Case Report

Ossifying Fibromyxoid Tumor: A Rare Subcutaneous Tumor

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Abstract

Description

The following case study demonstrates a 26-year-old male that presented to the dermatology clinic with an enlarging, raised skin nodule located on the left inferior lateral lower back. The patient reported it had persisted for two years, and he had not received prior treatment. He noted a family history of nonmelanoma skin cancer but had no other dermatological issues in the past. Physical examination revealed a pink, firm and well-circumscribed subcutaneous mass with a prominent follicular pore. It was assumed the lesion was an epidermal inclusion cyst, and surgical excision was performed. Histopathology revealed lobules of epithelioid cells with indistinct cytoplasm in a fibromyxoid hyalinized matrix surrounded by lamellar bone and a collagenous pseudocapsule. Immunohistochemical staining showed moderate desmin immunoreactivity and negative immunoreactivity for CD34, S-100, EMA, actin and pancytokeratin. Based on the findings, a diagnosis of ossifying fibromyxoid tumor was made. Given the uncertain biological potential of this lesion, re-excision was performed. No residual tumor was identified on repeat pathological evaluation. The patient was scheduled for close follow-up to survey for recurrence or possible metastasis.

Keywords

fibromyxoid tumor; ossifying fibromyxoid tumors; OFMT; subcutaneous tumor; desmin positivity; ossifying fibroma; fibroma; ossifying; soft tissue neoplasms

Introduction

Ossifying fibromyxoid tumors (OFMTs) are rare, soft tissue neoplasms that develop in the subcutaneous layer of the skin. They were first described in 1989 by Enzinger et al. in an article detailing 59 cases of a histologically unique neoplasm.[1] Histologically, they are characterized by lobulated chords of bland, round cells organized in a fibromyxoid hyaline matrix with a peripheral shell of woven bone.[2] Although OFMTs can present in all age groups, they usually arise in adults with a median age of 50, with a slight predilection towards males (1.5:1).[3] Clinically, an OFMT tends to present as a small, painless mass that persists over years most commonly arising on the extremities. Most OFMTs are benign and can be treated with excision; however, local recurrence has been seen in 17% of cases. Furthermore, malignant OFMTs have been identified in 5% of cases and have a metastatic potential of 60%.[3] The cellular origin of these tumors is still unknown, although the neuroectoderm is suspected in light of cyotarchitectural findings and positive staining to markers such as S100, desmin, CD56, CD99 and neurofilament.[4] This case study aims to demonstrate an exemplary presentation, work-up and management of an OMFT in order to shed further light on these rare tumors as well as to consider the origin of development in these patients.

Case Presentation

A 26-year-old male presented to our dermatology clinic for a chief complaint of a skin lesion located on his left inferior lateral lower back. He reported that the lesion was enlarging, painful and hard to the touch. Nothing had improved or worsened the lesion. He received no treatment for this lesion in the past. Physical exam-

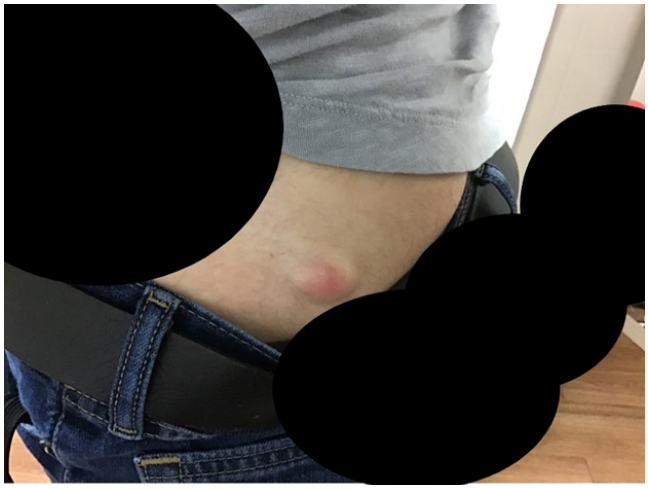

Figure 1. Clinical image demonstrating a 2.3 x 2.0 cm subcutaneous nodule.

ination revealed a 2.3 x 2.0 cm painful subcutaneous nodule. (**Figure 1**) Initial assessment of the skin lesion was an epidermal inclusion cyst, and the patient elected to undergo surgical excision. During surgical excision, it was noted that the lesion had a different consistency than an epidermal inclusion cyst, a fact that raised concern for an odd neoplasm. The specimen was submitted for dermatopathological evaluation.

Upon evaluation, the diagnosis of ossifying fibromyxoid tumor was given. The patient returned for re-excision, which on pathology demonstrated dermal scar. The patient recovered well from surgery and therefore, was scheduled for routine follow-up. Over 1.5 years later, the patient does not report recurrence.

