Diagnosis of bone metastasis from thyroid carcinoma: a multidisciplinary approach

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Abstract
Sarcomas are rare tumors originating from soft tissue or bone. Diagnosis and treatment of sarcomas should be performed at specialized sarcoma centers, where patients are evaluated at a multidisciplinary tumor conference. We present a case where sarcoma was suspected from magnetic resonance imaging (MRI), but histology revealed a metastasis from thyroid carcinoma, although the patient had no previous history of thyroid malignancy and resection of the thyroid gland was without malignancy. Ultrasound-guided biopsy was possible due to cortical destruction and the multidisciplinary approach with re-evaluation of previous pathology and a thorough patient history enabled a final diagnosis.

Keywords
Ultrasound, biopsy, magnetic resonance imaging (MRI), skeletal – appendicular, thyroid, metastases

Introduction
Sarcomas are rare tumors deriving from skeletal, muscle, and connective tissue. The incidence of sarcomas is low (45 bone sarcomas annually and 220 soft tissue sarcomas annually) in Denmark, making metastases to the musculoskeletal system a far more common cause of bone or soft tissue tumors. In most patients suspected of sarcoma the initial imaging examinations are performed at their local hospital with conventional X-ray, ultrasound, and magnetic resonance imaging (MRI) and often the suspicion of malignancy is proven wrong (1). The patient is referred to a specialized sarcoma center if the suspicion of sarcoma remains after imaging, in Denmark 4–600 patients are referred annually. At the sarcoma center, patient history and all previous imaging are evaluated at a multidisciplinary conference with participation of orthopedic surgeons, radiologists, and a pathologist. If sarcoma is still suspected, biopsies and treatment are performed (2).

Case report
A 64-year-old man with possible fracture of the shoulder was referred to an X-ray examination of his left shoulder. The X-ray visualized an osteolytic tumor in the proximal part of the left humerus and destruction of the cortex at the greater tuberosity (Fig. 1a). Supplemental MRI showed a heterogeneous tumor of 4 x 6 cm, which was enhancing on the T1 sequences after contrast administration, and a periosteal reaction at the distal part of the tumor (Fig. 1b). The cortical destruction and the contrast enhancing areas in the bone by MRI may suggest malignancy. The patient was referred to a national sarcoma center where a thorough medical history revealed that the patient had undergone left sided hemithyroidectomy 2 years previously due to a 5 cm follicular adenoma. He also had a malignant melanoma excised 8 years earlier from his left upper arm.

A whole-body PET-CT confirmed the suspicion of malignant tumor in the proximal part of the left humerus and cortical destruction at the greater tuberosity (Fig. 1c). A fat layer separated the tumor from...
the surrounding soft tissue, indicating that the tumor was only located to the bone. The PET-CT also revealed a small lymph node at the angle of the left mandible, suspected of being malignant. It was impossible to perform a biopsy of the lymph node due to its small size and location. Instead an ultrasound-guided histological biopsy was performed from the tumor in the left humerus, where cortical destruction enabled the needle to pass (Fig. 2a). Histology revealed a carcinoma with morphology and immunohistochemical profile indicative of metastasis from the thyroid gland. The cells where characterized by abundant granular cytoplasm due to aberrant accumulation of mitochondria, which is a characteristic of oncocyes (3) (Fig. 2b).

Due to this, the patient underwent thyroidectomy of the right side and isthmus of the gland, excision of the lymph nodes on the right side of the neck, and excision of the PET-positive lymph node on the left side of the neck. None of the excised tissue did contain malignancy. Because the primary cancer originating from thyroid tissue had not been located, the 2-year-old resected left lobe of the thyroid gland was re-evaluated. It had identical cytomorphology and the same immunohistochemical profile as the specimen from the tumor in the left humerus. There was no histological evidence of malignancy in any of the samples of the 5cm tumor of the left thyroid lobe (Fig. 2c). The patient was referred to the department of oncology in order to start medical therapy.

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**Fig. 1.** (a) X-ray examination of the left shoulder in frontal projection. (b) MRI of the left shoulder in the coronal view (T1-weighted fat saturated sequence with contrast). (c) PET-CT of the left shoulder in the coronal view.

**Fig. 2.** (a) Ultrasound scan of the proximal part of the left humeral bone. (b) HE stained histological preparation with 400 times magnification from the thyroid metastasis. The oncocytary tumor cells were demonstrating solid growth, few follicular structures and were strongly positive to TTF-1. In the bottom of the picture bone destruction in the periphery is visualized. (c) HE stained histological preparation with 200 times magnification from the follicular carcinoma of the thyroid gland. The oncocytary cells are arranged in micro follicles with colloid in the lumen. There were no signs of ingrowth in the capsule or the vasculature.
Discussion

Oncocytary adenoma and carcinoma of the thyroid gland are considered variants of follicular adenoma and carcinoma (4). Minimally invasive follicular carcinoma is separated from adenoma by histological characteristics – growth through the capsule and/or invasion of the vasculature by neoplastic cells. It is impossible to perform histological examination of the whole capsule volume when the tumor is large. This means that a malignant part of a tumor may not be recognized histologically, which may lead to a false benign diagnosis. When a patient has an oncocyty tumor in the thyroid gland and a metastasis with the same morphology and immunohistochemical profile, the tumor in the thyroid gland should be regarded as malignant as long as there are no other tumors in the thyroid gland or in ectopic thyroid tissue (5).

In this case report the patient had a tumor excised from the thyroid gland by hemi-thyroidectomy, which was not classified as malignant histologically. The tumor of the thyroid gland was retrospectively re-evaluated and compared to the tumor in the proximal part of the left humerus. Because the two tumors had resembling cytomorphology and immunohistochemical profile it was concluded that the tumor of the left thyroid lobe was the primary site of the bone metastasis in the proximal part of the left humerus and thus a follicular carcinoma.

MRI visualizes bone tumors with a soft-tissue component and can guide the ultrasound-guided biopsy. An ultrasound-guided biopsy is a less extensive procedure than a surgical bone biopsy. By evaluating the imaging examinations, pathology, and clinical history at a multidisciplinary conference in a sarcoma center, the diagnostic strategy may be optimized as shown in this case. Multiple histological sections can be evaluated and a conclusion reached.

In conclusion, this case report illustrates the importance of multidisciplinary tumor conferences with presence of clinicians, radiologists, and pathologists in highly specialized centers.

Acknowledgements

The authors thanks the Department of Radiology, Rigshospitalet – Copenhagen University Hospital.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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