio of 1.3:1 and demonstrates a bimodal age distribution [1,2]. PC mostly arises in the head and neck, and usually presents as a nodular, violaceous, firm, painless lesion that grows rapidly with overlying ulceration [1,3]. Metastasis occurs in 10–16 % of cases mostly to the pulmonary and lymphatic system [2,4]. Dermatoscopy can be helpful in recognizing it, however histological examination remains the gold standard for diagnosis. Although there are

no gold standard protocols for the management of PCs, most studies recommend wide local excision with clear margins, with or without radiotherapy [1,3,5]. To our knowledge, 52 PC cases have been reported in literature in the last 10 years including only 4 reported cases in the lower extremities. Here, we report the case of a 40-year-old man who presented for the evaluation of an asymptomatic, slow-growing, firm nodule with an overlying ulcer on his left thigh. This report was written in accordance with the Surgical CAse REport (SCARE) criteria [6].

2. Case presentation

We report the case of a 40-year-old Caucasian male patient, with a past medical history of familial adenomatous polyposis, who presented

Abbreviations: PC, Pilomatrix carcinoma; CT, Computed tomography; LEF, lymphoid-enhancing factor; Bcl-2, B-cell lymphoma; BAX, Bcl-2-associated X protein; CD, Cluster of differentiation; MMS, Mohs micrographic surgery.

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to our hospital to evaluate an asymptomatic, slow-growing nodule localized on his left thigh. Physical examination revealed a solitary, erythematous, firm nodule, 5 cm × 4 cm in diameter, without locoregional lymphadenopathy on the lateral third aspect of the left proximal thigh with an ulcer with scarring on the lesions surface. For further evaluation, Computed tomography scan (CT) with and without contrast was done, revealing a well-defined, enhanced lesion measuring 3.7 cm × 3.5 cm × 1.7 cm in size, located in the subcutaneous layer of the lateral aspect of the left thigh, with the presence of microcalcification within the lesion (Fig. 1A, B). Our differential diagnosis included complicated skin appendage lesion, sebaceous cyst and pilomatrixoma. Surgical excision was performed through an elliptical skin incision, followed by an “en bloc” resection of the lesion from the surrounding subcutaneous tissue. The postoperative course was uneventful. On pathological examination, an ellipse of skin with central friable mass measuring 4.5 × 3.5 × 2 cm was identified. Microscopic examination showed a dermal encapsulated, partially cystic, proliferation, composed of peripheral, monomorphous, basophilic cells and elements with eosinophilic cytoplasm and empty nuclear space, so-called “shadow-cells” (Figs. 2A, 2B). Numerous atypical mitotic figures were seen with areas of necrosis (Fig. 3). Calcifications and occasional multinucleated giant cells were also encountered.

3. Discussion

Pilomatrix carcinoma (PC) is a rare, locally aggressive neoplasm originating from follicular matrix cells. In the last 10 years, there have been nearly 52 reported cases of PC worldwide [1]. It presents in a bimodal prevalence with the first peak occurring within the first three

decades and the second occurring between sixth and seventh decades of life with male-to-female ratio of 1.3:1 [1,2]. 62 % of the reported cases were found in the head area and only 8 % reported in the lower extremities [1]. PC was reported more commonly on the left side throughout the body, except in the lower extremities, where it has been reported on the right side [3]. In most PC cases, the tumor remains localized. However, in 10–16 % of cases, metastasis occurs mostly affecting the regional lymph nodes, lungs and bones, and in 60 % of these cases it arises in men [2,4].

Both de novo PC development and the malignant transformation of pre-existing pilomatrixomas have been found to share a common CTNNB1 gene mutation suggesting a common pathogenesis [2,3,7]. CTNNB1 gene is the responsible gene for encoding β-catenin; a cell-signaling protein that is considered a central component of the WNT signaling pathway [2,8]. Cytoplasmic β-catenin translocates to the nucleus where it interacts and activates T-cell factor/lymphoid-enhancing factor 1 (LEF1) transcription complex which has roles in both follicular morphogenesis and hair cell differentiation [2]. Exon 3 of CTNNB1 is a key exon that encodes the phosphorylation site of GSK-3β which in turn activates the degradation of β-catenin when the WNT ligand is absent [8,9]. Mutation in this gene leads to constitutive activation of the Wnt/β-catenin resulting in nuclear accumulation of β-catenin, which could be used as a surrogate marker of CTNNB1 mutation [2].

