A rare case of cutaneous metastasis of distal phalanx chondrosarcoma

Catarina Correia[1] MD, Sónia Fernandes[1] MD, Paulo Filipe[1-3] MD PhD, Heinz Kutzner[4] MD PhD, Luís Soares-de-Almeida[1-3] MD PhD

Affiliations: [1]Dermatology Department, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte (CHULN), Lisbon, Portugal, [2]Dermatopathologie Friedrichshafen, Friedrichshafen, Germany, [3]Dermatology University Clinic, Faculty of Medicine, University of Lisbon, Lisbon, Portugal, [4]Dermatology Research Unit, Instituto de Medicina Molecular (IMM), University of Lisbon, Lisbon, Portugal

Corresponding Author Catarina Sofia Junqueira Correia, Hospital Santa Maria, Avenida Prof. Egas Moniz, 1649-028 Lisbon, Portugal, Tel: 351-21 780 5196; Fax: 351-21 795 4447, Email: catarinacorreia03@gmail.com

Abstract

Chondrosarcoma is the second-most common primary malignant bone tumor but chondrosarcoma of small bones of the hand is extremely rare, representing less than 2% of all cases, with exceedingly rare skin metastases. Cutaneous metastases of chondrosarcoma represent less than 3% of all cutaneous metastases. According to PubMed, there are only four previous case reports of cutaneous metastases originating from chondrosarcoma of small bones of the hand. We present an additional case of cutaneous metastases of phalangeal chondrosarcoma with a unique immunophenotype.

Keywords: bone, chondrosarcoma, metastases, neoplasms, skin

Introduction

Chondrosarcoma, a cartilage-forming neoplasm, is the second most common primary malignant bone tumor [1,2]. The most common sites of involvement—with a 50% prevalence—are the long tubular bones [2]. In contrast, chondrosarcoma of the small bones of the hand is extremely rare, representing less than 2% of cases. Chondrosarcomas of the small bones of the hand usually have low malignant potential, with rare concomitant skin metastases [1–4].

Case Synopsis

We describe the clinical case of a 71-year-old man with a previous history of chondrosarcoma of the proximal phalanx of the second left finger, without systemic involvement. The primary treatment consisted of disarticulation at the base of the second metacarpal with close follow-up monitoring by the orthopedic team. Two years after surgery, the patient was referred to the dermatology department for a 10-week history of disseminated cutaneous papules and nodules. The first cutaneous lesion appeared on the pulp of the distal phalanx of the first left finger. Further inspection revealed multiple pink exophytic papules and subcutaneous nodules scattered all over the integument, predominantly on the chest, abdomen, and buttocks (**Figure 1**). Skin biopsies revealed multiple intradermal nodules of pleomorphic chondrocytes (**Figure 2A**, **B**). Immunophenotypically, tumor cells were diffusely positive (nuclear stain) for MDM2, p53, p21, and

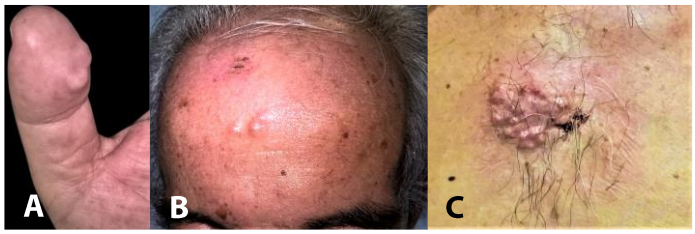

Figure 1. *Cutaneous metastases of phalangeal chondrosarcoma with multiple pink exophytic papules, subcutaneous nodules, and plaques, respectively, on the **A)** first left finger, **B)** forehead, and **C)** chest wall.*

