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Coexistence of secondary chondrosarcoma and lung carcinoma metastasis in the humerus of a patient with Ollier's disease: A case report

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ABSTRACT

Tumor-to-tumor metastasis in the same bone is an extremely rare condition. Limited number of case reports exists for coincidence of benign and malign neoplasms but none for malignant to malignant metastasis. Occurrence of several individual malignancies in the same patient may eventually cause such coexistences. We report an Ollier's disease patient with malignant transformation to chondrosarcoma complicated by a pathologic fracture and eventually whose pathological examination revealed that the lesion was not only the chondrosarcoma but an accompanying metastasis from existing lung adenocarcinoma. This report includes clinical, radiological, histological diagnostic challenges in an unexpected lesion and a review of literature.

Introduction

The coincidence of two distinct tumors in the same bone is a rare entity.[1] "Tumor-to-tumor metastasis" or "collision tumors" is a novel experience for the surgeons, although limited number of case reports defining the term tumor-to-tumor metastasis for coexistence of benign lesions with benign or malignant lesions have been published.[2–4] Ollier's disease is a rare, non-hereditary disorder, characterized by asymmetrical skeletal involvement with multiple enchondromas.[5–7] In approximately 40% of the patients with Ollier's disease solitary or multiple chondrosarcomas may develop during their lifetimes.[8,9] The metastasis of lung cancer to appendicular skeleton, especially to humerus is also rarely seen.[10–12] This report aims to define this tumor-to-tumor metastasis entity due to collision of a secondary chondrosarcoma, which developed from existing Ollier's disease and a lung adenocarcinoma metastasis in the humerus of a patient.

Case report

A 49-year-old Caucasian female attended to emergency service with pain, after a low-energy trauma to the left arm. Ecchymosis and deformity was evident in the lower two-third of the arm which raised the suspicion for a possible fracture. No neurovascular injury was evident.

The patient had the history of Ollier's disease which was diagnosed by detection of multiple enchondromas on both hands and mid-diaphysis of the left humerus at the age of 10 and followed-up annually since then (Fig. 1A–C). In May 2002, the patient had complained of hearing loss. The radiological evaluation revealed a mass on the left petrous bone and the patients had experienced wide resection of the left petrous bone with the diagnosis of low-grade chondrosarcoma, which developed secondary to enchondroma. In February 2013, with the complaints of palpable mass and pain in the left breast the patient was evaluated and diagnosed as having lobular breast cancer. The patient had undergone mastectomy and received postoperative chemotherapy. In May 2013 the patient was also diagnosed as primary lung adenocarcinoma during routine follow-ups and had been included in an additional chemotherapy regimen till July 2013. In August 2013, the liver metastasis from lung

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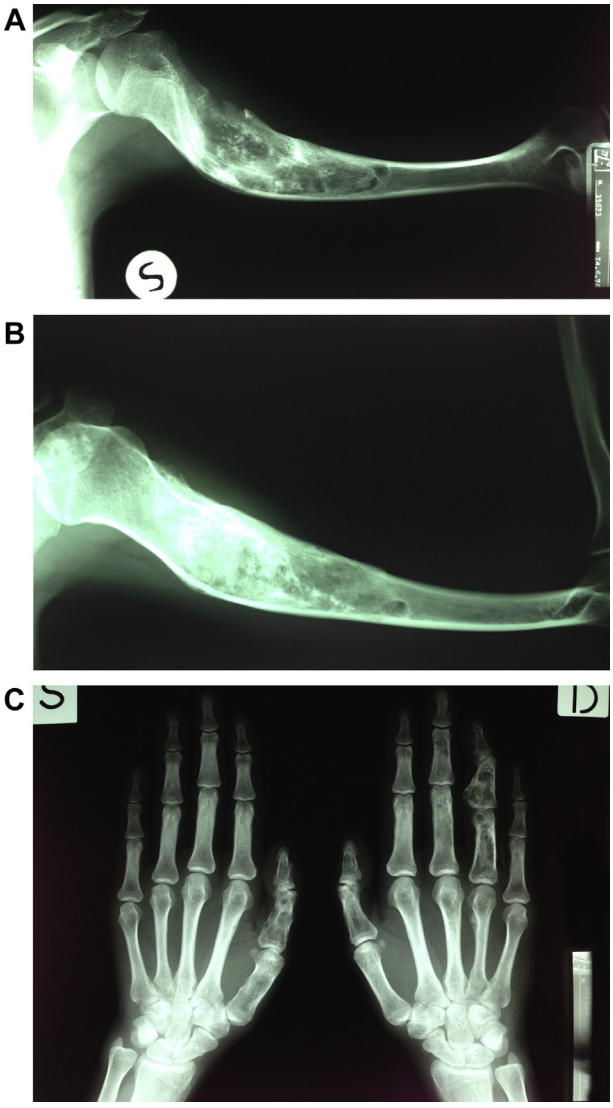