The two hit hypothesis has been proposed in PC, with the first mutation resulting in initial β-catenin accumulation within the nucleus resulting in the formation of pilomatrixoma in young patients, and the second mutation hits tumor suppressor and proto-oncogenes, conveying malignant potential and the formation of PC in older patients [2]. Considering the tendency of these tumors to arise on the neck and head,

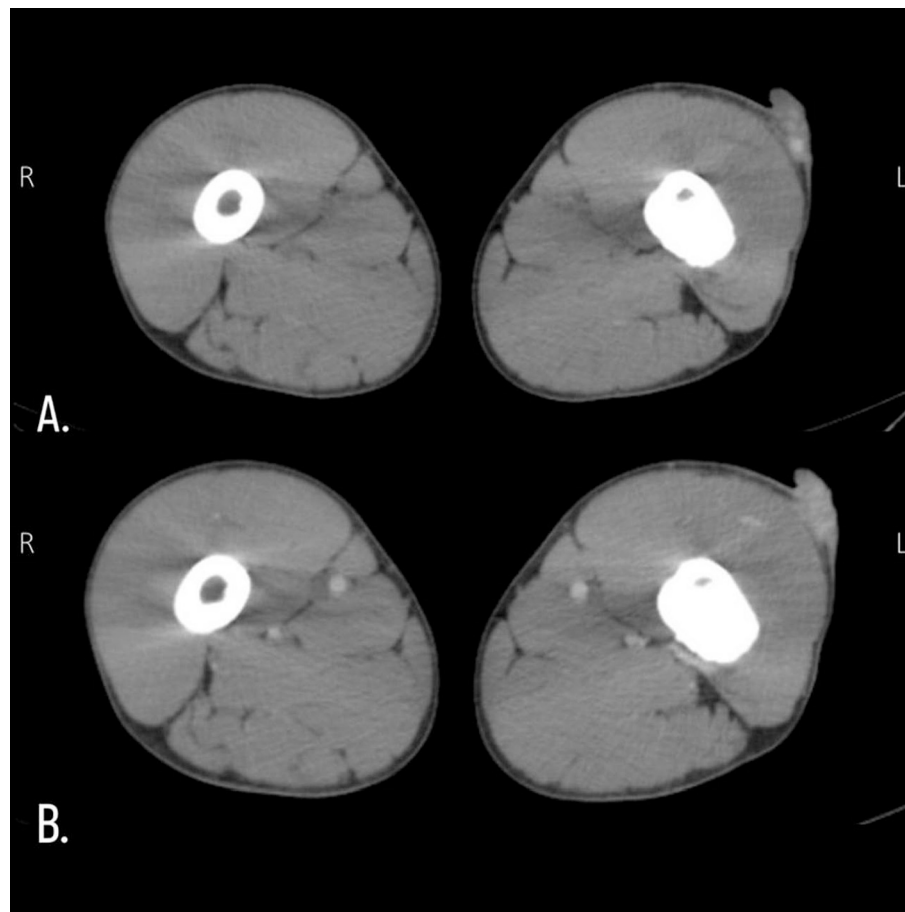


Fig. 1. A. - Non-contrast CT imaging displaying a pilomatrix carcinoma located on the lateral aspect of the upper left thigh, notable for the presence of microcalcifications. B. - Contrast-enhanced CT scan (IV contrast) highlighting enhancement of the lesion.

