Malignant mixed tumor of the skin: a case report and review of the literature

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ABSTRACT

Introduction: Malignant mixed tumor (MMT) is an exceedingly rare cutaneous adnexal carcinoma with a significant risk for aggressive behavior and a propensity for metastasis. This tumor occurs in a wide age range and is twice as common in woman than in men. MMT shows a predilection for the trunk and the extremist's foremost hands and feet. MMT may be confused clinically with many benign and malignant lesions. Therefore the histopathological and immunohistochemical examination is required for the correct diagnosis and treatment.

Purpose: To present a case of MMT localized in the left toe with a special attention focused on its histopathology and differential diagnosis.

Case presentation: A 56-year-old female was admitted with a nodular lesion on the left toe. A painless mass had been presented for one year with a significant increase in size within the past three month. The patient underwent wide surgical excision. Histopathologically for the lesion was diagnosed it as a malignant mixed tumor. Immunohistochemical examination revealed positive reaction for cytokeratin AE_1/AE_3/PCK26, vimentin and S-100. Histochemical reaction for PAS in the chondromyxoid tumor stroma was negative.

Conclusion: Correct histopathological diagnosis and complete excision with wide disease-free margins before metastasis result in MMT free survival.

Key words: malignant mixed tumor, skin, histopathology

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INTRODUCTION

Mixed tumor (MT) or chondroid syringoma (CS) is rare, benign tumor of the skin. In 1892, Nasse first described a mixed tumor of the skin due to its histopathological resemblance to the benign mixed tumor originating from salivary gland [1]. In 1961, Hirsch and Helwig suggested the term ''chondroid syringoma '' in view of mixed tumor of the skin. They defined '' chondroid syringiona'' as ''a neoplasm of epithelial origin with the capacity to form cutaneous adnexal-like structures, especially sweat gland-like structures, and to produce a chondroid matrix'' [2]. Headington divided CS into the two groups, including apocrine type and eccrine type, based on their histopathological appearance [3].

Mixed tumors most often occur as solitary slowly growing, solid, painless, subcutaneous or intracutaneous nodules on the head and neck. Most lesions are between 1-3 cm in diameter. They often affect adults with a male to female ratio of 2:1 [4 - 6].

Malignant mixed tumor (MMT) is an exceedingly rare cutaneous adnexal carcinoma with a significant risk for aggressive behavior and a propensity for metastasis. It occurs in a wide age range from 15 months to 50 years and is twice more common in women than in men [7]. In contrast to its benign counterpart MMT shows a predilection for the trunk and extremities, foremost hands and feet [8, 9]. MMT is usually much larger (2-15cm in diameter) at the time of presentation than its benign counterpart [7, 10]. Most malignant mixed tumors are firm, circumscribed, asymmetrical cutaneous or subcutaneous lesions with no distinctive clinical appearance [11 -13].

We present a case of MMT localized in the left toe with a special attention focused on its histopathology and differential diagnosis.

CASE REPORT

A 56-year-old female was admitted with nodular lesion one the left toe. A painless mass had been presented for one year with a significant increase in size with the past three months. During that time she had not experienced any functional or sensory loss. Her past medical history was unremarkable. On examination, a firm, lobulated 3,5cm x 3cm lesion was noted. The mass was not tender and mobile in the skin and subdermal structures.

The patient underwent wide surgical excision. Grossly the tumor was firm, circumscribed and asymmetrical. The tumor cut surface revealed myxoid material. Histo-pathologically the tumor was asymmetrical, poorly circumscribed, lobulated, with infiltrative margins and had biphasic nature. Examined neoplasm consisted of epithelial and connective tissue elements. Epithelial tumor aggregations presented as a confluent cords and nests of variable size and shape, with interspersed zones of gland-like structures. They were composed of atypical columnar or cuboidal cells with high mitotic count (Fig. 1 a, b).

The connective tissue elements were mainly presented in the center of the lesion. They were myxoid or chondroid like structures composed of spindle-shaped and polygonal cells surrounded by haloes like those around chondrocytes (Fig. 1c). Zones of necrosis were presented in examined tumor (Fig. 1d).

Immunohistochemical examination revealed positive reaction for cytokeratin AE_1/AE_3/PCK2 6 (Fig. 2a), vimentin (Fig. 2b) and S-100 (Fig. 2c). Histochemical reaction for PAS in the chondromyxoid tumor stroma was negative (Fig. 2d).

DISCUSSION

Malignancy of the skin accounts for considerable morbidity worldwide. Skin tumors can be generally divided into melanoma and non-melanoma types [14]. Basal cell carcinoma and squamous cell carcinoma comprise approximately 98% of the non- melanoma group. The incidence of malignant mixed tumor of the skin is less than 0,005% among all dermal malignant epithelial neoplasms [15].

