Concurrent Pilomatrix Carcinoma and Diffuse Large B-Cell Lymphoma

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ABSTRACT

Pilomatrix carcinoma is a rare cutaneous tumor derived from follicular matrix cells. It may arise de novo or from a malignant transformation of a pilomatrixoma. The latter process has been associated with impaired immune system surveillance of the host caused by UV radiation or the onset of an underlying malignant neoplasm. We report a case of a 58-year-old man presenting with a long-standing pilomatrix carcinoma on the inner right leg after 10 years of repeated curettage of the lesion, concurrent with a high-grade B-cell lymphoma on the same extremity. We describe a rare association which highlights the necessity of close follow-up of patients with long-standing malignant skin tumors.

Keywords: Lymphomas; Long-standing skin lesion; Pilomatrix carcinoma; Pilomatrixoma; Skin tumors

INTRODUCTION

Pilomatrix carcinoma or malignant pilomatrixoma, first described in 1980 by Lopansri and Mihm as the malignant variant of pilomatricoma [1], is a rare cutaneous tumor derived from follicular matrix cells. Up to 50% of pilomatrix carcinomas are located on the head, followed by other locations such as lower extremities [2]. It has a high tendency to grow through deep planes, which makes it locally aggressive, with high rates of local recurrence. Less frequently it infiltrates lymphovascular structures. Fewer than 130 cases of pilomatrix carcinoma have been reported in the literature, the vast majority as case reports. In addition to its rarity, pilomatrix carcinoma is often clinically misdiagnosed as a sebaceous cyst or...
other common skin tumor, which may delay tumor resection [2]. Pilomatrix carcinomas may arise de novo or from a malignant transformation of a pilomatrixoma. In the latter case, it is not clear what triggers the malignant transformation, but it has been reported to be related to an alteration in the immune system surveillance of the host caused by UV radiation or the onset of an underlying malignant neoplasm [3].

We report, for the first time, a case of a patient diagnosed with pilomatrix carcinoma after 10 years of a long-standing lesion in the right lower extremity, concurrent with a high-grade B-cell lymphoma on the same extremity. In our patient, whether this tumour developed de novo or transformed from its benign counterpart, pilomatrixoma, remains unclear.

CASE REPORT

A 64-year-old healthy man presented with a 10-year history of a painless exophytic lesion on his inner right leg, treated at home by repeated curettage. The patient was asymptomatic and had no significant medical or surgical history. Physical examination revealed an exophytic ulcerated mass, adhered to deep planes, of 6.5 cm greater dimension in the inner part of the lower right leg. A swollen subcutaneous mass in the right groin was also present, clinically suggestive of positive lymph nodes. The lesion was surgically removed with a 1-cm margin and closed with a split-thickness skin graft. The histopathological study showed a nodular proliferation of basaloid cells from the dermis to subcutaneous fat tissue, with poor circumscription. The lesion was ulcerated, and revealed an invasive tumor containing irregular nests (Fig. 1). The central part showed the transition of basaloid cells into shadow cells. The anaplastic basaloid cells in the periphery were proliferating with numerous mitoses, and exhibited an infiltrative growth with extensive areas of necrosis. The tumoral nests were surrounded by dense desmoplastic stroma, containing a variable amount of inflammatory infiltrate composed mainly of lymphocytes (Fig. 2). The surgical margins on microscopic examination were negative.

A lymph node dissection of the groin was performed on a second surgery. Lymph nodes showed complete effacement of the nodal architecture and proliferation of monomorphic large cells with oval or cleaved nucleus, with vesicular chromatin and several nucleoli. Immunophenotypic analysis demonstrated CD20-, CD79α-, BCL-6- and BCL-2-positive cells, confirming the diagnosis of diffuse large B-cell lymphoma (DLBCL). The remainder of the parenchyma constituted a mixed population of B and T cells of normal appearance.
Positron emission tomography–computed tomography (PET-TC) and bone marrow biopsy revealed no systemic disease. The patient was treated with R-CHOP chemotherapy for his lymphoma. After 10 months of treatment, his general condition was good; no abnormalities were found on clinical examination, and there was no evidence of any disease on the last PET-CT. Clinical examination was also scheduled by his dermatologist every 6 months.

Informed consent was obtained from all patients for being included in the study.

