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Case Report

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Locally-Invasive Lytic Phosphaturic Mesenchymal Tumor of The C7 Vertebrae: A Case Report

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Abstract

Case: This case describes a primary, lytic, and locally-invasive C7 vertebral tumor. Pathology following operative removal demonstrated an intraosseous spindle cell lesion with features favoring an oncogenic phosphaturic mesenchymal tumor (PMT).

Conclusion: Extant literature review confirms the rarity of this tumor with only 300 - 450 reported cases(1,2). In this report, we review the case and follow-up, extant literature, and diagnostic imaging and treatment modalities for this rare clinical entity.

Level of evidence: Case Report; Review

Keywords: Phosphaturic mesenchymal tumor, tumor-induced osteomalacia, Case report

Introduction

Background

Phosphaturic mesenchymal tumors (PMT) are rare tumors of uncertain incidence **[1,3]**, occurring in acral soft tissues and osseous lesions of the appendicular skeleton **[1]**. PMTs may cause Tumor Induced Osteomalacia (TIO) via expression of fibroblast growth factor 23 (FGF23) and other phosphatonins **[4]**. FGF23 decreases renal phosphate re-absorption and intestinal phosphate absorption. Resultant secondary hyperparathyroidism mobilizes calcium and phosphate from bones leading to total body phosphate depletion and osteomalacia **[3,5]**.

Clinically, individuals present with vague symptoms including diffuse muscle and bone pain, weakness and stress fractures **[1,3]**. One 2022 systematic review of 895 cases of TIO caused by a mixed group of tumors (65% PMTs), found a diagnostic delay of longer than two years in over 80% of cases, with a fracture reported in at least 39% of all cases **[7]**. Malignant transformation of PMTs is uncommon; the majority of tumors are benign and curable via resection **[2,6]**.

Herein we report a patient diagnosed with osteomalacia due to an expansile lytic mass in the C7 vertebra, found to be a PMT. Surgical management was corpectomy and mechanical stabilization with postoperative endocrinology management in the setting of ongoing FGF23 secretion from residual tumor. Therapeutic options for persistent paraneoplastic FGF23 secretion are discussed.

Case Report

The patient was informed that data concerning the case would be submitted for publication and she provided consent.

History/presentation reduced to pertinent findings

On presentation, patient was a 69-year-old female with history of hypertension and tubular adenoma of the sigmoid colon six years prior. She denied alcohol or recreational drug use and quit smoking more than 30 years prior to presentation. Surgical history included remote cholecystectomy. She was active and worked at a group home for people with special needs. Home medications included albuterol and cetirizine for a dry cough, lisinopril and verapamil for hypertension, a multivitamin, and omega-3 fatty acid. Family history was significant for a mother with ovarian cancer, a son with melanoma, sister with immune thrombocytopenia, younger sister with Down syndrome who passed at age 48 from a cardiac issue, and older half-brother with early onset Alzheimers (age 65).

Prior to presentation, she noted approximately five years of intermittent left rib pain with no clear inciting or alleviating factors. She had also complained of intermittent left knee pain with no fracture or dislocation and minimal osteoarthritis on radiologic evaluation (X-ray). She had no other prodrome.

Five months prior to presentation, she experienced bouts of severe intermittent abdominal pain, worse on the right, for which workup, including an abdominal computed tomography (CT) scan, surveillance colonoscopy, and abdominal ultrasound (US), was unrevealing. Cutaneous nerve entrapment was suspected and a

referral placed for abdominal wall lidocaine and steroid injection, which she declined.

On intake presentation to the emergency department (ED), she complained of acute right-sided rib and shoulder pain, worsened with movement.

Pertinent physical examination

The patient was pleasant, well groomed, and communicative. She appeared fit and healthy with a body mass index (BMI) of 26. Her vital signs, including temperature, pulse, respirations, and oxygen saturation were within normal limits. Her blood pressure was elevated to 167/95, and she described a history of white-coat hypertension. She was breathing comfortably on room air. She denied bowel or bladder incontinence and gait instability.

To bilateral upper extremities, skin was intact and with sensation grossly intact to median, radial, and ulnar nerve distributions. Radial pulse was palpable and fingers were warm and well-perfused. To bilateral lower extremities, sensation was intact grossly to deep peroneal, superficial peroneal, tibial, and sural nerve distributions. Dorsalis pedis and posterior tibial arteries were palpable and toes were warm and well-perfused. The spine was nontender to palpation along spinous processes and paraspinal musculature. She had a negative Hoffman's, no clonus, no saddle anesthesia, and intact rectal tone and perineal sensation. Motor nerve roots and dermatomal sensation was tested and found to have 5/5 strength bilaterally. Reflex exam was normal (2/4) to biceps, brachioradialis, triceps, quadriceps, and gastrocnemius/soleus muscles bilaterally.

