A rare case of skin metastasis from a chordoma

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Abstract

Chordoma is an uncommon, indolent malignant tumor arising from notochordal remnants. The incidence of distant metastasis varies between 30 and 40% in different series. Even though local involvement of the skin by direct invasion of chordoma is common, distant skin metastasis are rare, with less than 30 cases reported in the literature. The present clinical case illustrates the slow-growing natural history of a sacral chordoma, which evolved with lung metastasis, followed three years later by skin metastasis, thus giving us the opportunity to review the diagnostic approach, as well as the clinical and histopathological characteristics of this rare tumor.

Keywords: chordoma, metastasis, skin

Introduction

Chordoma is an uncommon, indolent malignant tumor arising from notochordal remnants, which typically occurs in the axial skeleton and accounts for 1-4% of all bone tumors and approximately 20% of primary spine tumors [1]. In adults, 50% of chordomas involve the sacrococcygeal region; 35% occur at the base of the skull; and 15% are found elsewhere in the vertebral column. Although it is a slow-growing tumor, it presents with local aggressiveness and recurrence [2,3].

On gross examination, chordomas are gelatinous pink or gray masses with solid and cystic areas [2]. Histologically, chordomas are composed of lobules that contain epithelioid cells arranged in cords or clusters and separated by fibrous strands in a mucinous matrix. The tumor cells have vesicular nuclei and abundant vacuolated, soap bubble-like cytoplasm (physaliphorous cells) that contains glycogen (periodic acid-Schiff positive) or mucin.

These tumors can be classified into four different variants classical, choncroid, dedifferentiated, and sarcomatoid [1]. The histology is diagnostic, but immunochemistry also helps in the identification. Tumor cells in almost all chordomas are diffusely and strongly positive for cytokeratin (mainly AE). Staining for epithelial membrane antigen (EMA) is present in more than 80% of cases. Expression of brachyury, a key transcription factor in notochord development, appears to be a sensitive and specific biomarker of chordoma. Other immunostains are variable, such as vimentin or S100 protein [4,5].

The incidence of distant metastasis varies between 30 and 40% in different series [3]. The most common site of metastasis is the lung. Local involvement of the skin, by direct invasion of chordoma is common. However, distant skin metastases are rare, with less than 30 cases reported in the literature [1,6,7]. We present a patient with distant skin metastases from sacral chordoma.

Case Synopsis

An 85-year-old man, followed in the dermatology clinic because of a history of non-melanoma skin cancers, presented with a one-month history of a lesion on the left nasal pyramid base. Notably, he had a history of chordoma of the sacrum diagnosed in May 2016 at another institution, in the context of prolonged lower back pain. At the time, he was treated with surgical resection of the tumor followed by adjuvant radiotherapy (66Gy in 33 fractions to the tumor bed) since the margin negativity was not able to be determined. This was completed in November 2016. Four months later, he presented with several suspicious lesions on a lung X-ray and biopsy confirmed metastasis of the previously diagnosed chordoma. The case was discussed in a multidisciplinary tumor board and given the several comorbidities and absence of symptoms, the patient was put on surveillance. Moreover, he had arterial hypertension, dyslipidemia, type two insulin-dependent diabetes mellitus, stage three chronic kidney disease, chronic disease anemia, and gastritis. A dermatology consultant, noted a 20×9mm, erythematous and pseudocystic nodule at the left nasal base (**Figure 1**).

The nodule was excised and sent for histopathological evaluation which revealed skin involvement by metastasis whose morphology was very suggestive and compatible with the previously diagnosed and treated-chordoma of the sacrum (**Figure 2A**). The immunohistochemical (IHC) studies carried out revealed positivity for cytokeratins AE1/AE3, cytokeratins 8/18 (**Figure 2B**), EMA (**Figure 2C**), vimentin, and CD10; there was very focal positivity (-/+) for p63, negativity for cytokeratin 5, cytokeratin 7, cytokeratin 20, MOC31, p40, CD117, protein S100, melanA, PSA, HepPar1, and TTF1. Immunostaining with Ki67 exhibited extensive staining (**Figure 2D**). From this IHC study, it was noted that the metastasis was not positive for S100 protein, contrary to the original chordoma.