DISCUSSION

Because specific histopathological diagnostic criteria for pilomatrix carcinoma have not yet been described, a diagnosis of malignancy relies on certain microscopic features. Pilomatrix carcinomas are poorly circumscribed lesions with asymmetric growth, central necrosis and ulceration; they are usually composed of ill-defined nodules of pilomatrical cells with foci of central necrosis. Two types of cells are commonly found, basaloid cells and “shadow” or “ghost” cells. Basaloid cells have hyperchromatic and pleomorphic nuclei with prominent nucleoli and numerous atypical mitoses. Ghost cells contain pale eosinophilic cytoplasm, faint degenerated nuclear outlines and no nuclei, and the transition between basaloid and ghost cells is mostly abrupt. In all cases, tumor nodules are surrounded by dense desmoplastic stroma containing a variable amount of inflammatory infiltrate, comprising mainly lymphocytes, plasma cells and histiocytes [4–6]. Multinucleated giant cells, dystrophic calcifications and melanophages can also be observed in the periphery. Occasionally, infiltration of blood vessels or lymphatics may also be found.

Histological differential diagnosis between pilomatrix carcinoma and its benign counterpart can be very challenging [12]. In addition to the rarity of pilomatrix carcinoma, its nonspecific clinical presentation frequently leads to misdiagnosis. There are currently no reliable immunohistochemical markers that allow for accurate differentiation of benign pilomatrixomas from pilomatrical carcinomas. Similarities between the two in the patterns and intensity of nuclear expression of β-catenin support the use of hair matrix differentiation [4–13]. Increased Ki-67 expression in some portions may indicate that the tumor is highly proliferative and has a tendency to invade the surrounding tissues. In addition, the stronger accumulation of p53 in recurrent lesions compared to primary tumors may suggest higher malignancy of the recurrent tumor.

Physical examination of our patient also revealed a hard, ill-defined subcutaneous mass in his right groin, suggesting the presence of lymph node metastases, even though these have been rarely reported in the literature.
Surprisingly, a wide resection of the mass revealed a high-grade B-cell lymphoma. Concurrent carcinomas and lymphomas have been described in other locations, but to the best of our knowledge, this is the first study reporting a concurrent pilomatrical carcinoma and high-grade B-cell lymphoma. Liegl et al. reported five malignant trichogenic tumours arising in long-standing benign adnexal neoplasms, four of which were associated with an underlying systemic malignancy. Three of these patients had a history of B-cell chronic lymphocytic leukaemia (B-CLL), and one patient had a history of colonic adenocarcinoma. The authors reported the case of a 76-year-old woman with an 8-year history of B-CLL who suffered a malignant transformation of a nodule on the forearm that had been present for at least 10 years. The tumor was interpreted as a pilomatrix carcinoma [3].

Several studies have documented a greater risk of various types of skin cancer in patients with non-Hodgkin’s lymphoma and an increased incidence of non-Hodgkin’s lymphoma following skin cancer [8, 9]. The authors posited that this may be related to shared etiological factors such as UV radiation and associated immunosuppression [8]. Malignant transformation of benign adnexal tumors may be related to impairment of the immune system caused by UV radiation or the onset of lymphoproliferative disorders. Repeated trauma is also known to induce malignant transformation. The patient in our study had a history of repeated self-treatment using curettage.

No standard has yet been established for the treatment of pilomatrix carcinoma. However, wide excision was found to lower the risk of recurrence from 64% to 20% [9]; however, whether this reduces the likelihood of metastasis is still under debate [2]. Furthermore, even with negative margin assessment by histology, tumor recurrence is still possible [7]. Two cases treated with Mohs micrographic surgery were reported in the literature, with no local recurrence 5 and 6 months post-surgery [9]. Cytotoxic or immune-modulating agents seem to be largely ineffective. Radiation and electron beam therapy have also been used as primary treatment or as an adjuvant to surgery, but their role is still unclear, as there have been reports of both cure and progression [10].

Recurrence and malignant transformation of long-standing pilomatrixoma or the residual component after surgical excision have been reported, indicating the need for careful examination and follow-up of these patients for sudden changes in preexisting benign tumors or in the surgical site. In addition, patients presenting with pilomatrixoma or other skin tumors in association with systemic lymphoid neoplasms or while undergoing chemotherapy treatment should be carefully monitored for recurrence or malignant transformation.

In conclusion, pilomatrix carcinomas are extremely rare neoplasms, and may either arise de novo or develop in benign adnexal neoplasms which have been evolving for many decades. Although it is not clear what triggers the malignant transformation in previously benign tumors of such long duration, research has demonstrated that pilomatrix carcinoma and its benign counterpart share a mutation in exon 3 of CTNNB1, a gene that encodes β-catenin [4]. As mentioned above, most tumors are located in the head and neck, suggesting that sun exposure may play a role in the acquisition of new genetic events contributing to malignant transformation. In addition, a change in host
immune surveillance may be of special importance in this specific setting, as was shown previously [3, 11]. Here we report, for the first time in the literature, a case of pilomatrix carcinoma concurrent with a high-grade lymphoma, thus highlighting the necessity of close follow-up in patients with persistent skin tumours not responsive to repeat treatment.

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Compliance with Ethics Guidelines. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964, as revised in 2013. Informed consent was obtained from all patients included in the study.

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