Laboratory values, including complete blood count and basic metabolic panel were within normal limits with the exception of low phosphorus to 0.9 mg/dL (reference 2.2 – 4.5 mg/dL), hypocalcemia to 8.5 mg/dL (reference 8.8 – 10.2 mg/dL), decreased C-terminal assay for parathyroid hormone-related peptide (PTH-RP) to 8 pg/mL (reference 11 – 20 pg/mL) **[8]**, and mild elevation in parathyroid hormone to 66.6 pg/mL (reference 15.0 – 65.0). Alkaline phosphatase (ALP), 25-D, and 1,25-D were within normal limits.

Radiographic findings

A CT of the cervical spine with contrast demonstrated an expansile lytic mass in C7 **(Figure 1)**, an age-indeterminant fracture of the posterior left first rib and multiple small long nodules measuring up to 6 mm. Pre-contrast magnetic resonance image (MRI) re-demonstrated the C7 lesion with lateral epidural extension and mild spinal canal stenosis without cord compression **(Figure 2)**.

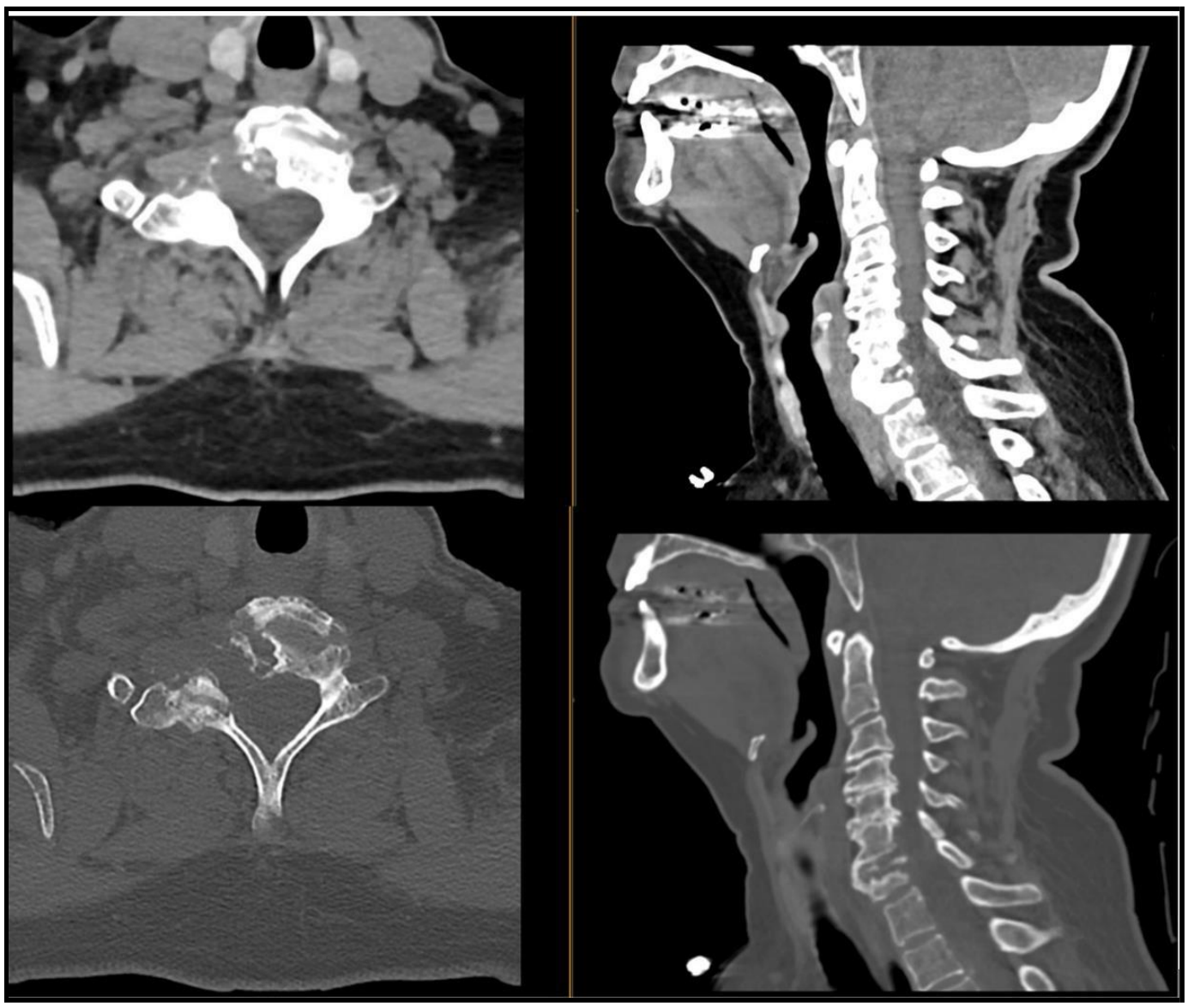

Figure 1: Sagittal and axial slices of CT cervical spine without IV contrast demonstrating lytic lesion measuring up to 3.5 cm in transverse dimension with the epicenter at the right C7 pedicle. Soft tissue components extended to adjacent right C6-C7 neural foramen and lateral epidural soft tissues. Included are bone (panel one) and soft tissue (panel two) windows.

