Synchronous metastatic skull base chordoma to the breast: case report and literature review

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ABSTRACT

Clinical Scenario During routine staging work-up for a left breast mass, a 68-year-old woman complained of dysphagia and dysphonia. During further investigations, a left-sided lesion at the foramen magnum was observed on brain imaging. Both lesions were biopsied and showed a classical chordoma.

Management The skull-base lesion and the breast lesion were surgically resected, and adjuvant radiotherapy was given.

Summary Chordoma is a rare primary central nervous system tumour that seldom metastasizes. The lung is the most common site of metastasis. Synchronous breast metastasis from a skull-base chordoma is very rare, and a safe management option includes a maximum resection followed by adjuvant radiotherapy.

Key Words Chordoma, synchronous metastasis, radiotherapy, surgery

INTRODUCTION

Chordomas are rare tumours that constitute fewer than 1% of bone tumours in the skull base and spine. They occur within the sacrum in 50% of cases, at the skull base in 35%, and on the remainder of the spine in 15%1. They originate from remnants of the notochord. Malignancy is mainly local; however, the risk of metastasis is on the order of 5% and occurs mainly to lung. The most common other sites of distant metastasis are liver, bone, and skin2.

In terms of chemotherapy, no regimen has been found to be very effective, and chordoma patients should be included in clinical trials. Surgery and radiotherapy are the main modalities of treatment. Although metastasis might occur, synchronous metastases are rare. Here, we report a case of skull-base chordoma presenting with a synchronous breast metastasis, and we review the local therapy of metastatic chordoma in our patient and in the available literature.

CASE DESCRIPTION

A 68-year-old woman reported a 1-year history of mild headaches. She was otherwise healthy. She has family history positive for malignancy: Her daughter had died of breast cancer at age 37, a maternal aunt had been diagnosed with breast cancer, and 2 sisters had been diagnosed with basal cell carcinomas.

The patient sought medical advice after a 5-month history of progressive tongue weakness, imbalance, dysarthria, and worsening headaches. Her examination revealed a left hypoglossal palsy and mild ataxia, with normal motor and sensory function in the extremities. Otherwise, she has a good performance status.

Contemporaneous routine screening mammography showed a 2-cm mass in the left breast. Magnetic resonance imaging of the brain (Figure 1) revealed a left-sided extra-axial lesion in the foramen magnum, causing compression on the medulla and upper cervical spine, which encompassed the left hypoglossal nerve and jugular foramen.

Urgent biopsy of the breast mass revealed an invasive carcinoma with mucinous features, positive for brachyury staining (Figure 2), overall grade 2, and triple-negative (estrogen, progesterone, and HER2 receptors). Computed tomography imaging of chest, abdomen, and pelvis, and a bone scan excluded the presence of other metastatic lesions.
FIGURE 1  Magnetic resonance images of brain show the left-sided foramen magnum lesion (arrows). From left to right, sequences are T2 weighted turbo spin echo, T1, and FLAIR (fluid attenuation inversion recovery).

FIGURE 2  Histopathology slides with brachyury staining. (A) Breast lesion, 20× original magnification, with hematoxylin and eosin (HE) staining. (B) Breast lesion, 10× original magnification. (C) Skull base lesion, 20× original magnification and HE staining. (D) Skull base lesion, 40× original magnification.
A segmental mastectomy was performed, with 2 sentinel lymph node biopsies that were negative. The patient was found to have a painful left shoulder skin lesion, which was also removed and confirmed to be a basal cell carcinoma.

Two weeks after the mastectomy, the patient underwent a left far lateral approach and near total resection of the skull-base tumour, which, on frozen section, was consistent with chordoma. The lesion completely involved the left hypoglossal nerves, which were resected with the tumour. The tumour was survised, intraoperatively, to be intradural. A small remnant over the lower cranial nerves entering the jugular foramen was left in situ. Postoperative magnetic resonance imaging confirmed a near-total resection. The patient had an uneventful postoperative period and recovered well, apart from left hypoglossal palsy and some increased difficulty in swallowing, which improved without the need for percutaneous gastrostomy.

Histology examination of the skull-base tumour (Figure 2) showed a morphology compatible with chordoma (anastomotic cords of cuboidal cells floating in a myxoid and chondroid matrix). In some areas, the cells appeared more stellate within a chondroid background. No marked nuclear atypia was seen, and only 1 mitotic figure was identified. Immunohistochemistry was positive for S100, brachyury, cytokeratins AE1 and AE3, and negative for E-cadherin, cytokeratins 7 and 20, estrogen receptor, progesterone receptor, HER2 receptor, and mammaglobin.

Re-analysis of the breast lesion, including brachyury staining (Figure 2), was conducted at Montreal Neurological Institute and Hospital. That analysis confirmed that the tumour was in fact consistent with chordoma. Based on a histopathologic analysis by Barresi et al., brachyury staining was found to be a highly sensitive and specific nuclear stain for chordomas.