Fig. 1. A: AP X-ray view of the left humerus of the patient obtained 38 years ago. Note the deformity of the humerus and the irregularity of lateral cortex by a lesion with calcific matrix which occupies proximal two thirds of the medulla. The patient was decided to be followed up with the diagnosis of Ollier's disease. B: AP X-ray view of the left humerus of the patient obtained 20 years ago. The lesions matrix was more calcified and deformity was relatively corrected by the time, when compared with the X-ray of the humerus obtained 18 years ago. No malignant degeneration was detected. C: The AP X-ray view of both hands of the patient which was obtained at annual follow-up visits 20 years ago. Multiple lesions can be detected in phalanges and metacarpals.

adenocarcinoma was detected. The patient denied the history of any genetic disease and laboratory test results were within normal limits.

Anteroposterior (AP) and lateral radiograms of the left humerus revealed a pathologic fracture on a preexisting diaphyseal mass. The proximal half of the humerus was enlarged and cortical borders were thinned with a more lytic, and expansive lesion. A slightly oblique fracture line in the junction of proximal and mid-third of humerus with punctate cartilaginous calcifications was evident (Fig. 2A and B).

Further evaluations with CT indicated a 100 × 50 × 50 mm osteolytic mass with calcification and almost complete lysis of the medial cortex. An oblique fracture line with calcification brimming over the cortex was detected. A skip lesion was also evident just proximal to the lesion (Fig. 3 A and B).

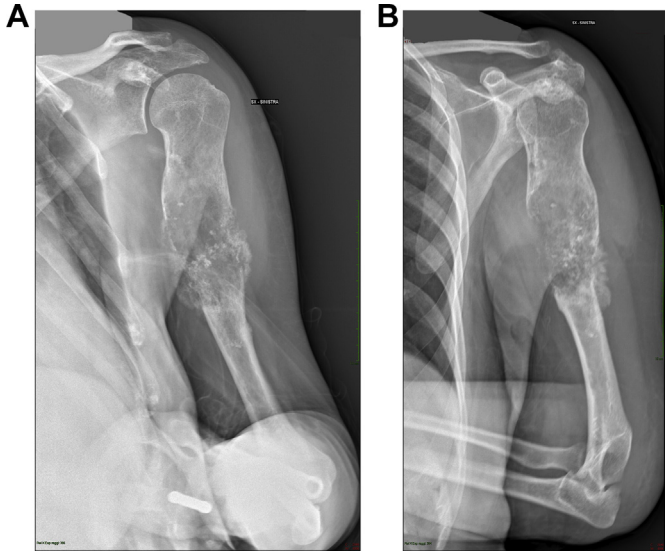

Fig. 2. A: The AP x-ray view of the left humerus of the patient at referral. Note the discontinuity in medial and lateral cortices between the proximal and mid-third of humerus. The matrix of the lesion demonstrates irregular punctate calcifications in the distal part. The proximal third seems more lytic without a transition zone. An oblique middiaphyseal fracture line is evident. B: The lateral X-ray view of the left humerus of the patient at referral. The anterior cortex is lytic. Posteriorly a sunburst-like calcification pattern which extends from the cortex is observed in the mid-third of humerus. The oblique fracture line can be detected at distal part of the lesion.