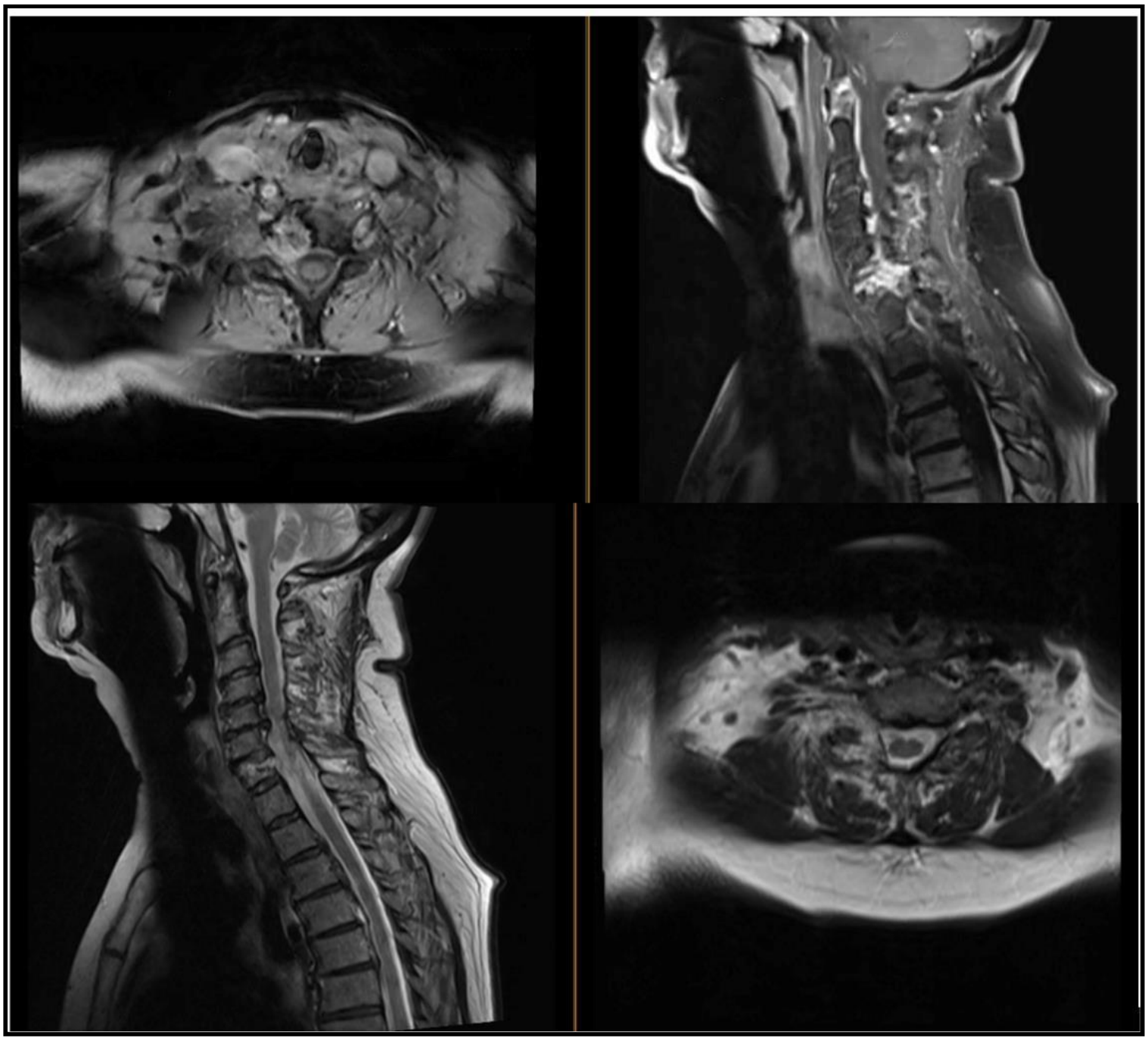

Figure 2: T2-weighted (panel 1) and T1-weighted (panel 2) magnetic resonance imaging (MRI) sagittal and axial cuts of the cervical spine demonstrating an expansile lesion at the right aspect of C7 with involvement of the right aspect of the vertebral bodies, pedicle, lateral mass, transverse process, and lamina, measuring 2.9 x 2.1 x 3.7 cm. Noted is right lateral epidural extension, resulting in mild spinal canal stenosis, without cord compression. Extension to the right neural foramina at C6-C7 and C7-T1 is noted.