In our case, the patient had a history of slowly growing left toe lesion for 1 year with a significant increase in size within the past 3 months. Malignant mixed tumor may occur *de novo* or rarely develop in benign mixed tumor. In contrast to the benign counterpart, which is common in the head and neck region, the malignant variety occurs predominantly on the trunk and extremities [8, 9]. Our patient was 56 year-old woman with MMT on the left toe. The female preponderance of that tumor is reported in many studies [12, 16].

MMT may be confused clinically with many benign and malignant lesions. Therefore the histopathological and immunohistochemical examination is required for the correct diagnosis. Differentiation of MMT from other skin malignancies is important clinically because prognosis and treatment differ from the more commonly encountered dermal cancers [16].

MMT probably does not originate in association with its benign counterpart but develops *de novo* [17]. A myoepithelial origin of MMT appears to be the most plausible [18]. In 1961, Headington divided mixed tumors of the skin into wo groups, including apocrine and eccrine type, based on their histopathological appearance [3].

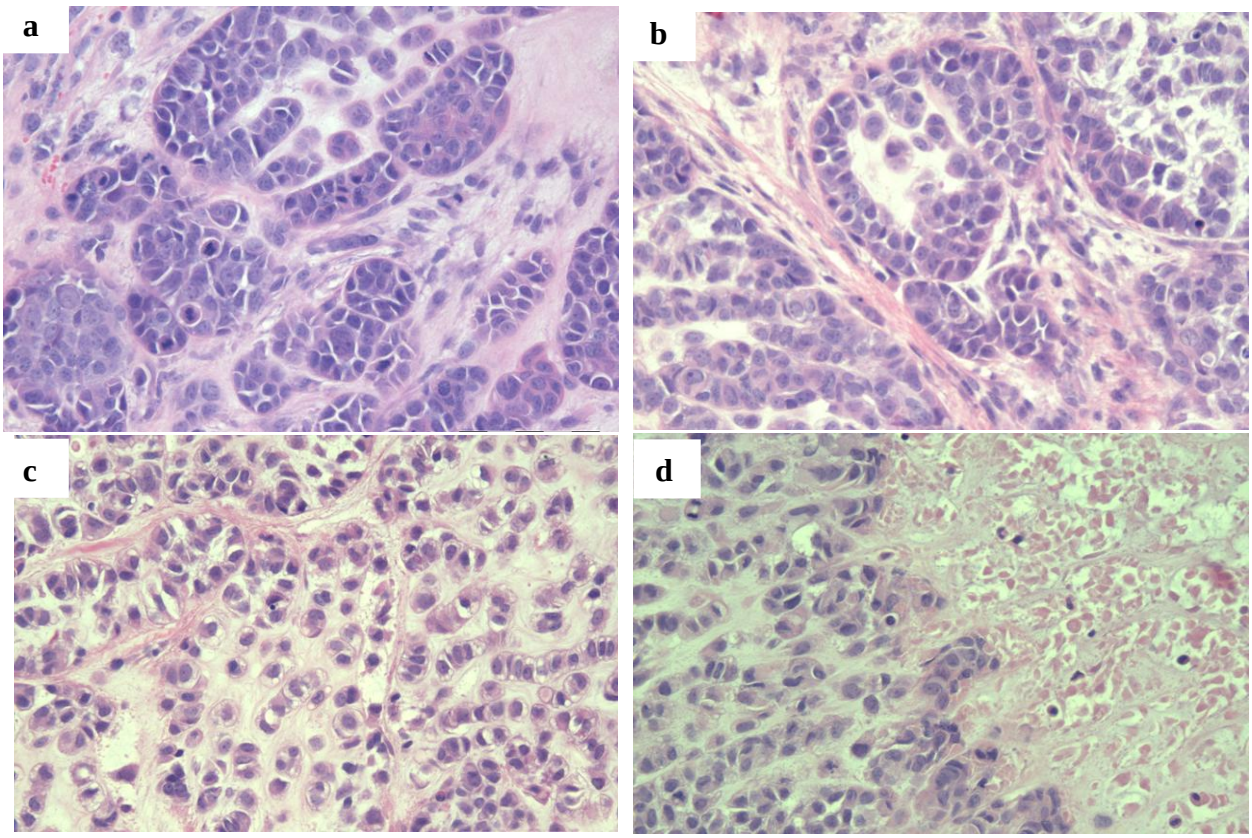

Figure 1. Histopathological features of MMT. Epithelial tumor aggregations presented as a confluent cords and nests with interspersed zones of gland-like structures. (a,b) Tumor composed of atypical columnar or cuboidal cells with high mitotic count (c), and necrotic area (d).