MRI revealed that the cancelous bone was replaced by a 100 × 50 × 50 mm, heterogeneous, hypointense, and parenchymal tissue-like expansile lesion on T1-weighted sequences. Necrotic areas were heterogeneously scattered throughout the lesion. A diffuse edema was evident in adjacent soft tissues, however neurovascular structures were free of edema. The proximally located skip lesion was evident in all MRI sequences (Fig. 4A–C). Overall, radiologically, a pathologic fracture secondary to a malignant lesion, which was highly suggestive of a secondary chondrosarcoma was detected. Conclusively, a wide resection and reconstruction with tumor endoprosthesis was planned.

The proximal 150 mm of the left humerus and overlying soft tissue were resected leaving wide margins intact, and sparing radial and brachial neurovascular bundles. The resected segment was reconstructed by a modular proximal humerus tumor endoprosthesis.

Macroscopic histopathological evaluation demonstrated the presence of a 100 × 50 × 40 mm cortical bone which contained a focal area of a grayish lesion (Fig. 5A). The skip lesion was indeed a small focus of enchondroma from Ollier's disease according to macroscopic evaluation. During microscopic examination a distinct Grade I/II central chondrosarcoma and surprisingly, a metastatic, poorly differentiated carcinoma with squamoid aspects and desmoplastic reaction around metastatic region were detected in this patient with Ollier's disease (Fig. 5B–D). The morphological comparisons between the previous biopsy specimens obtained from breast and lung carcinomas of the patient revealed that the metastatic focus originated from pulmonary adenocarcinoma (Fig. 5E). The surgical margins were negative.

At six weeks follow-up, the patient was radiologically stable, no sign of peripheral neurologic deficit was detected and the mobility of the left hand was preserved (Fig. 6). At 12 weeks the patient was hospitalized for lung adenocarcinoma by the oncologist and no chemotherapy or radiotherapy was administered.

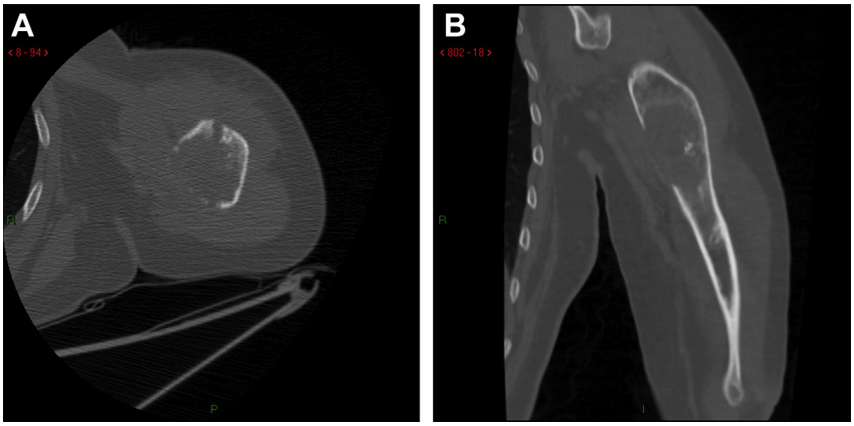

Fig. 3. A, B: CT views of the left humerus indicate a 10 × 5 × 5 cm lytic lesion which expands and thins the cortices of proximal half of the humerus. The lesion includes frequent calcifications in matrix distally and causes an almost complete cortical deletion of medial and posteromedial cortices in proximal and mid-third collisions. An oblique fracture line can be detected.