Pathology Report

The specimen was received in formalin and consisted of a portion of skin measuring 3.0 x 2.0 x 1.5 cm and a firm subepidermal mass measuring 1.3 x 1.0 cm. The mass was composed predominantly of sheets of vague lobules of epithelioid cells, with indistinct cytoplasm, set within a fibromyxoid to hyalinized matrix. The cells were relatively monomorphous. Neither atypical mitotic activity nor necrosis was identified. The tumor was surrounded by a "partial shell" of lamellar bone as well as a collagenous pseudocapsule. (**Figure 2**) The metaplastic bone was normal in appearance and lacked atypical cytologic features. (**Figure 3**) The lesional cells were moderately immunoreactive for desmin. (**Figure 4**) These cells failed to demonstrate immunoreactivity

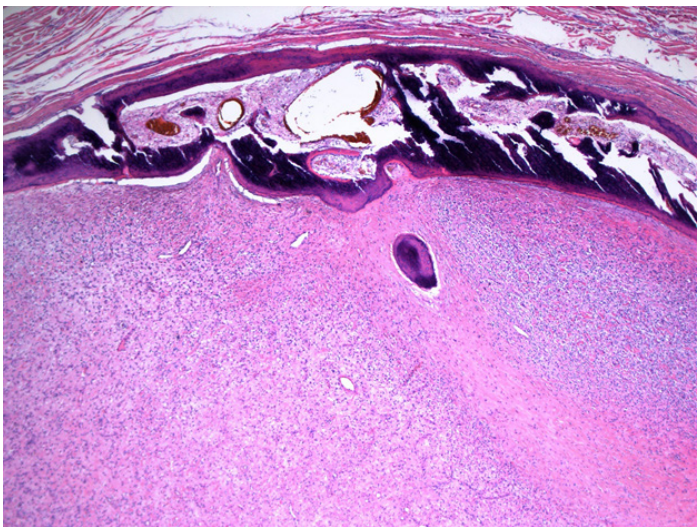

Figure 2. H&E at 10x demonstrates lobules of epithelioid cells set within a fibromyxoid matrix surrounded by a "partial shell" of lamellar bone as well as a collagenous pseudocapsule.

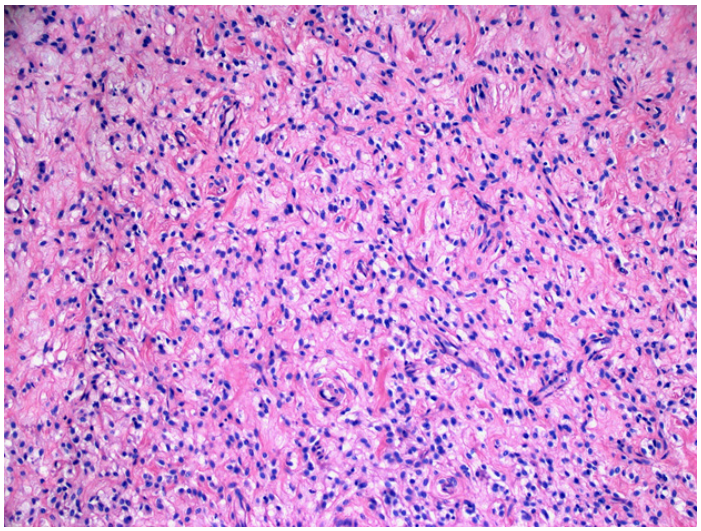

Figure 3. H&E at 100x demonstrates relatively monomorphous, epithelioid cells with indistinct cytoplasm set within a fibromyxoid to hyalinized matrix. Neither atypical mitotic activity nor necrosis was identified.

for CD34, helping to exclude a vascular lesion, such as an angiomyxoma. Other negative markers included S-100, pancytokeratin, EMA and actin. Colloidal iron staining confirmed the presence of subtle background mucin. By evaluable features, the lesion was predicted to be benign. Other than high cellularity, other poor prognostic features were absent. No high-grade nuclear atypia, high mitotic count (>2/50 per high power field [HPF]), or infiltrative growth were identified. There is no reliably distinguishing immunoprofile for this lesion. The diagnosis of an OFMT was reached at the conclusion of histopathological evaluation.

Although the features did not meet the criteria for malignancy, there was some uncertainty of biologic potential, and thus, conservative re-excision to ensure complete removal was advised. Molecular studies were not preformed.

Discussion

OFMTs are a unique mesenchymal tumor that can mimic other dermatological disorders and go undiagnosed in many patients. According to the Folpe and Weiss classification model, there are typical, atypical and malignant OFMTs. A typical OFMT is histologically characterized by low nuclear grade, low cellularity and a mitotic rate <2/50 per HPF. By contrast, malignant OFMTs possess high nuclear grade, high cellularity and mitotic activity >2/50 per HPF.