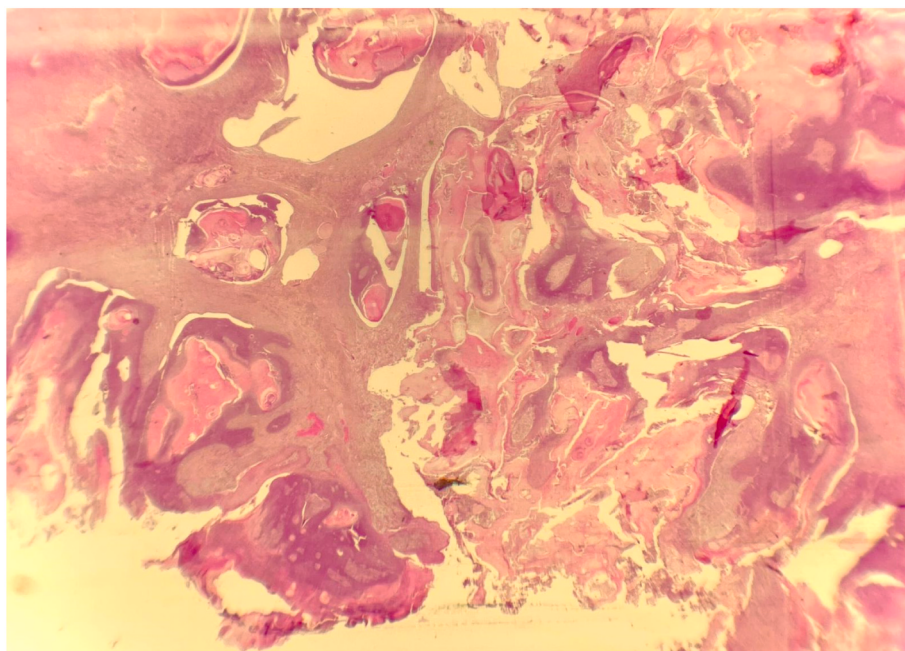


Fig. 2A. H&E: Low power of the lesion shows lobulated dermal neoplasm composed of islands of basaloid cells exhibiting abrupt keratinization along with Ghost/shadow cells.

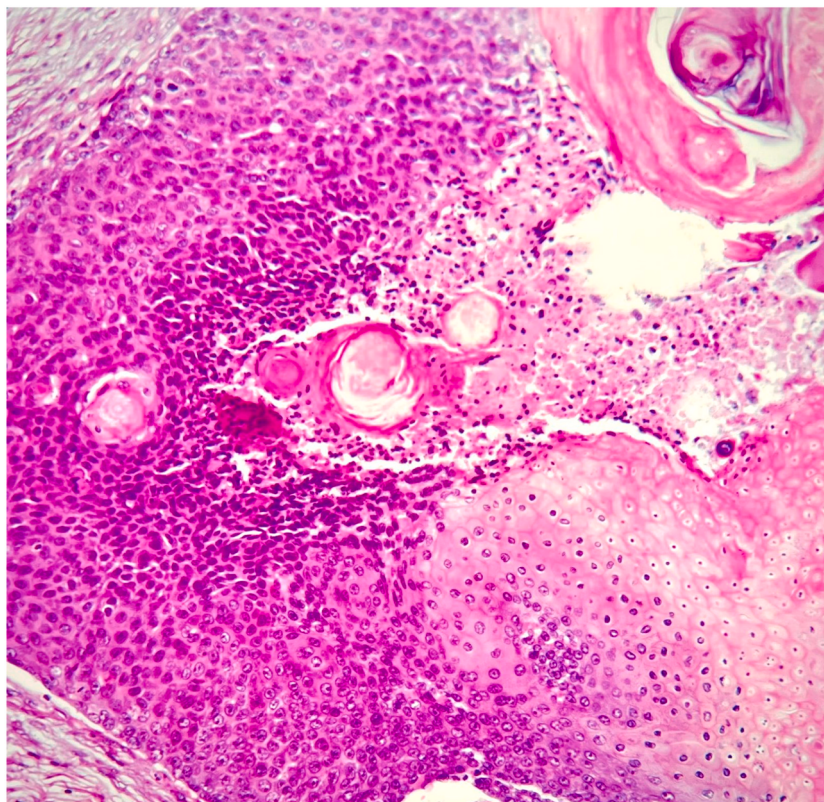


Fig. 2B. H&E 20X: Basaloid tumor cells with “ghost cells” and keratinization.

photodamage via ultraviolet light has been proposed to supply the requisite second mutation [2].

