Atypical Mixed Tumor of the Skin in the Gluteal Region with Strong and Diffuse Nuclear Expression of the p16 Stain: A Case Report

Andreja Petrović[1], Vesna Cerfalvi[2], Davor Tomas[2,3], Monica Stephany Kirigin[2], Božo Krušlin[2,3]

[1]Merkur University Hospital, Zagreb, Croatia; [2]Sestre milosrdnice University Hospital Center, Zagreb, Croatia; [3]School of Medicine, University of Zagreb, Croatia,

Corresponding author:
Andreja Petrović, MD
Merkur University Hospital, Zagreb, Croatia
petrovic.andrea@gmail.com

Received: May 5, 2022
Accepted: September 1, 2022

ABSTRACT Benign, atypical, or malignant chondroid syringoma (mixed tumor of the skin) have almost identical clinical presentation with similar histological features, except for infiltrative growth, and perineural and vascular invasion in the malignant type. Tumors with borderline features are described as atypical chondroid syringoma. Immunohistochemical profiles in all three types are similar, with the the main difference in the expression of the p16 stain. We present a case of an atypical chondroid syringoma in an 88-year-old female patient with a subcutaneous, painless nodule in the gluteal region and with diffuse, strong nuclear immunohistochemical staining for p16. To our knowledge, this is the first such reported case.

KEY WORDS: mixed tumor, atypical, skin, chondroid syringoma, p16

INTRODUCTION

Benign, atypical, or malignant chondroid syringoma (mixed tumor of the skin) is a very rare tumor of the skin with an incidence of 0.01% to 0.10%. Only 10% of benign chondroid syringoma present atypical features, and just a few cases of atypical chondroid syringoma have been reported. Cutaneous mixed tumor is a mostly benign tumor of the sweat glands that presents as a circumscribed solitary mass in the dermis or subcutaneous fat (1,2). Mixed tumor of the skin is very similar to pleomorphic adenoma of the salivary glands. The most common manifestation is an asymptomatic, slowly growing nodule in the skin of the head and neck region, with predominance in middle-aged males (1-4). Its malignant version is also known as malignant chondroid syringoma, with female predominance mainly affecting the extremities. The reported age range in both types is wide, between the ages of 13 and 89 (1,2). The tumor size is variable, with a diameter ranging from 2 mm to 10 cm (3). Clinical presentation is the same as its benign counterpart, but sometimes it can present as multiple nodules with sudden rapid growth and distant metastases (1,3,4). We present a case of an atypical chondroid syringoma in an 88-year-old female patient with a subcutaneous, painless nodule in the gluteal region and diffuse and strong nuclear immunohistochemical staining for p16.

CASE REPORT

An 88-year-old female patient presented with an asymptomatic, nodular, subcutaneous mass in the right gluteal region. The overlying skin was normal. The patient could not specify the exact time when the mass appeared or whether it was increasing in size. The patient had no previous relevant diseases. Pre-operative ultrasound showed a heterogeneous,

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2022;30(3):163-165

mostly hyperechogenic, and vascularized mass in the lower lateral gluteal area. The tumor measured up to 3.3 cm in its largest diameter. On gross examination, a solid, gray-white, well-circumscribed nodular mass was observed (Figure 1, A). The cut surface was firm and yellowish-white, without necrotic or hemorrhagic areas. Microscopic examination of the specimen showed the tumor consisted of an abundant atypical epithelial component embedded in a benign mesenchymal component. The epithelial component was composed of larger solid parts with increased cellularity (Figure 1, B) and increased mitotic activity (up to 4 mitoses per HPF) (Figure 1, B). There was high expression of the proliferation marker Ki-67 in approximately 20% of the tumor cells (Figure 1, C). Epithelial cells showed some pleomorphism with hyperchromatic nuclei and irregular nuclear borders. Ductal and tubular differentiation was also focally present in the epithelial component (Figure 1, D). There was no necrosis or perineural or vascular invasion. The mesenchymal component was composed of fibrous and myxoid tissue without atypia. The tumor partially contained a fibrous capsule and had pushing borders.

Immunohistochemical staining revealed positivity for S100, SMA, calponin, and p63, indicating myoepithelial differentiation. The aforementioned was positive in the outer layer of the tubular and ductal structures, while the solid part of the tumor was negative (Figure 2, A and B). The outer layer of the tubular and ductal structures was positive for BCL2, while the inner layer was positive for CKPAN and EMA, as was the solid part of the tumor (Figure 2, C). All tumor cells expressed diffuse and strong nuclear staining for p16 (Figure 2, D) but were negative for estrogen, progesterone, and D2-40.