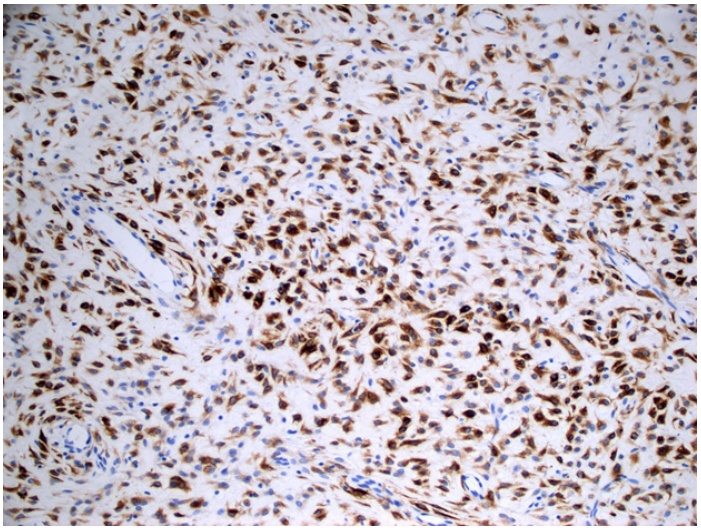

Figure 4. CImmunostain showing moderate immunoreactivity for desmin.

Atypical OFMTs differ from typical OFMTs in architectural and cytologic features; however, they do not meet the proposed criteria for malignancy.[5] One of the most useful staining markers for OFMTs is S-100, which has been identified on average in 75% of cases. Another common marker is desmin, identified in about 25% of cases.[3] Additionally, some studies note neurofilament staining presence in over 80% of cases.[6] A few other stains that can be used include smooth muscle actin, pancytokeratin and epithelial membrane antigen. Immunohistochemistry has identified some similarities and differences between nonmalignant and malignant OFMTs. Compared to typical OFMTs, malignant tumors are more frequently positive for pancytokeratin, EMA and actin, and less frequently positive for S-100 and desmin.[7] Given the pathology report for this case, the lesion did not meet malignant criteria. However, typical OFMTs do have metastatic potential (found in 4% of cases). Additionally, these lesions can be persistent and bothersome for many patients. As was performed in this case, local excision with negative margins is the typical treatment for OFMTs. Non-malignant OFMTs have a recurrence rate of about 8%, and thus, close post-surgical surveillance is necessary so that new lesions can be identified and treated. In addition to excision, adjuvant radiation may be utilized for certain cases with malignant features. Chemotherapy may be considered if there is extensive metastasis.[3]

Molecular studies have provided useful insight to the molecular drivers of these neoplasms, as well as possible lines of differentiation. PHF-1 gene rearrangement on 6p21 has been found in up to 80% of tumors in studied case series.[8] This gene encodes a protein that controls embryonic stem cell differentiation via interaction with the protein associated with the polycomb-repressive complex 2 gene (PRC2), ultimately governing changes in chromatin structure during fetal development.[3] Furthermore, fluorescence in situ hybridization studies have demonstrated mosaic INI-1 (integrase interactor 1) loss that was identical in both histologically typical and malignant OFMTs.[7] Furthermore, OMFTs have shown upregulation of EAAT4 and MUC4 protein expression, and downregulation of PMP22 and MYEF2.[9] Although the origin of these tumors is unknown, there are some leads based on immunological and histological findings. Schwannian origin has been cited as a possible precursor in light of histological findings of replicated external laminas and S-100 expression. However, PMP22 and MYEF2 are usually upregulated in nerve sheath myxomas and schwannomas.[9] Cartilaginous differentiation is also possible given cytoarchitectural findings of irregular borders with short processes and intracellular microfilaments, as well as S-100 positivity and weak collagen II expression.[9] Myoepithelial origin can also be argued as they share certain low power microscopic characteristics such as lobularity, epithelioid cells and chondromyxoid stromas. However, cytokeratin, smooth muscle actin and SOX-10 are relatively infrequent markers found in OFMTs compared to myoepithelial tumors.[3] Lastly, neuronal cell origin is argued on the basis of prominent neurofilament staining, as well as proteomic markers such as katanin, a neuron microtubule protein, and versican, a neuron-associated glycoprotein. Nonetheless, the origin remains unclear, and more research is warranted to unveil the exact line of differentiation of these tumors.

Conclusion

OFMTs represent a group of mesenchymal neoplasms of unknown origin with certain features used to aid in identification. However, classic immunohistochemical markers such as S-100, desmin and others employed may not always be expressed. Furthermore, other tumors share immunological and cytoarchitectural features with OFMTs such as myoepithelial neoplasms, epithelioid schwannomas and fibromyxoid sarcomas, to name a few. Thus, strong clinical suspicion must be utilized in combination with the diagnostic tools available. Although rare and usually benign, certain OFMTs can possess histologically malignant features and have the potential to metastasize and be life threatening. Close clinical surveillance is crucial in these patients not only to identify and treat recurrences, but also to monitor for signs of metastatic lesions.

Conflicts of Interest

The authors declare they have no conflicts of interest.

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