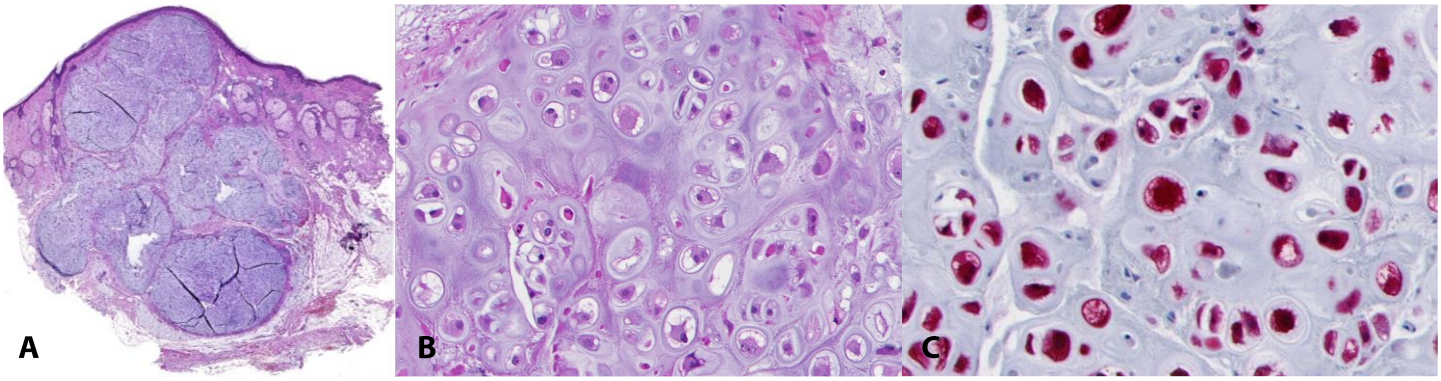

Figure 2. *Cutaneous metastasis of phalangeal chondrosarcoma.* ***A)*** *Asymmetrical exophytic tumor composed of multiple sharply circumscribed nodules with abundant hyaline matrix and atypical pleomorphic chondrocytes that vary in size and shape. H&E, 25×.* ***B)*** *There is no mitotic activity. H&E, 200×.* ***C)*** *Nuclear pleomorphism of atypical chondrocytes is highlighted by strong expression of S100 protein; the cytoplasm is mostly spared. S100 immunostain, 200×.*

FOSB. Additionally, there was mostly nuclear coexpression of S100 (**Figure 2C**) and concomitant negativity for SATB2 and p16. Proliferative activity (Ki67) was low; there was no detectable mitotic activity. Additional imaging studies revealed extensive pulmonary, hepatic, splenic, renal, mesenteric, and retroperitoneal metastases; there were multiple metastases in cutaneous/subcutaneous layers of the chest wall and buttocks. Clinicopathological correlation and imaging studies were consistent with the diagnosis of metastasizing chondrosarcoma. The patient succumbed to metastasizing sarcoma one month later.

Case Discussion

Chondrosarcoma commonly occurs between forty and sixty years of age, is more usual in men, and frequently arises from the pelvic bones. Clinically, local swelling and pain of long duration are the foremost symptoms. Radiographic findings are essential for primary diagnosis of the tumor, although magnetic resonance imaging and CT help delineate its extent [1].

Conventional chondrosarcoma of bone, as in the present case, comprises approximately 85% of all chondrosarcomas and can be categorized according to its location in the bone into primary central (85%), secondary peripheral (15%), and juxtacortical (periosteal) chondrosarcoma (1%). Central and peripheral chondrosarcomas are histologically identical.

Like the present case, conventional chondrosarcoma presents histopathologically, with a nodular tumor pattern composed of proliferating atypical chondrocytes with clumped chromatin. Hypercellularity and pleomorphism vary greatly and require pathological grading [5]. Grade I chondrosarcomas, as in our case, exhibit only a limited range of differentiation and pleomorphism and have low cellularity with an abundant hyaline cartilage matrix. A lobulated growth pattern is often recognized and lobules can be regularly shaped, varying in size. However, they rarely metastasize, contrarily to the case presented [2]. By contrast, grade II and III chondrosarcomas have an overall lobular configuration in which the tumor lobules permeate and entrap the pre-existing bone trabeculae. The tumor cells are embedded within the cartilaginous matrix, which can still be hyaline but often shows myxoid changes to a variable extent. The cellularity is higher than in grade I chondrosarcomas and mitoses are present. Nuclei vary in size with open chromatin and a visible nucleolus. Nuclear atypia can be present but is usually not severe. Binucleation can be seen and necrosis can be present, with metastases developing in up to 70% of patients [4,6].