Initial Management

The patient was started on PhosNaK 250 mg QID and calcitriol 0.5 mcg BID. Wide margin resection was not possible due to location. Distant metastases were unlikely based on slow clinical progression and absence of DOTATATE-uptake outside of the C7 tumor. As such, she underwent posterior C6 to C7 laminectomy and decompression, C2 – T2 posterior fusion, and biopsy of the right C6 – C7 foraminal tumor. She was extubated in the operating room, observed to be grossly moving bilateral upper and lower extremities, and transferred in a cervical collar to the intensive care unit to maintain mean arterial pressures (MAP) greater than 85 mm HG for 24 hours, then transferred to the surgical floor on postoperative day 1. She was discharged to short term rehab on postoperative day 11 in a hard cervical collar, and discharged home from rehab on postoperative day 15.

Pathology and Diagnosis

Pathology demonstrated a benign intraosseous spindle cell lesion with features favoring an oncogenic phosphaturic mesenchymal tumor **(Figure 3)**. Mitotic activity was not observed. Tumor cells were noted to diffusely express SATB2 and variably express CD56 **(Figure 4)**, which coupled with low serum phosphate values favor phosphaturic mesenchymal tumor.

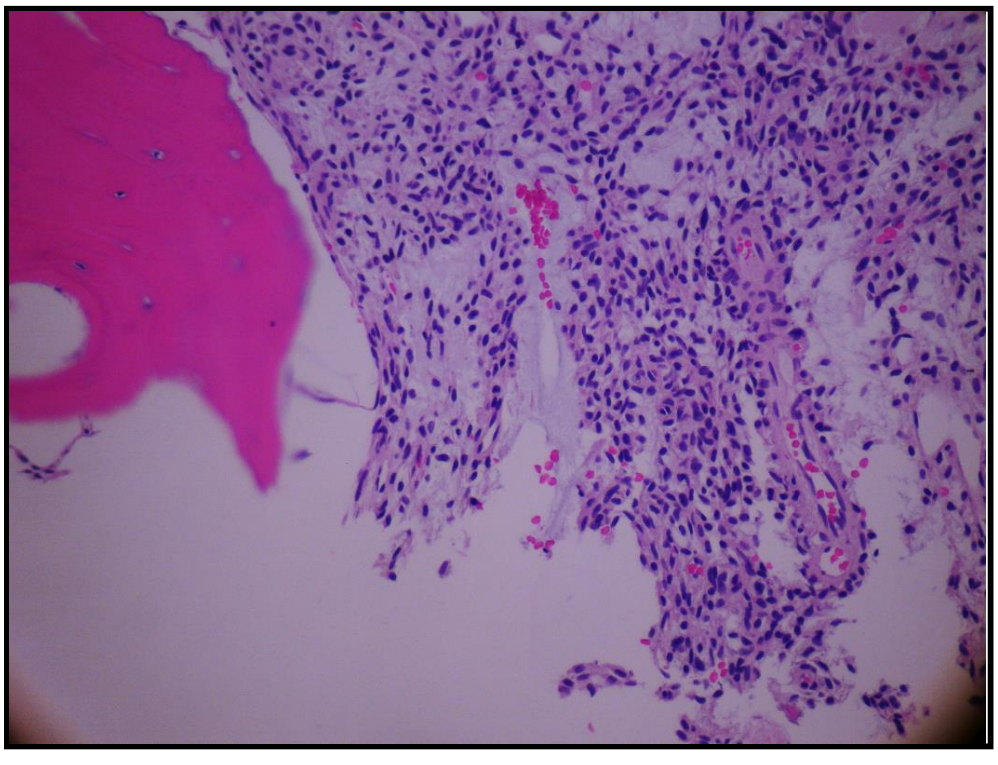

Figure 3: Microscopic slides of fresh frozen section of cervical tumor cut at 5 microns with hematoxylin and eosin (H&E) staining. To left of the field (pink) bone is observed with tumor to the right. The tumor consists of a cellular infiltrate of short, cytologically bland spindled cells with an accentuated capillary vascular element and a very focal myxochondroid matrix. Mitotic activity is not observed. Pictured are spindle cells (elongated dark purple), accentuated capillary vascular element (bright red blood cells contained within capillaries), and myxochondroid matrix (lighter purple, "fluffy" in quality)