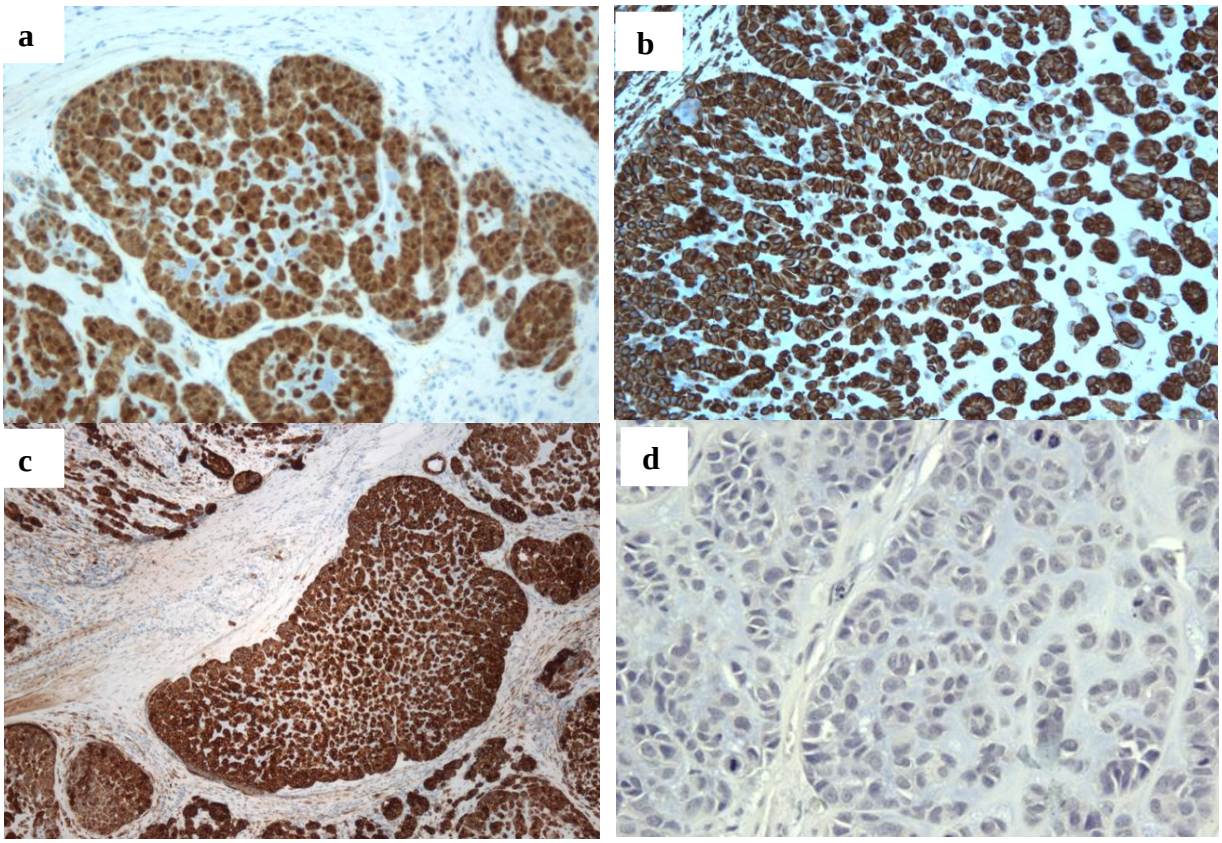

Figure 2. Immunohistochemical and histochemical examination of MMT. Positive reaction for pancytokeratin (a), vimentin (b) and S-100 (c). Histochemical reaction for PAS was negative (d).

In our case the epithelial component of MMT showed hybrid morphology between apocrine and eccrine appearance. The epithelial structures were composed of pleomorphic columnar and cuboidal cells, with nuclear atypia and high mitotic activity what help us to diagnose malignancy. The non- epithelial elements required for diagnosis of MMT were composed of myxoid and chondroid like structures. Differential diagnosis of MMT takes extraskeletal myxoid chondrosacroma and mucinous carcinoma into consideration. Extraskeletal myxoid chondrosarcoma consists of non-cohesive elongated tumor nests without ductal or tubular structures and the cells are cytokeratin negative [18]. In our case, epithelial tumor aggregations presented as a confluent cords and nests with a tendency to form gland-like structures were cytokeratin positive. Mucinous carcinoma shows distinct PAS positivity of the extracellular myxoid stroma (18). Our case was PAS negative.

MMT tends to follow on unpredictable clinical course. Of the reported cases, 50% had local recurrences [19]. Nodal metastases and distant metastases were observed in 39% and 36% of the cases, respectively. The most common site for distance metastasis was lung, followed by bone and brain [19, 20].

Treatment consists of complete excision of the tumor. Though local radiotherapy is often unsuccessful, skeletal metastasis has been shown to respond to radiotherapy. Combination chemotherapy in patients with metastasis is not reported to be beneficial [19].

In conclusion, correct histopathological diagnosis and complete excision with wide disease-free margins before metastasis result in MMT free survival.

Conflicts of interest

The authors declare that they have no competing interests in the publication of the manuscript.

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