Multifocal, recurrent malignant chondroid syringoma with visceral metastases: A case report and literature review

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Case Report

Abstract

We present the unusual case of malignant chondroid syringoma (MCS) in a 64-year-old male with recurrent nodular skin lesions and visceral metastases. The patient underwent repeated excisions, with eventual development of widespread nodules and multiple pulmonary and hepatic nodules. Systemic chemotherapy was planned. MCS is a very rare skin adnexal tumor of the sweat glands with only around 50 cases reported worldwide. To the authors’ knowledge, this is the first reported case of MCS with a multifocal presentation and mucosal involvement.

Keywords: Malignant Chondroid Syringoma; Malignant Mixed Tumor; Sweat Gland Carcinoma; Eccrine Carcinoma; Adnexal Carcinoma

1. Introduction

Skin cancer causes significant morbidity worldwide. However, apocrine-eccrine carcinomas are rare, with a reported incidence rate of 2.6 per 1 million person-years. Still, these adnexal neoplasms are associated with a prolonged course and a poor prognosis in the presence of metastatic disease, with a 5-year relative survival rate of 51%.2,3

Malignant chondroid syringoma (MCS), also called malignant mixed tumor of the skin, is an extremely uncommon eccrine sweat gland neoplasm with epithelial and mesenchymal components. Due to the absence of a distinct clinical presentation, it is difficult to distinguish from other cutaneous tumors.4

2. Case presentation

We present the case of a 64-year-old male with recurrent nodular skin lesions on his right arm. The patient underwent repeated excisions, followed by wide excision with axillary lymph node dissection. A 10-cm firm, lobulated mass with skin ulceration and muscle involvement was removed. Microscopic examination revealed infiltrating nests of medium to large epithelial cells embedded in a chondromyxoid matrix with few scattered plasmacytoid myoepithelial cells (see Figure 1). There was brisk mitosis as well as large areas of tumor necrosis. All axillary lymph nodes were negative for tumor. The final histopathologic diagnosis was malignant chondroid syringoma. However, the patient was lost to follow-up.

Figure 1: (1000x magnification). Cuboidal to polygonal tumor cells embedded in a chondromyxoid matrix, with moderate to abundant eosinophilic cytoplasm, round to ovoid nuclei, and prominent nucleoli.

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The patient’s surgery was closely followed by the appearance of multiple similar-looking nodules over the scalp, face (including the buccal mucosa), trunk, right upper extremity, and right foot (see Figure 2). The patient also developed hepatomegaly accompanied by progressive weight loss and anorexia. Subsequent imaging studies revealed multiple pulmonary and hepatic nodules. The patient was then referred for palliative chemotherapy. At the time of consult, he had an Eastern Cooperative Oncology Group (ECOG) performance status of 2 and was advised a trial of doxorubicin-based chemotherapy. However, his clinical condition rapidly deteriorated and he eventually expired before starting treatment.

Figure 2: Multiple firm, erythematous nodules with indurated edges and central ulceration (scalp).

3. Discussion

Chondroid syringoma is a rare type of syringoma that histologically resembles benign mixed tumors of the salivary glands. Its cancerous subtype, malignant chondroid syringoma, is the rarest variant, with an estimated incidence of <0.005%. In contrast to its benign counterpart, MCS is more common in women, affects a wider age range, and usually involves the trunk and extremities. Malignant lesions are usually much larger and appear as firm, circumscribed, asymmetrical skin nodules. They may progress very slowly, with late metastatic spread.

Due to the lack of a distinct clinical presentation, MCS may be confused with various skin tumors, making histopathological and immunohistochemical examination of paramount importance due to differences in its treatment and prognosis. Upon literature review, MCS has been most commonly misdiagnosed as benign chondroid syringoma, unclassified benign sweat gland tumor, and basal cell carcinoma. Histopathologically, MCS consists of clusters of epithelial cells and ductal structures with intervening chondromyxoid matrix and scattered myoepithelial cells. The most reliable histologic features that favor malignancy include cellular atypia, nuclear pleomorphism, increased mitotic activity, focal necrosis, infiltrative borders, invasion of adjacent soft tissues, satellite tumor nodules, and metastasis. Immunohistochemical features include reactivity for epithelial markers such as cytokeratin (CK), epithelial membrane antigen (EMA), and carcinoembryonic antigen (CEA), as well as mesenchymal markers like vimentin, S-100, neuron-specific enolase (NSE), and glial fibrillary acidic protein (GFAP), similar to their salivary gland counterparts.