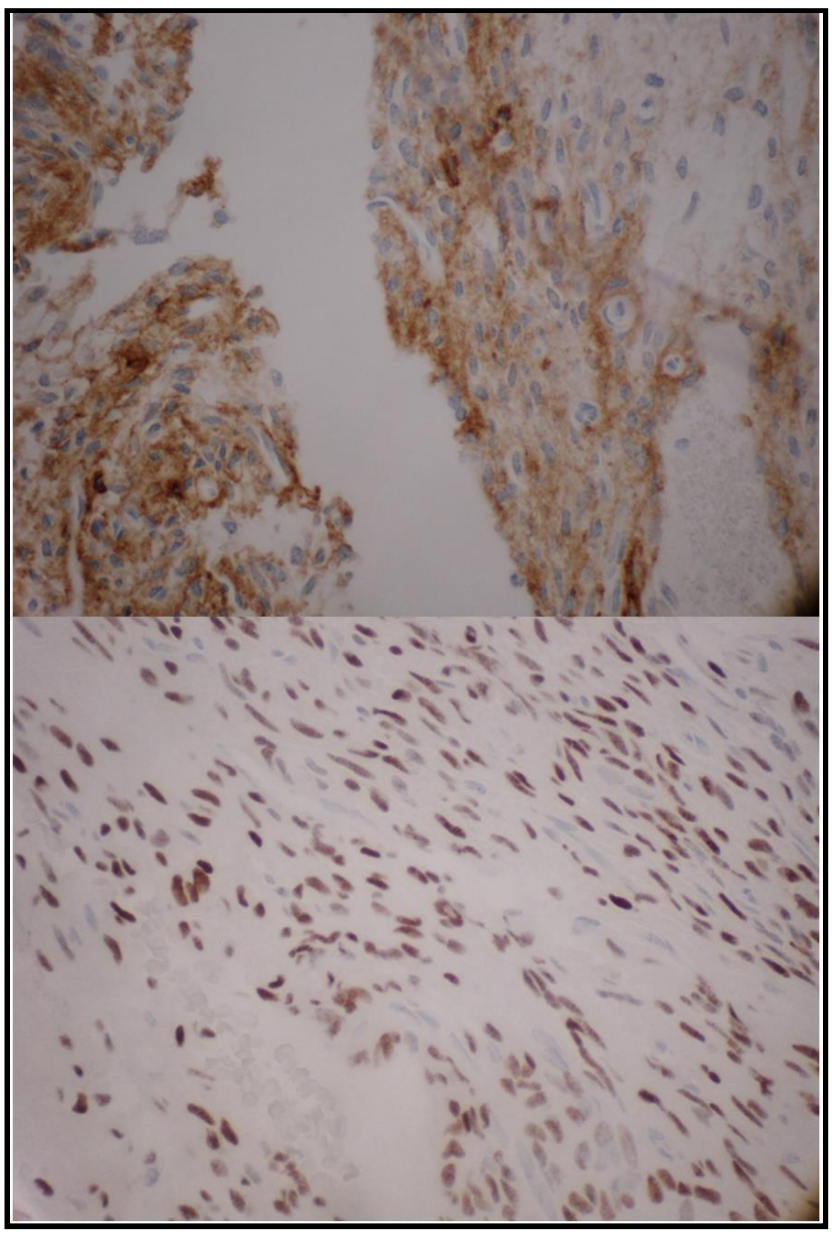

Figure 4: Microscopic slides of fresh frozen section of cervical tumor cut at 5 microns with immunoperoxidase SATB2 stain (left) and CD56 stain (right). In this stain, brown demonstrates antigenic presence, or a "positive" stain demonstrating that these tumor cells diffusely express SATB2 and variably express CD56.

Definitive Management and Follow-Up

One month out from index surgery, the patient underwent anterior cervical corpectomy of C7 with diskectomy of C6 to C7 and C7 to T1, with anterior fusion of C6 – T1 via cervical cage and iliac crest autograft. Representative intraoperative fluoroscopic images **(Figure 5)** and postoperative computed tomography (CT) scan **(Figure 6)** are included. Postoperative pathology of C6-C7 and C7-T1 discs

(adjacent to tumor pathology) demonstrated no evidence of tumor. The patient was discharged on postoperative day two to acute rehabilitation, and returned home on postoperative day five with home health care services.

Postoperative laboratory studies suggested persistent tumor-induced osteomalacia (TIO) with phosphorus decreased to 1.8 mg/dL (reference range 2.2 – 4.5 mg/dL), calcium decreased to 8.5 mg/dL (reference range 8.8 – 10.2 mg/dL) and fibroblast growth factor 23 (FGF23) elevated to 105 pg/mL (reference less than 59 pg/mL). Tumor resected from the patient's second procedure were sent for special FGF23 antibody from Novus (# MAB26291) which confirmed residual tumor FGF23 secretion **(Figure 7)**. Supplementation with PhosNaK 250 mg four times daily and calcitriol 0.5 mcg twice daily initiated with normalization of phosphorus to 3.4 mg/dL, 2.5 mg/dL, and 3.1 mg/dL (reference range 2.2 – 4.5 mg/dL) and calcium to 9.9 mg/dL, 9.5 mg/dL, and 9.7 mg/dL (reference range 8.8 – 10.2 mg/dL) on 3, 6, and 12-month outpatient follow-up respectively.