A tumour board decision was made to manage the patient with adjuvant radiotherapy to both sites. The patient received hypofractionated whole-breast radiation (42.5 Gy plus a 15-Gy boost in 22 fractions) and was then referred to a proton-beam centre for intensity-modulated proton-beam therapy for the skull-base tumour remnant and operative cavity, receiving an equivalent dose of 68 Gy cobalt.

**DISCUSSION**

Chordomas are considered to be slow-growing tumours, but they behave like other sarcomas and tend to recur after local treatment. Because of the proximity of these tumours to critical structures, treatment is potentially difficult, requiring highly specialized techniques and great precision.

Chordoma has 3 histologic subtypes: conventional (sometimes called classical), chondroid, and dedifferentiated. Chondroid chordoma shows a low-grade growth pattern, has a favourable long-term outcome, and tends to be less aggressive than conventional chordomas. By contrast, dedifferentiated chordoma (which is observed in fewer than 5% of cases) exhibits high-grade behavior and an aggressive clinical course, growing rapidly and being more likely to metastasize.

The full picture of predisposing factors that might increase the risk of a chordoma developing is not clear. A large proportion of chordomas occur sporadically. Some genetic conditions might be associated with the development of the disease, but most patients who develop sporadic chordoma have a brachyury single-nucleotide polymorphism. In some families with multiple members who have chordoma (“familial chordoma”), a duplication in the brachyury gene is present. Furthermore, changes in either of two genes involved in tuberous sclerosis complex—TSC1 and TSC2—can cause a predisposition to developing chordoma.

As far as survival is concerned, the median survival in metastatic disease was described to be less than 12 months in a series of 28 chordoma patients. In nonmetastatic disease, the overall median survival was estimated to be approximately 6 years, with a 70% survival rate at 5 years that falls to 40% at 10 years.

Synchronous metastatic chordoma is rare. Badwal et al. reported a 36-year-old man who presented with multiple extraosseous intraspinal chordomas. Similarly, Ahmed and colleagues presented a case of synchronous clival and lumbar vertebral chordomas. Su and colleagues described cutaneous involvement by chordomas in 19 patients.

Breast metastasis from chordoma is extremely rare, but has also been previously described. In 2006, Tot described a metastatic breast lesion mimicking mucinous carcinoma in a 74-year-old woman with history of resected sacral chordoma 8 years earlier. Similarly, Gupta and colleagues reported a 51-year-old woman who presented with a breast lump 3.5 years after a primary diagnosis of chordoma. Fine-needle aspiration showed the classical physaliferous cells in a fibrillary background and anaplastic cells in magenta. Fine-needle aspiration biopsy was reported to be used for preoperative diagnosis of chordomas, with application of electron microscopy, histochemical, and immunocytochemical examination.

Our case involved a skull-base primary lesion and a synchronous breast metastasis. Maximum safe resection to the skull base and segmental mastectomy to the breast lesion were performed. Based on the natural behavior of chordoma, with its tendency to recur locally, aggressive treatment was implemented in a form of adjuvant radiotherapy which was delivered to both locations.

The cornerstone in the management of chordomas is maximum safe resection and radiation therapy. There is well-established consensus that adjuvant radiotherapy in the postoperative setting provides an added advantage. Because the tolerance doses to the spinal cord, brainstem, and cranial nerves are much lower than the effective dose required to treat chordoma, delivery of a high dose is limited. Treatment with conventional radiation therapy at doses of 40–60 Gy has led to 5-year local control rates of only 10%–40%. The most recent advances in radiation techniques have helped to achieve better tumour irradiation at higher doses, simultaneously with better protection of noble structures in the vicinity of the tumour bed.

In metastatic disease, many reports support wide local excision (metastasectomy) plus adjuvant radiotherapy, as for primary disease. Erkmen et al. reported successful treatment of recurrent chordoma and bilateral pulmonary metastases after surgery and adjuvant radiation for all locations.

The introduction of hadron therapy (protons or charged particles) has led to even higher dose escalation,
with minimum radiation-induced toxicities and improved radiobiologic effect. In terms of high relative biologic effectiveness and reduced oxygen-enhancement ratio in the tumour, hadron therapy provides biologic and physical advantages over photon therapy. Many studies have demonstrated the use of hadron therapy in chordomas of the skull base, cervical spine, and sacrococcygeal region, with local control at 5 years being 50%–60%, leading to uniform agreement that hadron therapy seems to be at least as effective as photon therapy. More specifically, carbon-ion radiotherapy has been considered for the treatment of unresectable chordomas. Using the stereotactic technique, proton therapy was able to deliver up to 74 Gy equivalents to the treatment volume.

SUMMARY

Chordomas are rare tumours of the skull base and spine. Synchronous presentation with a distant metastasis is even less common. Our review of the literature demonstrates the benefit of adjuvant radiotherapy to both the primary site and the metastasis.

CONFLICT OF INTEREST DISCLOSURES

We have read and understood Current Oncology's policy on disclosing conflicts of interest, and we declare that we have none.

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