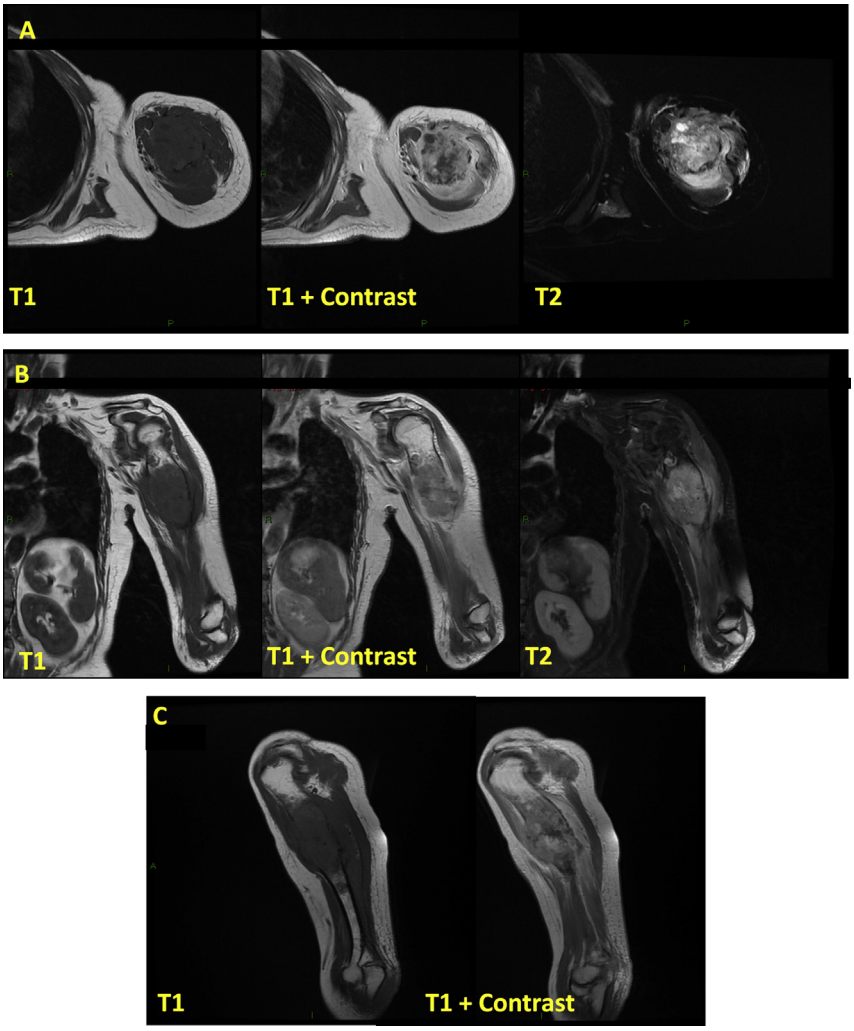

Fig. 4. The MRI of the left humerus exhibits a parenchymal tissue-like lesion which is heterogeneous, and hypointense in T1-weighted, and heterogeneous-hyperintense in fat suppression sequences. Numerous millimetric hypointense foci and necrotic-like areas are unevenly distributed throughout the lesion. Note the mid-diaphyseal diffuse edema effecting the fibers of triceps brachialis muscle which is highly suggestive of pathologic fracture. A possible skip metastasis like lesion is evident in proximal medial humerus with the same characteristics as the lesion.