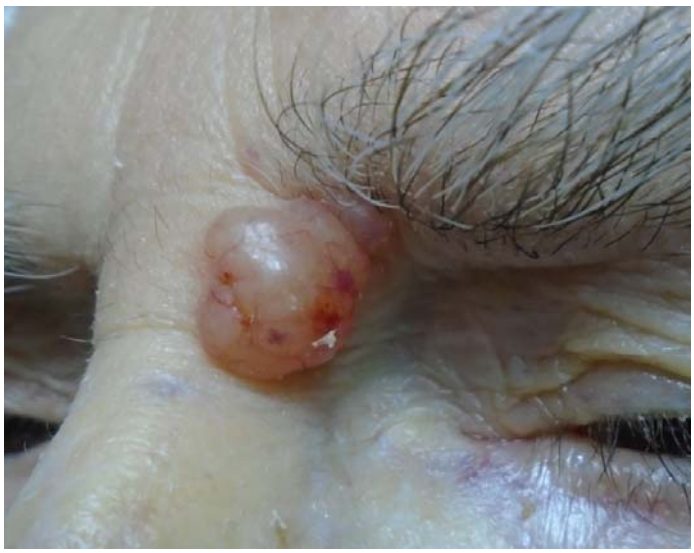

Figure 1. *Pseudocystic, erythematous nodule.*

At the next consultation, the patient exhibited a debilitated general condition, with Karnofsky performance score of 60%. On physical examination had multiple fixed and painful nodules on the lateral side of the left thigh and palpable lymphadenopathy (3cm) of the right cervical region three. At tumor board, supportive care was suggested.

Case Discussion

Chordomas are rare, low-grade, slow-growing, malignant neoplasms that remain asymptomatic until advanced stages when they present with locally aggressive behavior. Local skin involvement by chordoma is frequently described, but distant metastases are rare. A retrospective study that reviewed 207 cases of chordoma, found that 9%

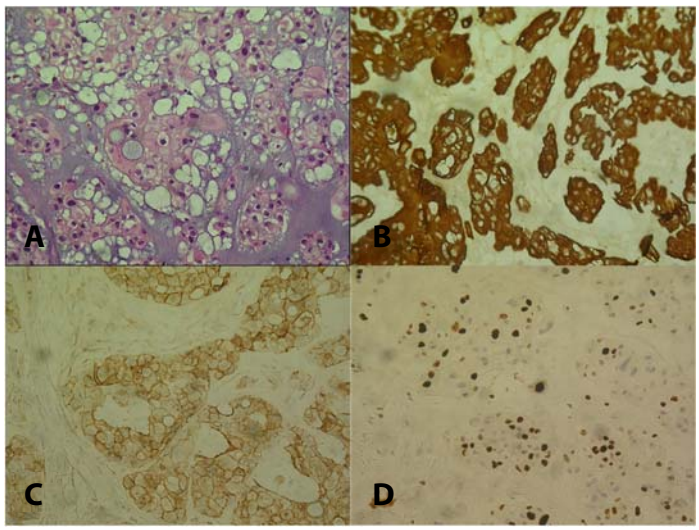

Figure 2. ***A)*** *Chordoma characteristic histology in hematoxylin and eosin staining with encapsulated groups of densely packed spindle-shaped fibroblasts cells, 100×.* ***B)*** *Positive immunohistochemistry staining for cytokeratins AE1/AE3, 100×.* ***C)*** *Positive immunohistochemistry staining for EMA, 100×.* ***D)*** *Immunohistochemistry staining for Ki67 that demonstrates high proliferation, 100×.*

(N=19) had skin involvement but only one case was related to distant metastasis [8].

Chordoma skin metastases present as reddish, firm, non-tender nodules of variable size, which tend not to ulcerate [9]. The most common locations are the face or back, but they may also occur on the scalp, trunk and extremities [7]. They usually occur in patients with advanced disease when metastasis in other sites, mainly the lung, are already present. Histologically, the chordoma metastasis shows the same histological features of the primary tumor. Immunohistochemistry of primary chordomas may show positivity for keratin, vimentin, S100 protein, EMA, and brachyury. However, most of the described skin metastases lose the reactivity to S100 protein [1,10].

Our patient presented with an erythematous and pseudocystic papule of unknown primary site and key IHC markers excluded metastasis from a second primary cancer. Cytokeratin 5, cytokeratin 7, cytokeratin 20, and MOC31 positivity would have suggested an adenocarcinoma metastasis. Negative melanA ruled out melanoma. Prostate-specific antigen, is essential in metastasis of unknown primary in all men. In addition, HepPar1 for hepatocarcinoma and TTF1 expression would favor pulmonary small cell carcinoma [11]. On the other hand, the skin metastasis expressed some of the chordoma characteristic markers as cytokeratins AE1/AE3, cytokeratins 8/18, EMA, and vimentin. In this way, the comparison of the skin lesion and the original chordoma tumor histology, together with the IHC studies were sufficient to reach the diagnosis of a chordoma skin metastasis; there was no need to carry out the characteristic brachyury immunostain. Brachyury is a useful marker for chordoma diagnosis, but other similar reports in the literature also did not perform brachyury IHC to confirm the diagnosis [12,13]. Therefore, dermatopathology findings were consistent with skin metastasis from a chordoma and were consistent with previous reports in the literature.