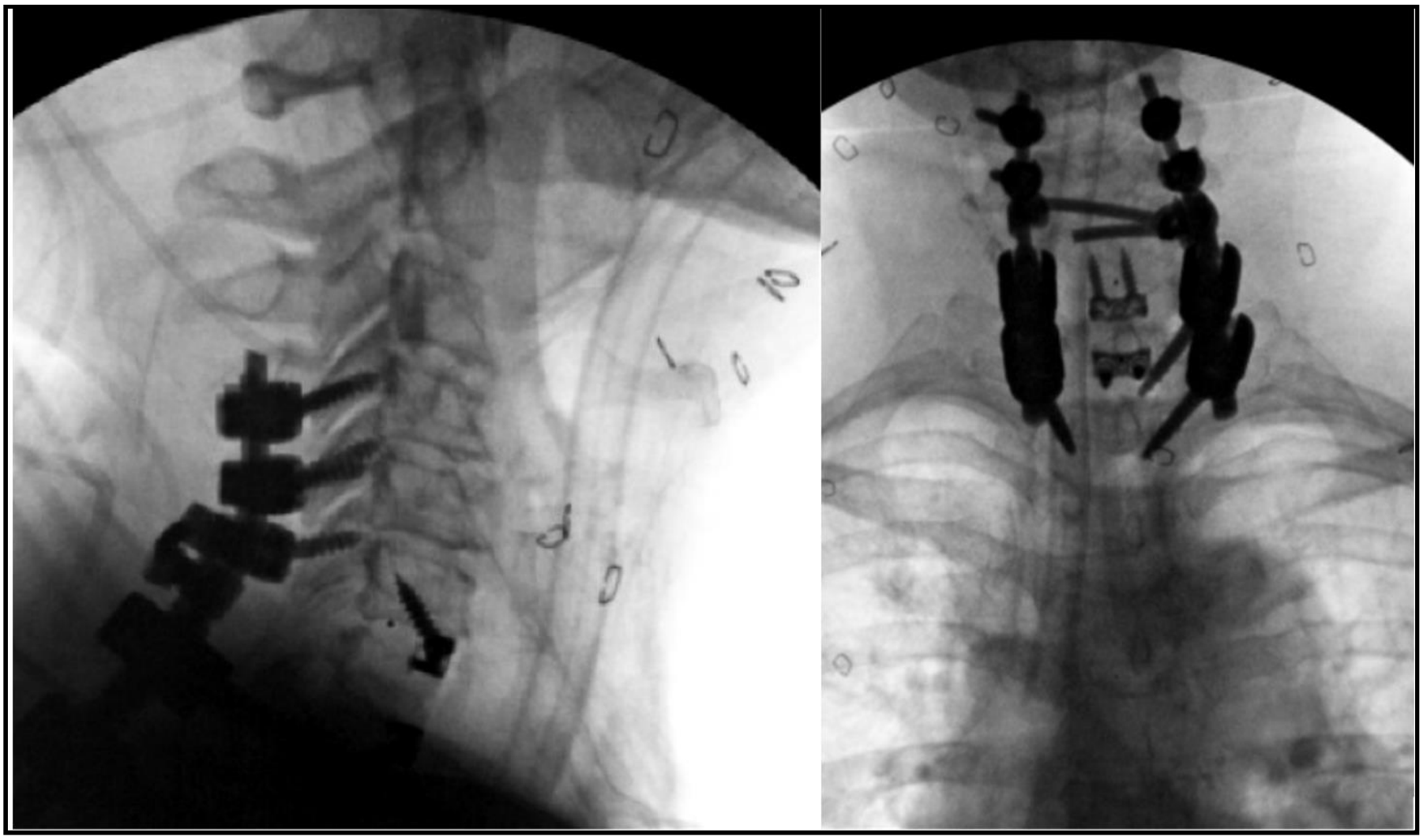

Figure 5: Antero-posterior and lateral intraoperative fluoroscopic images of cervical spine with demonstrated posterior instrumented fusion of C4, C5, C6 and T1, T2 and anterior interbody cage at C7

