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A Peculiar Primary Paraganglioma of the Distal Thumb

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Abstract

A paraganglioma is a highly vascularized neuroendocrine tumor, most commonly found within the adrenal gland as a pheochromocytoma. Extra-adrenal paragangliomas, are frequently located in the head, neck, thorax and abdomen. We report the first documented case of a primary paraganglioma found within the appendicular skeleton. Only two additional cases of paragangliomas in the extremities have been documented, one in the soft tissue of the forearm and other within the median nerve. Our patient underwent amputation of the distal phalanx, with no sign of recurrence at greater than 1-year follow-up. Given the geographic and clinical similarity to a benign enchondroma, radiographic imaging alone may not be sufficient to rule out malignancies inside of bones. Thus paraganglioma should remain in the differential and immunohistochemistry is both vital and necessary to confirm the diagnosis. Vigilant and appropriate follow up is necessary to detect metastases early in these cases.

Keywords

Paraganglioma; neuroendocrine tumor; distal thumb

Introduction

Paragangliomas, also known as glomus body tumors, are neuroendocrine tumors of the chromaffin system, which are derived from neural crest cells called paraganglia. Those that present within the adrenal medulla are referred to as pheochromocytomas and account for approximately 90% of these tumors.¹ The extra- adrenal paragangliomas can arise within sympathoadrenal or parasympathetic paraganglia.¹ Sympathic paragangliomas can arise anywhere along the sympathetic chain, with the majority located in the abdomen. The parasympathetic ganglia derived tumors most commonly present in the neck and skull base.² In the past it was believed that chromaffin tissues did not exist within the human extremities. Presentations of extra-adrenal paragangliomas are rare, but the presentation of a paraganglioma in the appendicular skeleton, to the best of our knowledge, has only been documented twice in the literature. We present a case of a primary paraganglioma diagnosed in the distal phalanx of the right thumb. The patient was informed that data concerning the case would be submitted for publication and she provided informed consent.

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Case Report

A twenty-three-year-old female student presented with tenderness, swelling and slow-onset pain over a four-months duration along the distal aspect of her right thumb. She presented on account that the nail on her right thumb had clubbing, which she reported progressed over the past two weeks. Her history was negative for prior surgery, injection or therapy in her hand. She had no specific family history. Upon inspection there was a slight positive curvature of the nail. There was no pain aggravation upon palpitation. Radiographs revealed a mass in the bone.

Magnetic resonance imaging of the thumb showed a $2 \times 1 \times 0.2$ cm geographic lesion in the distal phalanx (Figure 1). The cortex appeared thin but intact and there was expansion of the medullary cavity. No soft-tissue extension, abnormal fluid, tendon or ligament damage was noted. The mass closely resembled a chondroid matrix lesion, likely to be an enchondroma by both the radiologist and surgeon.

The patient underwent thumb curettage and bone grafting with synthetic allograft. Pathologic evaluation of tumor material revealed poorly-differentiated, mostly rounded cells in nests, which appeared to grow mainly in the sheaths (Figure 2). Tumor cells (chief cells) were strongly and diffusely immunoreactive for synaptophysin and chromogranin A, and negative for pankeratin, epithelial (EMA, GFAP, SMA, Pax-8), and histiocytic markers (CD34, CD31). S-100 protein was focally positive with sustentacular cells. Hematoxylin and eosin staining suggested both metastatic well-differentiated neuroendocrine carcinoma (carcinoid tumor) or metastatic paraganglioma. However, no primary lesions were found under magnetic resonance imaging of the abdomen, chest, head and neck. The CT scan, octreotide scan, and PET were all normal and negative for distant disease. Biochemical markers including chromogranin A, serum metanephrine, CBC and CMP were normal and unrevealing. The patient had no evidence for active malignancy. A diagnosis of primary paraganglioma was made based on immunohistochemical and morphologic profiles.

After consultation with a tumor specialist, the patient underwent amputation of the distal phalanx of the right thumb (Figure 3). Post-operative urinary catecholamines were negative. Six months status post amputation of her distal phalanx of her right thumb, she received a PET CT of her full body and repeat MRI of her right hand which revealed no recurrence of disease or concern for metastasis. There was nonspecific low-grade uptake in the soft tissues surrounding her right elbow and MRI of this elbow revealed, synovial hypertrophy and joint effusion not consistent with malignancy. The patient continues to be closely followed by an orthopedic oncologist in the area where she has moved, she has no recurrence or health concerns.

Discussion

A paraganglia arising in the sensory-somatic nervous system within an extremity has been documented only twice previously in the literature.^{3, 4} Both cases describe a spontaneous paraganglioma development in the upper extremity. In 1996, Wang et al. described the first case in the literature of a primary malignant extra-adrenal paraganglioma in the forearm,

which was significantly larger than our patient's tumor. This forearm paraganglioma had metastasized to the lymph nodes, and was found to secrete neuronal hormones all unlike the smaller paraganglioma found in our patient.⁴ The only other case in literature was documented to be within the median nerve of a 22-year-old woman.³ Both patients presented with a solid, palpable mass after a period of progressively worse pain. No patient described in the literature has been found in the bone of the appendicular skeleton. Diagnosis was made based on histochemical analysis and microscopic appearance. Both patients were treated with surgical excision of the mass. Postoperatively, there was no recurrence in either case.

Paragangliomas are extremely rare and a vastly unusual diagnoses in the extremity. Radiographic imaging can provide non-specific guidance, and this neoplasm could be easily misdiagnosed as a benign enchondroma, a common primary tumor arising in the hand.⁵ Having an identical radiographic appearance. Enchondromas originates from cartilage and believe to be left as remnant inside the bone during development. Enchondromas most commonly presents in the proximal metaphysis of the proximal phalanx and produce cortex thinning and cortical expansion.^{6,7} Paragangliomas are similarly non-aggressive and geographic in appearance, but rarely appear inside a bone outside of the axial skeleton.^{8,9}

Due to the similarities with other tumors, immunohistochemistry is critical for diagnosis. Positivity of protein S-100, chromogranin A, and synaptophysin are considered confirmatory for the diagnosis.⁸ Extra- adrenal paragangliomas have been noted to have higher malignant potential than their intra-adrenal tumors counterparts and thus require clinical workup to rule out metastases.¹⁰ Our case serves as a reminder that clinical suspicion for malignancy is warranted in certain cases which would otherwise be assumed to be enchondromas. Malignancy masqueraded as enchondromas are only definitively rules out by pathologic evaluation of the specimen obtained at surgery. Vigilant and appropriate follow up may help to detect metastases early in the setting of paraganglioma.

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Figure 1.
Lateral, Oblique, and PA Pre-Operative Radiographs of the Right Thumb

Figure 2.
T1 and T2 Magnetic Resonance Imaging of the Thumb; reveals a $2 \times 1 \times 0.2$ cm geographic lesion in the distal phalanx. The cortex appears intact with expansion into the medullary canal.

Figure 3.
Immunohistochemistry: (a) H&E tumor 20×. (b) Chromogranin A 20× (c) Synaptophysin 20× (d)
S100 20×

Figure 4.
Amputation of the distal phalanx of the right thumb.