Surgical excision of the chordoma, as a single block, leaving the capsule intact and with negative margins is the treatment of choice and yields the best survival rate. In patients in which R0 margins can't be achieved, radiotherapy is the complementary strategy. There are few available options for systemic treatments. Cytotoxic chemotherapy is generally ineffective. Target therapy with inhibition of mTOR, EGFR, and MET have shown slight activity in the disease, with imatinib being the most used and promising agent [1]. In case of local or distant relapse, the approach is the same with surgery as the gold standard. The long-term prognosis of chordoma can be extremely poor and depends largely on the success of the primary surgery. Metastatic disease carries a 5-year survival rate of approximately 50%.

Our case shows the characteristically slow progression of chordoma malignant neoplasms, with metastasis to the lung and skin over the course of four years. The cutaneous lesions show similar histological features to the primary tumor. Our case also demonstrated the loss of S100 protein expression, as described in various literature cases.

Conclusion

Chordoma is a rare malignancy with few therapeutic choices. Distant skin metastases are infrequent, but should be considered in the differential diagnosis when new cutaneous lesions appear in a patient with a history of chordoma. Histology and immunohistochemistry are crucial in confirming the diagnosis and are usually concordant with the primary chordoma, except for S100 protein, which may disappear in the skin metastases. More studies are needed to understand the chordoma metastatic disease behavior and to improve treatment options.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Meng T, Jin J, Jiang C, et al. Molecular Targeted Therapy in the Treatment of Chordoma: A Systematic Review. *Front Oncol.*

2019;9:30. [PMID: 30775316].
2. Heffelfinger MJ, Dahlin DC, MacCarty CS, Beabout JW. Chordomas and cartilaginous tumors at the skull base. *Cancer*. 1973;32:410-20. [PMID: 4722921].
3. Vujovic S, Henderson S, Presneau N, et al. Brachyury, a crucial regulator of notochordal development, is a novel biomarker for chordomas. *J Pathol*. 2006;209:157-65. [PMID: 16538613].
4. Abenoza P, Sibley RK. Chordoma: an immunohistologic study. *Hum Pathol*. 1986;17:744-7. [PMID: 2424820].
5. Young VA, Curtis KM, Temple HT, et al. Characteristics and Patterns of Metastatic Disease from Chordoma. *Sarcoma* 2015;2015:517657. [PMID: 26843835].
6. Stacchiotti S, Sommer J, Ares C, et al. Building a global consensus approach to chordoma: a position paper from the medical and patient community. *Lancet Oncol*. 2015;16:e71-83. [PMID: 25638683].
7. McPherson CM, Suki D, McCutcheon IE, et al. Metastatic disease from spinal chordoma: a 10-year experience. *J Neurosurg Spine*. 2006;5:277-80. [PMID: 17048762].
8. Riesco-Martínez MC, Parrilla-Rubio L, Enguita-Valls AB, et al. A unique case of distant skin metastasis from chondroid chordoma. *JAAD Case Rep*. 2016;2:63-6. [PMID: 27051831].
9. Su WP, Louback JB, Gagne EJ, Scheithauer BW. Chordoma cutis: a report of nineteen patients with cutaneous involvement of chordoma. *J Am Acad Dermatol*. 1993;29:63-6. [PMID: 7686189].
10. Ruiz HA, Goldberg LH, Humphreys TR, Blacklock JB. Cutaneous metastasis of chordoma. *Dermatol Surg*. 2000;26:259-62. [PMID: 10759805].
11. Fizazi K, Greco FA, Pavlidis N, et al. Cancers of unknown primary site: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2015; 26 Suppl 5:v133-8. [PMID: 26314775].
12. Miettinen M, Wang Z, Lasota J, et al. Nuclear Brachyury Expression Is Consistent in Chordoma, Common in Germ Cell Tumors and Small Cell Carcinomas, and Rare in Other Carcinomas and Sarcomas: An Immunohistochemical Study of 5229 Cases. *Am J Surg Pathol*. 2015;39:1305-12. [PMID: 26099010].
13. Suarez Conde MF, Vallone MG, González VM, et al. Metastatic chordoma. *JAAD Case Rep*. 2019;5:852-854. [PMID: 31649971].