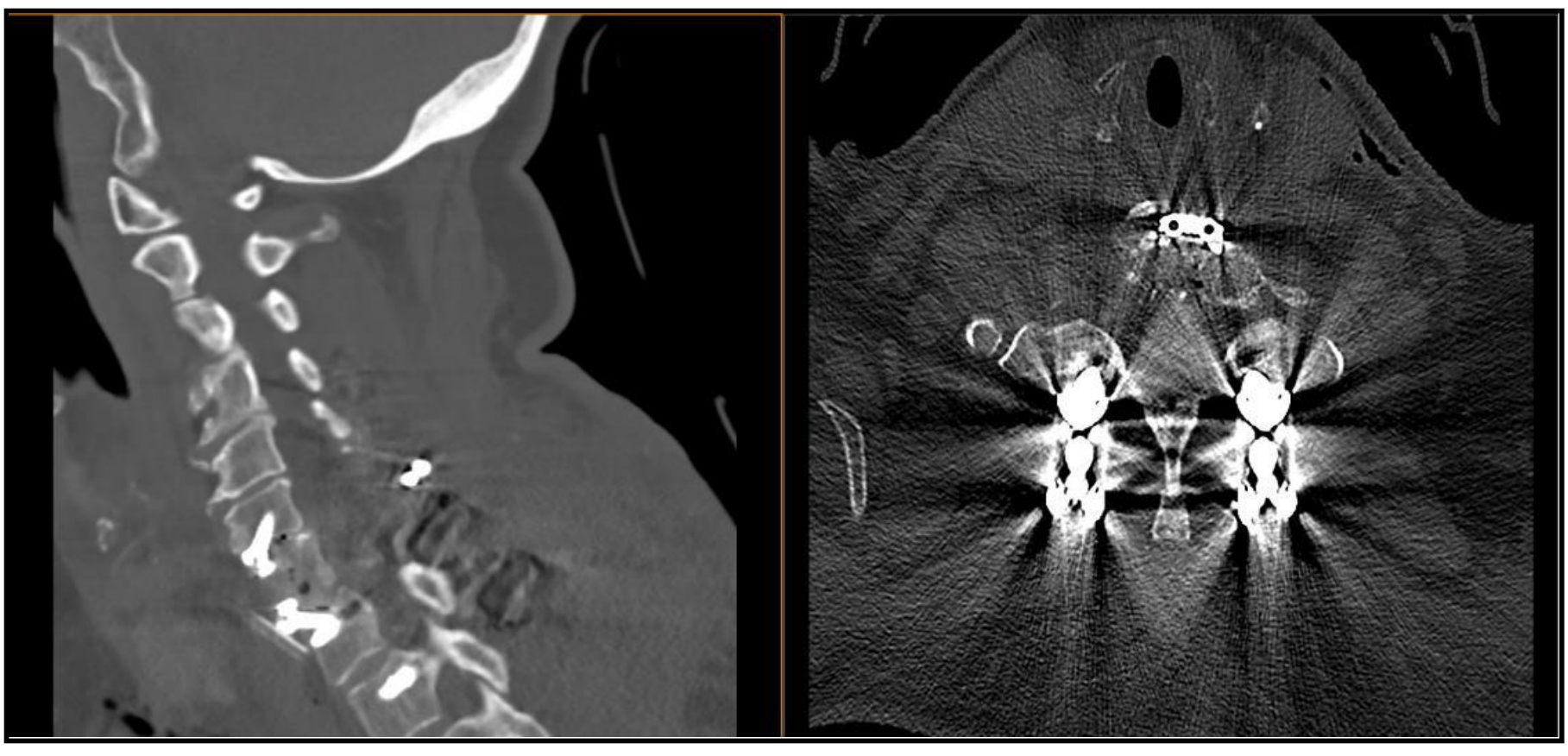

Figure 6: Postoperative computed tomography (CT) scan of patient cervical spine with sagittal (left) and axial (right) cuts demonstrating anterior interbody cage placement at C7. Incompletely appreciated on these thin slices is posterior instrumented fusion of C4, C5, C6 and T1, T2