PC usually presents as a single, firm, painless dermal or subcutaneous lesion associated with violaceous discoloration and ulceration of the overlying skin, the latter being considered as a significant indicator of malignancy [1,3]. The malignant tumor size ranges from 0.5 to 15 cm.

The rapid speed of growth is more indicative of malignancy than the overall size. PC is frequently misdiagnosed due to their nonspecific manifestations; a recent review of the 52 PC cases has stated that out of the 52 cases, none was initially diagnosed as PC. The most frequently implicated differential diagnoses include epidermal cyst, basal cell carcinoma, amelanotic melanoma and pilomatrixoma [1].

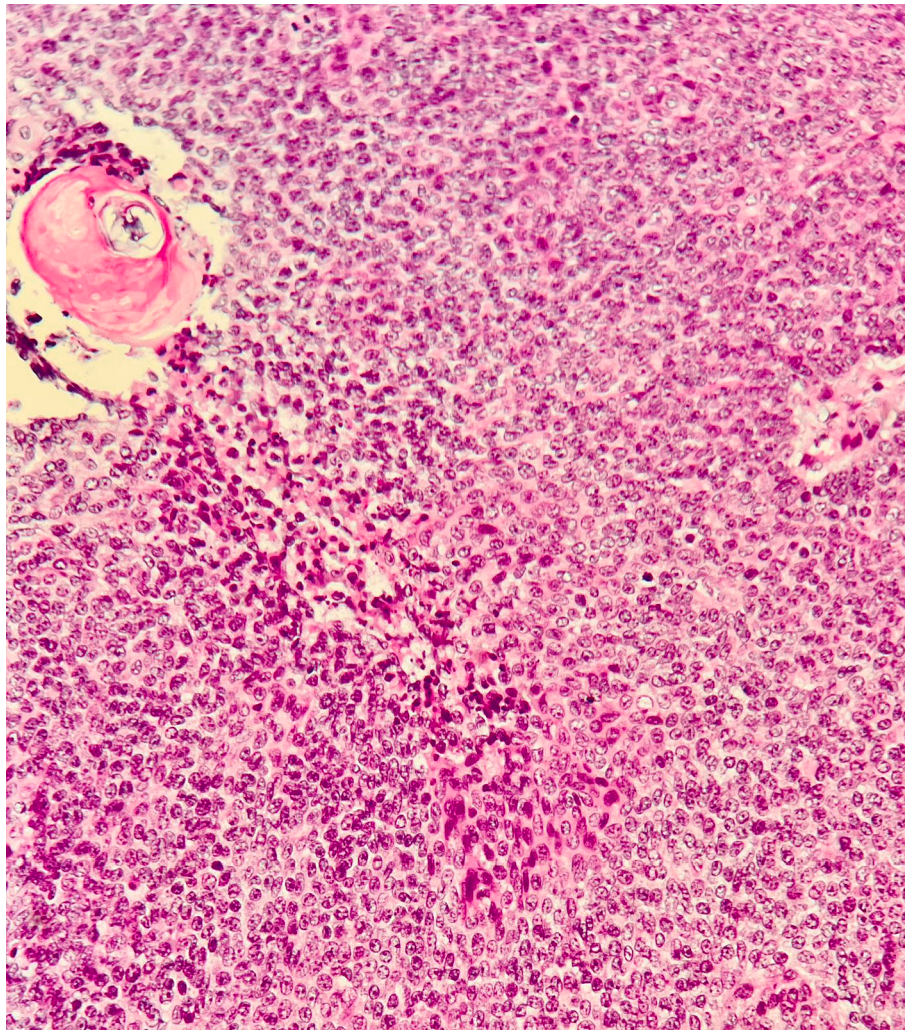


Fig. 3. H&E 20X: Basaloid tumor with frequent mitosis, karyorrhexis and foci of central necrosis.

