Malignant chondroid syringoma: A case report and literature review

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ABSTRACT

Introduction: Malignant mixed tumor of the skin/malignant chondroid syringoma (MCS) is a very rare adnexal tumor that is considered as the malignant counterpart of the benign mixed tumor/benign chondroid syringoma (BSC) of the skin. It usually arises de novo in the extremities and takes an unpredictable clinical course with high incidence of local recurrence, distance metastasis, and death. We present a rare case of malignant chondroid syringoma of the forearm which metastasized to the axillary lymph node despite aggressive local treatment.

Case Report: An 83-year-old male with history of numerous prior cutaneous neoplasms, presented with a forearm nodular keratotic lesion, clinically thought to be an invasive squamous cell carcinoma. Accurate histopathological examination revealed a completely excised malignant chondroid syringoma. The patient underwent wide local re-excision of the scar, followed by four weeks of local radiotherapy. Although there was no evidence of any local recurrence, he developed axillary lymph node metastasis four years after the initial diagnosis, for which he underwent axillary lymph node dissection.

Conclusion: Malignant chondroid syringomas are exceedingly rare tumors, but with a high incidence of recurrence, metastasis, and death. These cases need to be diagnosed with strict histopathological criteria. Current treatment of MCS comprises of complete excision with wide margins plus or minus local radiotherapy to prevent local recurrence. Close follow-up and staging are recommended to aid in early detection of recurrence or metastasis.

Keywords: Chondroid syringoma, Malignant mixed tumor, Metastatic, Skin adnexal tumor

INTRODUCTION

Malignant mixed tumor of the skin/malignant chondroid syringoma (MCS) is a very rare cutaneous adnexal malignancy that is biphasic in origin, with malignant epithelial and mesenchymal components [1, 2]. Its benign counterpart, benign chondroid syringoma (BSC) is also rare, comprising <0.01% of all primary skin tumors, and mostly occurring on the head and neck region [3]. The MCS (which has only about 40 cases being reported in the literature) is most often reported in the extremities and trunk, with only a few cases reported in the head and neck region [4, 5]. Most of the time there is anaplastic changes noted from early on [2, 6], with a requirement for the diagnosis of MCS to have some resemblance to its benign counterpart [7].
We present a case of malignant chondroid syringoma of the distal forearm in a patient with history of multiple prior cutaneous malignancies including a scalp melanoma. The MCS, which was treated with complete excision, wide re-excision of scar, and local radiotherapy; metastasized to the axillary lymph nodes, four years after the initial diagnosis. This case highlights some of the unique characteristics of this adnexal malignancy including a propensity for metastasis and probable resistance to radiotherapy. We also consider the possible utility of sentinel lymph node biopsy in the treatment of these highly malignant adnexal tumors [8].

CASE REPORT

An 83-year-old male with prior history of multiple cutaneous neoplasms (multiple basal cell and squamous cell carcinomas in the head and neck, a spindle cell melanoma of the scalp and an atypical fibroxanthoma of the forehead) presented with a new keratotic lesion on the dorsal of left distal forearm that was clinically suspected to be squamous cell carcinoma. Gross examination revealed a nodular keratotic 1.7 cm lesion. Microscopic examination revealed an ulcerated, completely excised, lobulated tumor in the dermis composed of both epithelial and mesenchymal components (Figures 1 and 2). The epithelial component was composed of irregular nests and cords of focally atypical cells with pleomorphic nuclei, prominent nucleoli, and eosinophilic cytoplasm (Figure 3). Mitotic figures were also identified (Figure 4). The stromal/mesenchymal component consisted of mainly a chondromyxoid and fibrous stroma with poor chondroid differentiation (Figure 5). The tumor showed focal close connection to the epidermis which also showed a hyperkeratotic and parakeratotic crust. There was a thin peripheral collarette of epidermis at places, however in the central deep portion of the tumor there were markedly irregular tumor cell clusters and isolated cells showing nuclear pleomorphism. Foci of glandular and squamous differentiation, necrosis as well as brisk mitotic and apoptotic activity were noted. There was no evidence of any lymphovascular or perineural invasion. All resection margins were negative, with the closest deep resection margin being 3 mm away. The epithelial cells were immunoreactive to CK 5/6, 34BE12, P63, CK7, and CAM 5.2 staining (Figure 6). The chondromyxoid area was immunoreactive to S100 and vimentin (Figure 7). This case was diagnosed as malignant chondroid syringoma following intradepartmental pathology consensus rounds. He underwent a wide re-excision of the scar, which showed no evidence of any residual malignancy. Subsequently he received four weeks of adjuvant radiotherapy, mainly with the intent of reduction of risk of local recurrence. No sentinel lymph node biopsy was done and the patient did not receive any adjuvant chemotherapy. Staging computed tomography (CT) scan was not performed at that time.
Four years later, the patient presented with enlarged left axillary lymph nodes (6 cm palpable mass). A core biopsy of the left axillary mass was performed at an outside facility and diagnosed as epithelioid-mesenchymal/chondromyxoid tumor with nuclear atypia and mitotic figures up to 6/10 high power fields, consistent with metastatic MCS. Left radical axillary lymph node dissection performed at our hospital. The specimen revealed 2/7 lymph nodes to be positive for malignant chondroid syringoma, with the overall tumor metastasis measuring 5.0 cm (Figure 8). The epithelial tumor cells were positive for AE1 AE3 and focally positive for epithelial membrane antigen (EMA) and carcinoembryonic antigen (CEA). The cartilaginous areas were positive for S100 and vimentin; and negative for glial fibrillary acidic protein (GFAP), actin, desmin, and caldesmon. A preoperative CT scan had revealed a
The mesenchymal components can be mucinous, cartilaginous, or osteoid in differentiation [3]. Aggressive behavior is associated with a large amount of mucoid matrix and poor chondroid differentiation of the tumor, the latter of which appears to be consistent with the findings and presentation in our case [11]. Dermal satellite nodules and osseous metaplasia have also been reported [6, 11]. Involvement of subcutaneous/deep structures and a local recurrence of a lesion also raises the possibility of malignancy [2, 3]. Due to the extreme rarity of MCS, no formal grading system has been suggested. In a single institute study of 50 cases of malignant adnexal tumors, less than half of the cases were assigned histological grade, and grade was not found to be predictive of overall survival rate [8].