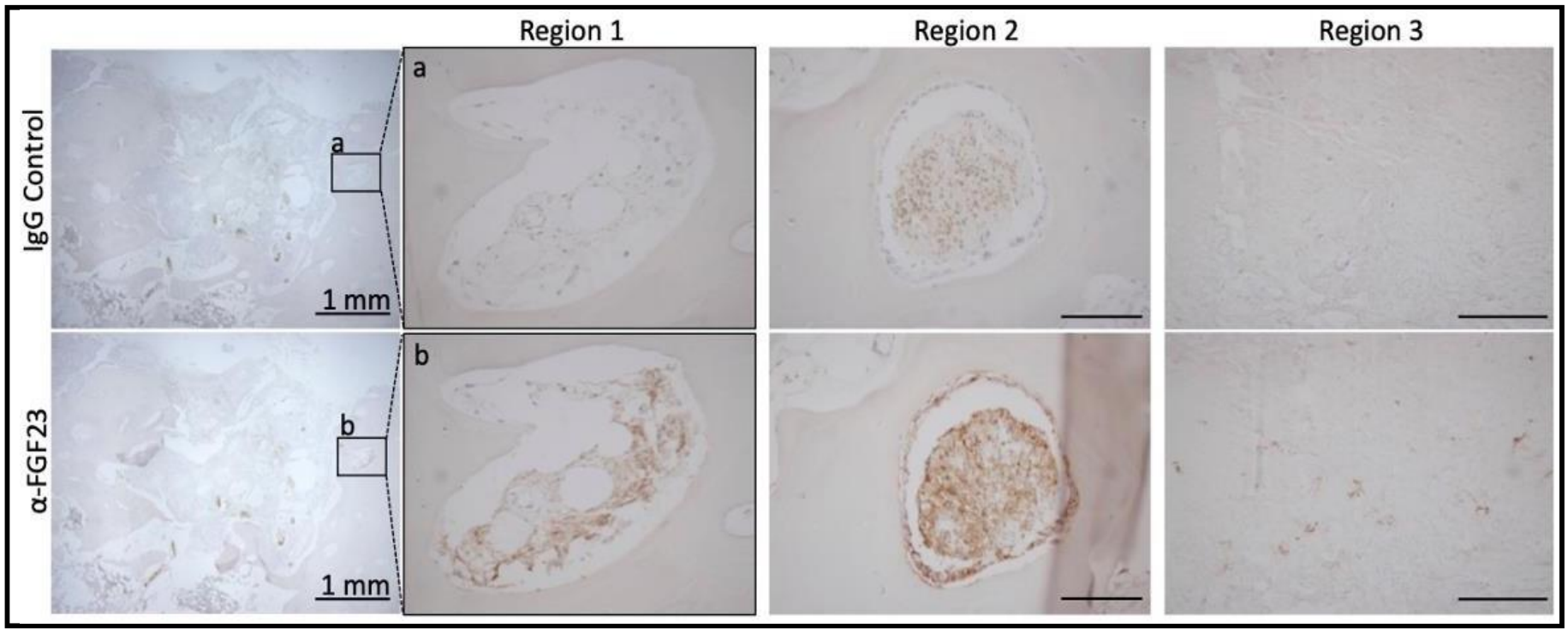

Figure 7: Figure #: FGF23 staining of the tumor. The bulk of the tumor is negative for FGF23, but foci adjacent to the main tumor are strongly positive. Three discrete regions of the biopsy are shown. Panels "a" and "b" highlight the same region in high resolution. Bar = 1 mm in low resolution image. Bar = 100 micrometers in high resolution images

Discussion

Herein we present the case of a 70-year-old woman, who presented aged 69 with a rare phosphaturic mesenchymal tumor (PMT) in C7. Pathology findings of CD56 and SATB2, radiologic findings of a C7 lytic lesion, insufficiency rib fracture, laboratory values of phosphorus depletion, elevated vitamin D and FGF23, and tumor FGF23 secretion on antibody staining are highly suggestive of PMT **[7,9]**. Due to tumor location at C7, wide margin resection was not possible; definitive management consisted of local resection and stabilization. Postoperatively, the patient continues on phosphate supplementation and calcitriol **[12]**. Positron emission tomography (PET) scanning was unrevealing for local recurrence or metastatic disease at the one-year postoperative mark. Ongoing long-term recurrence surveillance will continue.

Like the majority of presented cases **[1,11]**, this patient's nonspecific symptoms of fatigue, pain, and musculoskeletal weakness did not localize to the tumor region, and was likely contributory to the delay in her diagnosis. Advanced imaging (CT scan) ultimately prompted diagnosis **[13]**.

When possible, definitive management of PMTs is wide margin resection, typically resulting in complete resolution of TIO symptoms and bony remineralization **[14]**. In some cases symptom resolution, including normalization of FGF23, was observed as early as postoperative day three(14), with serum phosphate normalizing by postoperative day five(15). In our patient, elevated FGF23 and serum phosphate remained elevated two months postoperatively, necessitating ongoing medical management, including PhosNaK supplementation and calcitriol(16). Other therapies in development for the medical treatment of TIO include anti-FGF-23 antibody, which has shown to be safe and effective in X-linked Hypophosphatemic rickets, another FGF-23-related hypophosphatemic disorders **[17]**.

Conclusion

The finding of a phosphaturic mesenchymal tumor localized to the C7 vertebral body in a patient with primary complaint of right upper quadrant abdominal pain is a rare, but a typical diagnostic for the chameleon of Tumor Induced Osteomalacia (TIO) **[1]**. Paraneoplastic osteomalacia from FGF23 secretion may result in bone pain and stress fractures, such as the rib fractures observed in this case. Primary metastasis is unusual and local invasion is a characteristic feature of PMTs. Wide-margin resection may be curative, but careful follow-up important given resection limitations imposed by surrounding anatomical structures. Long-term calcitriol and phosphate supplementation may be necessary in addition to local recurrence surveillance.

Declarations

Ethics approval and consent to participate

The patient provided verbal, informed consent. This case report does not have a formal IRB.

Consent for publication

The patient provided verbal, informed consent for publication. The authors consent to the publication of this manuscript.

Availability of data and material

Corroborating de-identified material may be made available on request from the corresponding author.

Competing interests: The authors have no competing interests to declare.

Funding: This project received no funding.

Authors' contributions

CD participated in data collection, project conception, original draft writing, and draft editing. CB participated in data collection, project advising, and draft editing. TP participated in data collection and draft editing. JF participated in data collection and draft editing. SJ participated in data collection, patient interaction, and draft editing. JY oversaw the project, provided project guidance, performed patient interventions, and performed project conception and draft editing.

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We would like to acknowledge the patient who consented to have their de-identified information disclosed in this manner.

List of Abbreviations

BMI: body mass index

CT: computed tomography

ED: emergency department

FGF23: fibroblast growth factor 23

MRI: magnetic resonance image

PET: Positron emission tomography

PMT: phosphaturic mesenchymal tumor

TIO: Tumor Induced Osteomalacia

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