Excised tumors frequently appear as an asymmetric, encapsulated, cystoid lesion, with an overlying grayish surface [2]. Histologically, dermal proliferation of basaloid cells predominates. The basaloid cells are arranged in irregularly shaped nests and bands, containing small amounts of clear cytoplasm [2,10]. The nuclei of the basaloid cells appear slightly atypical with pleomorphic features, and high mitotic and apoptotic index [3]. Eosinophilic ghost or shadow cells, calcification and necrotic debris are scattered among cell types [10]. The presence of ulceration and infiltration into adnexal structures substantially supports the diagnosis, with some studies correlating it to the degree of malignancy [2]. Typically, a dense desmoplastic stroma containing lymphohistiocytic infiltration is found surrounding the tumor capsule [2,11].

A variety of immunohistochemical utilized profiles could be used to support, not confirm, the diagnosis of PC, by targeting different proteins, including β -catenin, Ki-67, p53, CK 14, LEF1, B-cell lymphoma 2 (Bcl-2), Bcl-2-associated X protein (BAX), and cluster of differentiation (CD)44 [2,3]. In contrast to tumors with focal germinative matrix cell nests such as basal cell carcinoma and trichoblastoma, both pilomatrixoma and PC show LEF1 and β -catenin pan-cellular staining [2]. Although LEF1 and β -catenin help narrow the differential diagnosis, they do not differentiate between benign and malignant variants. However, low levels of β -catenin suggest that metastasis is more likely. The CD44 isoforms have been found to be an indicator of metastatic potential, whereas a high BAX to Bcl-2 ratio indicates good prognosis and even high sensitivity to radiation [12].

Given its rarity, there are no definitive guidelines regarding

treatment protocols. Most studies recommend local excision with margins ranging from 5 to 30 mm, as it has the lowest risk of recurrence. However, some studies have reported metastasis equivalently in both tumors excised using both simple and wide approaches [1]. Mohs micrographic surgery (MMS) approach offers the highest cure rate, with superior margin control preserving healthy tissue and improving cosmetic outcomes [3]. When surgery is not possible or does not offer clear margins, radiotherapy could be extremely effective in limiting disease progression. Adjunctive radiotherapy could be effective in recurrent or metastatic cases [5]. Chemotherapy has also been proven to be effective [3].

The overall prognosis and recurrence of PC is dependent on identifying the suspicious lesion and the initial treatment approach. Local recurrence occurred in 50–83 % and 18–23 % of cases treated with simple excision and wide excision, respectively [5,11]. In 10–16 % of cases metastases occurred, mostly affecting the pulmonary and lymphatic system, followed by local bone infiltration, skull bone, brain and parotid gland [2,3,11]. Due to the high risk of local recurrence and metastasis, patients should have a total-body skin examination 2–3 times annually.

4. Conclusion

Pilomatrix carcinoma is an extremely rare malignant tumor with a high rate of metastasis and recurrence. PC is rarely suspected clinically. Given its rarity, there are no well-defined treatment protocols; however,

surgical excision with wide margins remains the best therapeutic option to avoid recurrence, and regular follow-up should be offered. Further studies should be done to give a better awareness and establish a clearer standard of management of this rare tumor.

5. Methods

Work has been reported in line with the SCARE criteria [12].

Ethical approval

This case report is exempt from ethical approval in our institute.

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Author contribution

AA, AO, and YD: Literature review and manuscript preparation. MM and AA: Manuscript review and editing IB: Pathology part and diagnostics.

Guarantor

Dr. Mohammed Maree.

Research registration number

None.

Informed consent

Written consent was not obtained due to distance between the

patient's residential city and the hospital.

Verbal informed consent on the phone was obtained from the patient for their anonymized information to be published in this article.

Conflict of interest statement

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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