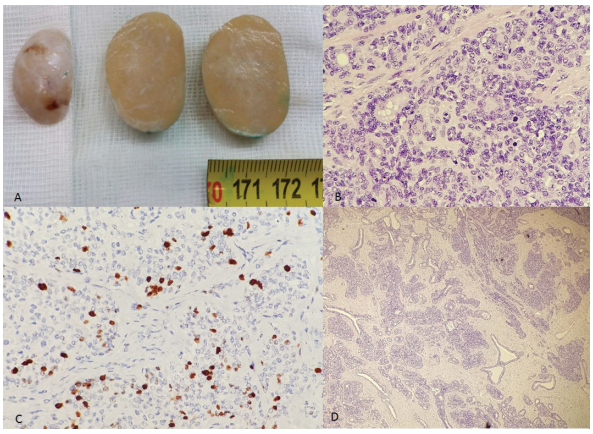

Figure 1. Macroscopic and microscopic description. (A) Well circumscribed nodular mass. (B) High mitotic activity (4 mitotic figures per high-power field) (hematoxylin and eosin, ×400). (C) Proliferation marker Ki67 (Ki67 ×100). (D) Ductal and tubular differentiation (hematoxylin and eosin, ×40).

The diagnosis of a potentially aggressive atypical mixed tumor was established based on clinical data, histological appearance of the tumor, and diffuse and strong nuclear expression of p16. Long-term follow-up was suggested to the clinicians. Currently, the patient is well and without recurrence 15 months after the surgery.

DISCUSSION

There are approximately 20 cases of atypical chondroid syringoma reported in the literature (2). Like its benign counterpart, malignant chondroid syringoma is composed of epithelial and mesenchymal components (1,4). The epithelial component consists of two types of cells that are distributed in cords, nests, and clusters, in tubular or ductal structures or arranged individually (1,2,4). Metaplastic changes can be observed in the epithelial component, with squamous metaplasia being the most common (1,4). The mesenchymal component varies; it can be myxoid, chondroid, hyalinized, fibroid, or a mixture of each (1,2,4). The histological criteria to identify malignant chondroid syringoma are architectural and cytological (1,4-8). When there is a chondroid syringoma with borderline features, the suggested term is an atypical mixed tumor (2,4,9,10).

Malignant mixed tumor of the skin has similar immunohistochemical staining results as its benign counterpart. Epithelial components present expression for CKPAN, CK 5/6, EMA, and CEA, while myoepithelial cells show expression for p63, SMA, S100, BCL2, calponin, and vimentin; however, this immunohistochemical profile can be variable (1,2,4,6,7).

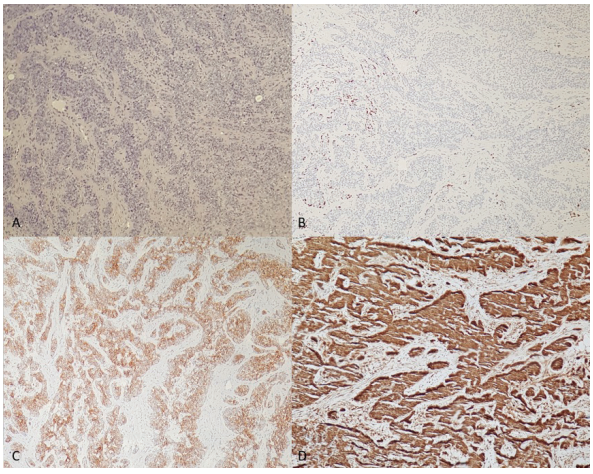

Figure 2. The solid part of the tumor and its immunohistochemical staining. (A) The solid part of the tumor (hematoxylin and eosin, ×100). (B) p63 (×100). (C) PANCK AE1/AE3 (×100x). (D) Diffuse and strong nuclear and cytoplasmic p16 staining (×100)

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Immunohistochemical staining for androgen receptors is negative (2). The marker Ki67 of cell proliferation is very low, ranging from 1 to 2% (6-8). According to the literature, the p16 immunohistochemical marker is helpful in the diagnosis of malignant chondroid syringoma (11,12).

The most important differential diagnosis is benign and malignant chondroid syringoma. Some of the benign tumors can have atypical features but still lack true features of malignancy (3,4,6), such as infiltrative growth pattern, cytological atypia, increased mitotic activity, necrosis, and perineural and vascular invasion. The term atypical chondroid syringoma has been suggested for tumors with borderline features (1-4,6). According to data from the literature, diffuse and strong nuclear expression of p16 favors malignant chondroid syringoma (11,12).

Atypical chondroid syringoma is a rare tumor of the skin with local recurrence if excision was incomplete, and they do not develop metastasis (2,4,9,10). The treatment of choice is surgical excision. Excision should be wide, and a clearance of 3 cm has been suggested (1,2,9,10). Because of its recurrence, long-term follow-up is recommended (9,10).

In our case, the diagnosis of malignant chondroid syringoma was difficult to establish. The clinical data suggesting malignancy were female sex and localization of the tumor. The histological features that pointed towards malignancy were increased cellularity, frequent absence of glandular structures, nuclear pleomorphism, and increased mitotic activity. Immunohistochemical staining without clinical data or histology is not helpful because both tumor types have an almost identical immunohistochemical profile except for p16 expression. However, our final diagnostic suggestion to the clinician was atypical mixed tumor of the skin.

Because of its rarity and potential use of the new marker, this case highlights the importance of clinical data along with histological morphology and immunohistochemical profile in diagnosing the atypical type of chondroid syringoma and differentiating it from its benign counterpart. After an extensive search of the relevant literature, we have concluded, to the best of our knowledge, that this is the first such described case.

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