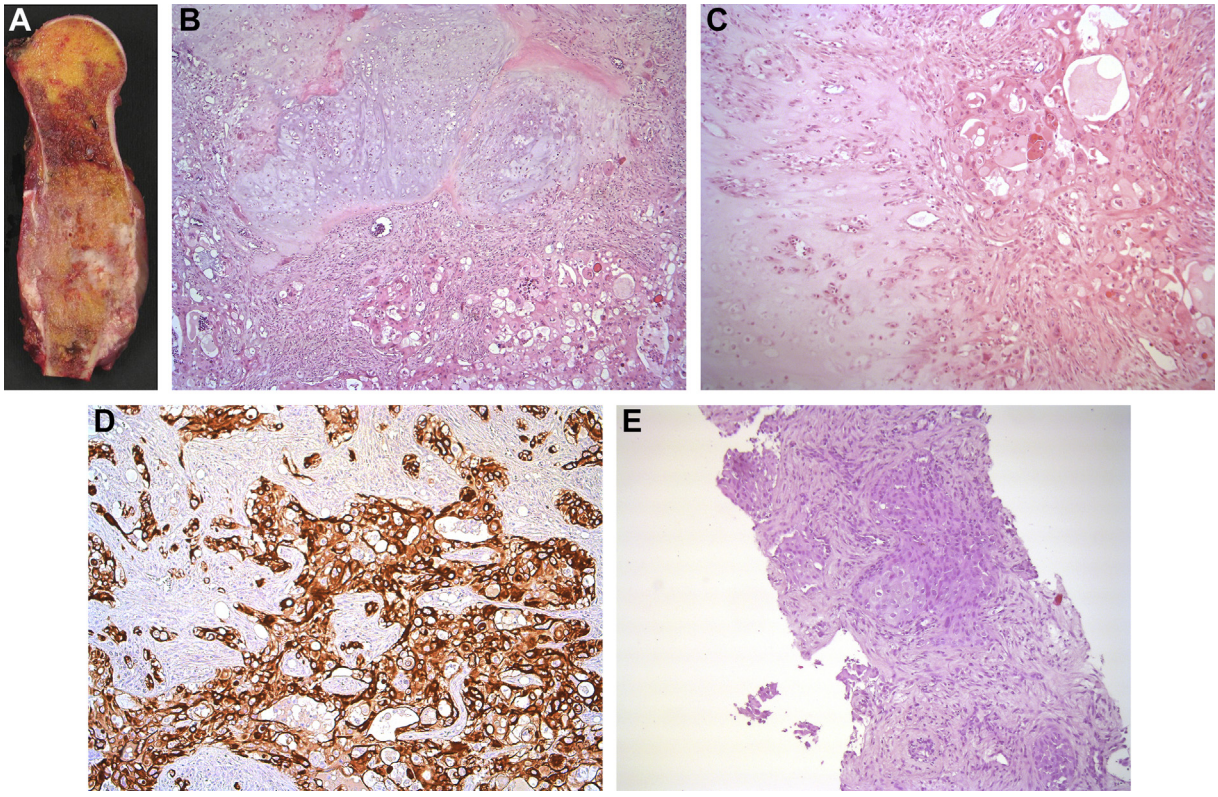

Fig. 5. A: The macroscopic view of the resected specimen. The coronal plane section at the level of midshaft demonstrates a heterogenous, grayish lesion, including a white foci of cartilage distally. The surrounding the bone is interrupted in different focal points by the soft tissue extension. B: The lesion in the humerus. A cartilaginous tumor with mild to moderate atypia and mixoid quality of the matrix which diffusely infiltrates the surrounding tissue. The tissue is neighbored to a proliferation of malignant epithelial cells which is growing in glands and solid nests. The lesion also demonstrates squamoid features and focal mucus production within a desmoplastic reactive stroma. These features are highly consistent with a metastatic cancer developed in a grade 2 chondrosarcoma on Ollier's disease (Haematoxylin&Eosin, 10x). C: The lesion in the humerus with higher magnification (Haematoxylin&Eosin, 20x). D: Cytokeratin 7 positivity in the metastatic cancer (10x). E: The previous biopsy from lung cancer. The proliferation of malignant epithelial cells growing in glands and solid nests, with squamoid features and focal mucus production which is set in a desmoplastic reactive stroma (Haematoxylin&Eosin, 10x).

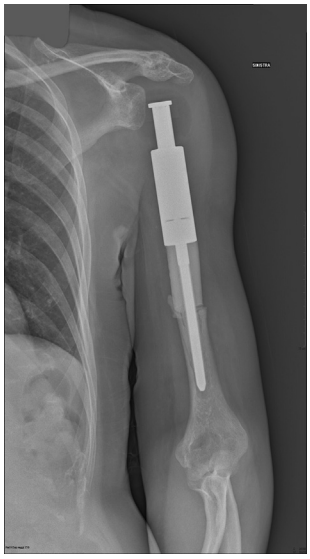

Fig. 6. Postoperative 6th week follow up AP x-ray of left humerus demonstrated no sign of allograft fracture or subluxation.

Discussion

Tumor-to-tumor metastasis was first reported by Fried et al in 1930 which included a case of bronchogenic carcinoma metastasizing into a meningioma.[13] Various case reports and series contributed to the literature concerning metastases of meningiomas or renal cell cancer into papillary thyroid cancers.[14,15] The definition of tumor-to-tumor metastasis and collision differs in terms, although both indicates coexisting lesions.[16] To name a lesion “tumor-to-tumor” or “cancer-to-cancer metastasis”; focus of the metastatic lesion must be at least partially enclosed by a histologically distinct host tumor tissue rim. Donor must be proven as a metastatic lesion (direct contamination by tumor is not accepted) and host lesion must be proven to be a true neoplasm.[16] The term “collision” on the other hand, defines two neighboring neoplasms that invade each other.[16] Our case can be clearly, and definitely defined as an example of tumor-to-tumor metastasis.