MCS is an aggressive tumor with a significant risk for metastasis via hematogenous and lymphatic spread. It carries a mortality rate of approximately 25%. It tends to follow an unpredictable course, with approximately 50% presenting with local recurrences, 42% with nodal metastases, and 40% with distant metastases. The most commonly identified site of distant metastasis was the lung, followed by bone and brain. Due to the small number of reported cases, prognostic factors are still difficult to establish, but these likely include size, histological type, lymph node involvement, and distant metastasis.

After a thorough literature search, 51 previous cases of MCS were retrieved. Including the present case, the age range was from 13 to 89 years, with a median age of 54 years. There was no particular age predilection, but there were slightly more cases in the fourth and seventh decades. More females were affected (58%). The most commonly affected primary sites were the extremities (54%), followed by the head and neck region (29%) and the trunk (17%). The present case is particularly exceptional because of the multifocal presentation and the presence of mucosal involvement. Most cases had recurrent disease (60%), and nodal involvement was present in 37%. Distant metastases were documented in 37% of all cases and in 71% of recurrent cases, most commonly affecting the lungs (24%), followed by the central nervous system (10%), pleura (10%), bone (8%), and liver (6%). These data are quite consistent with previously published literature. However, it is more difficult to draw conclusions regarding mortality data as most cases had short follow-up times and not all authors mentioned the outcomes of their patients. Nevertheless, 17% of the cases included in this review died of progressive cancer disease. Surgery was the most widely utilized first-line treatment option, followed by radiotherapy and chemotherapy.

At present, there are no established guidelines for the treatment of apocrine-ecrine carcinomas, particularly for those with distant metastases. Complete surgical excision of the primary tumor with wide margins and dissection of involved lymph nodes is the mainstay of treatment for localized disease, as incomplete removal could result in recurrences. Adjuvant radiotherapy and chemotherapy may also be recommended, but their
definite roles are currently not yet well established as the rarity of this type of tumor precludes clinical trials.\textsuperscript{6,42} Previous reports suggest a possible survival advantage in patients with aggressive tumors receiving adjuvant radiotherapy.\textsuperscript{16,18,24} In particular, bone metastases and spinal cord compression have been shown to be responsive to local radiotherapy.\textsuperscript{6,41} On the other hand, the benefit of combination chemotherapy in metastatic disease has not yet been confirmed. Chemotherapeutic regimens that have been tried include: (1) Cyclophosphamide, vincristine, doxorubicin, dacarbazine (CYVADIC regimen) \textsuperscript{31,51}; (2) Cyclophosphamide, vincristine, doxorubicin\textsuperscript{48}; (3) Cyclophosphamide, vincristine, dactinomycin\textsuperscript{6}; (4) Cyclophosphamide, vincristine, vinblastine\textsuperscript{19}; (5) Cisplatin, etoposide\textsuperscript{33}; (6) Cisplatin, paclitaxel\textsuperscript{31}; (7) 5-fluorouracil, cisplatin\textsuperscript{48}; (8) 5-fluorouracil, leucovorin, cyclophosphamide, doxorubicin\textsuperscript{33}; (9) Tegafur, gimeracil, oteracil potassium\textsuperscript{25}; and (10) Intrallesional methotrexate\textsuperscript{35}. However, no lasting clinical response has been observed with most of these regimens except for the CYVADIC protocol, with the treated patient still alive after 5 years of follow-up.\textsuperscript{51}

4. Conclusion
To the authors’ knowledge, this is the first reported case of malignant chondroid syringoma with a multifocal presentation and mucosal involvement. Because the disease has no distinct clinical presentation, its diagnosis relies on its characteristic histopathological and immunohistochemical findings. Complete surgical excision is the cornerstone of therapy for localized disease, while the role of other treatment modalities such as radiotherapy and chemotherapy has not yet been well established.

Conflict of interest
The authors declare that they have no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References