Immunohistochemically, it may show a polyphenotypic profile, including expression of CD99 (if there is a small cell component), S-100 protein (in the cartilaginous component), and focal positivity for actin, desmin, myogenin, and neuron-specific enolase [7]. In this case, there was mostly

Table 1. *Reported cases of hand metastatic chondrosarcoma to the skin.*

Case [ref]	Gender; age (y)	Primary site	Skin metastatic sites; interval (months)	Follow-up; outcome
1 [2]	Male; 66	Middle phalanx (left middle finger)	Face, neck, trunk; 26	Unknown
2 [3]	Female; 41	Proximal phalanx (right thumb)	Frontal, trunk, abdomen; 68	2 months; died of disease
3 [2]	Female; 76	Metacarpal (fifth bone)	Forearm; 6	Unknown
4 [2]	Female; 40	Metacarpal (left thumb)	Upper arm; 11	2 years; died of disease
5 current report	Male; 71	Proximal phalanx (left second finger)	Frontal, trunk, abdomen, glutes; 24	1 month; died of disease

nuclear coexpression of S100. Immunostaining with actin, desmin, myogenin, and neuron-specific enolase were negative. Interestingly, tumor cells were diffusely positive (nuclear stain) for MDM2, p53, p21, and FOS-B. The p53/MDM2 pathway seems to be involved in 40–50% of chondrosarcomas and is correlated with aggressive behavior. Although MDM2 has been a helpful marker in liposarcomas, few studies have been done in bone tumors. In one study, 32% of chondrosarcomas exhibited nuclear positivity for MDM2 in 2–40% of tumor cells [8]. FOS-B is not generally expressed in chondrosarcomas. Lam et al. demonstrated a strong and diffuse nuclear staining for FOS-B in all osteoid osteomas (22/22), in 57% of the osteoblastomas (12/21), and in one case with reactive callus formation, as opposed to chondrosarcomas [9]. Finally, Hiraoka et al. discovered the p21 expression in low-grade, well-differentiated chondrosarcoma cells, as in our case [10].

The histopathological differential diagnosis should include metastasizing extraskeletal osteosarcoma, which is usually replete with neoplastic bone in conjunction with variably pleomorphic spindle or polyhedral cells that are cytologically atypical and mitotically active. Cutaneous variants of benign soft-tissue chondroma (extraskeletal chondroma) and its chondroblastoma-like variant are composed of mature, hyaline cartilage lobules with abundant matrix and groups of chondrocytes that may exhibit mild-to-moderate pleomorphism. There are no abnormal mitoses. Additional benign tumors that are relevant in the differential diagnosis comprise chondroid lipoma, which exhibit an abundance of mature adipocytes and the monophasic ("eccrine") variant of chondroid syringoma (mixed tumor of the skin). Remarkably, both tumor cells of monophasic chondroid syringoma and the adipocytes, as well as chondrocytes of lipomas and chondromas, are S100-positive leading to the conclusion that the immunophenotype of these tumors is either misleading or "nonspecific." Although immunohistochemistry does not help distinguish chondrosarcoma from other cartilage-forming tumors, it is helpful in distinguishing chondrosarcoma from chordoma, which expresses epithelial membrane antigen, cytokeratins, and occasionally, CEA [6].

Cutaneous metastases of chondrosarcoma represent less than 3% of all cutaneous metastases [4,11]. Chondrosarcoma metastases can be single or multiple and usually appear in the head and neck region. A PubMed review of published skeletal chondrosarcomas metastatic to the skin retrieved a total of nine cases [2]. Remarkably, only four of these were cutaneous metastases of chondrosarcoma originating in the small bones of the hand (**Table 1**), affecting patients aged 40 to 71. The time interval between primary diagnosis of chondrosarcoma and the first appearance of cutaneous metastases varied between 6 and 68 months (mean 27 months). Cutaneous metastases appeared in the face, neck, trunk, abdomen, and arms. Average time of death was 9 months after the first appearance of cutaneous metastases [1-6]. Even though typical chondrosarcomas of small bones of the hand rarely metastasize, these tumors must be closely monitored as metastases may occur many years after the primary diagnosis [2]. Surgical treatment is critical for survival and prognosis: wide and free resection margins are paramount for higher survival and lower recurrence rates [2-4]. Cutaneous metastases of chondrosarcoma herald an unfavorable prognosis: most patients succumb to

the tumor within 6 months after the first onset of cutaneous metastases [1,4].

Conclusion

This case emphasizes the importance of clinicopathologic correlation to confirm the diagnosis of cutaneous metastases and identify the origin of the primary tumor. Cutaneous metastases represent a sign of acute and evolving tumoral activity, requiring complete examination of the patient to identify the origin of the primary tumor and identify metastatic progress at other organ sites [4].

Potential conflicts of interest

The authors declare no conflicts of interest.

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