As far as we have known, tumor-to-tumor metastasis of bone has not been defined, yet., however; very few reports indicating benign with benign or with malignant bone neoplasms are available in the literature.[1–4]

Our patient had the history of Ollier's disease secondary to chondrosarcoma of the skull base. Additionally the patient had a preexisting, asymptomatic enchondroma component of Ollier's disease in the left humerus, which later demonstrated malignant differentiation to chondrosarcoma. One of the most severe complications in Ollier's disease is malignant transformation of enchondromas to secondary chondrosarcomas.[5–9] A recent multicentered study reported a 40% malignant transformation.[6] The authors have also concluded that lesions limited to hands and feet, have relatively low risk for malignancies (14%), when compared to involvement of long and flat bones (44%–50%).[6]

The MRI evaluation of our patient revealed two components on T2-weighted sequences, one with a high signal which was suggestive of cartilage and the other one with a low signal which was suggestive of a dedifferentiated tumor. The presence of multiple hypointense foci, corresponded to cartilaginous calcifications in the chondrosarcoma. Cortical erosions, soft tissue invasions, irregular surfaces and less mineralized matrices may be radiological signs of malignant transformation in Ollier's disease.[17] Dedifferentiated chondrosarcomas are characterized with a low or intermediate signal on T1-weighted, and a high-signal intensity on T2-weighted images with lytic areas, which are commonly associated with cartilaginous calcifications resulting in a bimorphic pattern.[18]

It is essential to determine whether tumor involvement in the humerus is primary or secondary.[19] Metastatic involvement progressively destroys the bone, and pathologic fractures of humerus are reported in 10% of the cases.[20] Breast cancer is the most common source of metastatic humerus involvement, whereas lung cancer metastases are rare.[11]

Posttraumatic pain was evident in our patient and a lytic metastatic lesion was observed. Bone metastasis develops in approximately 65% of lung cancer patients.[21] In a recent study concerning bone metastasis of lung cancer; vertebral involvement was found to be the most common location (42%), whereas, humeral involvement was reported to be the least (1%).[12] Pain is a more prominent feature of osseous involvement in lung cancer metastasis when compared to bone marrow involvement.[22] Adenocarcinoma subtype is more prone to bone marrow involvement.[23,24]

Histopathologically, enchondromas usually present as multiple oval-shaped or round cartilaginous nodules, which are well demarcated from the surrounding bone.[17] The cartilage matrix is usually solid, with myxoid changes.[17] Heterogeneity and cellularity in enchondromas depend on age and localization.[17] The conventional histological criteria for chondrosarcoma cannot be used in Ollier's disease due to its increased cellularity, thus a distinction between enchondroma and Grade I chondrosarcoma is almost impossible.[17] Briefly, the detection of cortical destruction, soft tissue extension with accompanying clinical and histological criteria may differentiate between an enchondroma and a grade I chondrosarcoma.[17] The surgery is reserved for pathologic fractures, deformities or malignant transformations in Ollier's disease.[6] Dedifferentiated chondrosarcomas histologically exhibit a low-grade, cartilaginous tumor juxtaposed to a generally high-grade, mesenchymal, noncartilaginous component. The dedifferentiated component is most frequently an osteosarcoma.[25] In our case it was difficult to exclude a dedifferentiated component of a chondrosarcoma but the spindle cell elements around the chondrosarcoma were mostly consistent with the desmoplastic reaction around the metastatic cancer, which was also present in the lung biopsy specimen taken in July 2013. The possibility of a metastatic sarcomatoid carcinoma with cartilaginous differentiation was ruled out by the presence of Ollier disease.

Conclusion

The Ollier's disease has a potential to develop malignancies without predilection of age. The patients with complaints of pain and swelling should be monitored carefully. Coexistence of benign neoplasms with benign or malignant bone neoplasms is extremely rare in the literature. Tumor-to-tumor metastasis is a novel entity for bone malignancies. When a radiologically and histologically unusual malignant bone lesion is detected in a patient with high risk of metastases, tumor-to-tumor metastasis of bone should be included in the differential diagnosis and treatment plan should be done accordingly.

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