Although there are no immunohistochemical stains specific to MCS, the use of some stains may help confirm the biphasic/mixed differentiation of these lesions and to rule out metastasis [1, 6]. The epithelial component stains positive for cytokeratins including CK5/6, EMA, CEA (glandular differentiation), and p63 (myoepithelial or squamous differentiation) [6]. Our case demonstrated positivity for both high molecular weight (CK5/6, 34BE12) and low molecular weight (CK7, CAM5.2) cytokeratins as well as p63. The mesenchymal chondroid differentiation areas show S-100 and vimentin positivity as expected to occur in chondroid differentiation of other malignancies such as metaplastic carcinoma of breast [12]. Other site specific immunostains can be performed to rule out metastasis as has been widely discussed in reviews of utility of immunohistochemistry in unknown primary, although there may be some overlap with immunophenotype of salivary gland and mammary tumors [13].

Histological differential diagnosis includes primary cutaneous carcinosarcoma, a term which encompasses any biphasic malignant tumors arising within the context of other adnexal neoplasms, such as eccrine porocarcinoma, malignant cylindroma, malignant spiradenoma, and pilomatrical carcinosarcoma [6]. The current World Health Organization (WHO) classification emphasized the need of some benign chondroid syringoma like areas to confirm the diagnosis of MCS and to avoid using overlapping terms like cutaneous carcinosarcoma, when distinctive benign adnexal tumor is seen in the background [7]. Other differential diagnosis includes a BCS, a direct extension and/or metastasis of another malignant biphasic lesion such as malignant pleomorphic adenoma or metaplastic carcinoma of the breast. Careful histopathological examination in the view of clinical history can usually help in reaching a definitive diagnosis, although this may be difficult on small/partial biopsies [3].

The clinical course of MCS has been considered unpredictable, although based on the current literature it appears to be quite an aggressive malignancy. About 50% show local recurrence, up to 62% show nodal and distant metastasis and about 27% patients die of advanced...
metastatic disease [2, 4]. The most common site for distal metastasis is lung, followed by the bone and brain [4]. Local bone invasion has also been reported [14]. Death occurred as early as 9 weeks following surgery to about 12 years after diagnosis [11, 15].

Surgical excision is the mainstay of treatment for MCS. Although tissue conservation surgical technique such as Moh’s micrographic surgery has been recently proposed to be adequate treatment of this lesion on the face, most authors seem to be of the opinion that wide local surgical excision, or staged margin-controlled excision be preferred in these highly malignant lesions [1, 4]. Various chemotherapy protocols with or without radiotherapy have been administered to patients without significant response. Close follow-up is mandatory for early detection of local recurrence or metastasis [4]. A sentinel lymph node biopsy may also be offered to the patients with MCS, especially with the presence of high-risk features such as large amount of mucoid matrix, malignant chondroid differentiation, or extensive lymphovascular invasion [8]. Further accumulating literature may help to delineate better prognostic characterization and treatment guidelines.

CONCLUSION

Malignant chondroid syringomas are exceedingly rare tumors, but with a high incidence of recurrence, metastasis, and death. These cases need to be diagnosed with strict histopathological criteria and with attention paid to the amount of mucoid matrix, poor chondroid differentiation, and margin status. A wide local excision is so far the mainstay of treatment, although sentinel lymph node biopsy may be considered as part of a comprehensive surgical management of these highly malignant tumors. Adjuvant radiotherapy and chemotherapy have not proven to be useful in preventing metastasis.

REFERENCES


Author Contributions

Pooja Vasudev – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Guarantor of Submission
The corresponding author is the guarantor of submission.

Source of Support
None.

Consent Statement
This case does not use any specific patient identifiers, and the pictures are of microscopic histology and immunohistochemistry that cannot be used for patient identification purposes. In the department of pathology, we do not directly interact with patients, but all efforts have been made in great detail to anonymize the case as much as possible.

Conflict of Interest
Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.

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