

Unusual Presentations and Complications in Cancer

Metastasis to the Bones of the Hand

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The rarity with which cancer spreads to the distal skeleton can cause clinicians to miss this diagnosis. These authors describe two cases in which hand metastases were mistaken for infection.

Bony metastasis from a malignant neoplasm is common, with the proximal skeleton being the most frequent site of such lesions. By contrast, metastasis to the bones distal to the elbow (Figure 1) or knee is rare. When such distal metastases do occur, they usually arise from bronchogenic carcinoma.

The rarity of distal seeding in the skeleton, combined with the frequency of other disease processes in the extremities (such as infection, inflammatory arthropathy, and vascular compromise), can cloud the diagnosis and delay appropriate treatment. While such delays probably have little effect on overall patient prognosis, they may deprive patients of comfort and quality of life, subject them to unnecessary procedures, and expose them to adverse effects from inappropriate medications.

In this article, we aim to increase federal practitioners' awareness of distal metastasis. To that end, we describe the cases of two VA patients who were seen at the Orthopaedic

Hand Clinic at the John D. Dingell VA Medical Center in Detroit, MI over a six-month period. Both had a known diagnosis of lung carcinoma with local disease progression, despite intervention. In both cases, metastasis to the hand initially was misdiagnosed and treated as infection, based on clinical examination, imaging studies, and laboratory findings—but no confirming biopsy or culture.

CASE 1

A 58-year-old man with known squamous cell lung carcinoma presented to the oncology clinic with pain and swelling in his left ring finger. The patient previously had undergone three of four prescribed cycles of chemotherapy consisting of docetaxel and carboplatin, but had stopped this therapy prior to the last cycle due to intolerable adverse effects. Fewer than six months after the chemotherapy regimen was halted, a computed tomography scan of the thorax had revealed progression of his primary cancer. At that time, he was prescribed gefitinib, an epidermal growth factor receptor inhibitor used in cases of non-small cell lung cancer progression despite chemotherapy. This occurred three months prior to the present oncology clinic visit.

His significant medical history also included chronic obstructive pulmo-

nary disease, benign prostatic hypertrophy, and opioid dependence. His active medications included the gefitinib, an albuterol inhaler, an over-the-counter nasal spray for seasonal allergies, furosemide, loratadine, oral morphine, naproxen, ranitidine, sertraline, methadone, and a vitamin supplement.

The patient's substance use history included heavy tobacco and alcohol use, as well as cocaine and heroin use. After smoking two packs of cigarettes per day for 30 years, the patient had reduced his tobacco use over the past three years to one to two cigarettes per day. He had last consumed alcohol three years prior, and his last cocaine and intravenous heroin use had been two years prior.

At his presenting visit, his fingertip was warm, painful, and swollen but without fluctuance or significant erythema. There was no compromise of the skin. The oncology team diagnosed him with paronychia and performed an incision and drainage that yielded no appreciable purulence. Presuming infection to be the cause, the team initiated a course of oral antibiotics but did not collect a specimen for culture or other evaluation.

Two weeks later, the patient presented to the urgent care center at the same institution with persistent pain and swelling in the same finger. The urgent care team obtained radio-

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graphs that showed a fracture of the distal phalanx through an osteolytic lesion (Figure 2). The team scheduled the patient for an appointment with the Orthopaedic Hand Clinic, but before that appointment could occur (after only one week), he returned to the urgent care center with worsening pain. Radiographs at this time showed progressive bony destruction of the distal phalanx (Figure 3).

A new Orthopaedic Hand Clinic appointment was scheduled for the following week. At that time, physical examination revealed bloody drainage from the site of the incision made at his presenting visit. A drainage procedure yielded no expressible purulence, but there was exquisitely tender swelling and a deformity of the distal phalanx. The patient was presumptively diagnosed with bony metastasis of the hand and offered operative intervention for the purpose of pain control.

Subsequently, he underwent amputation through the distal interphalangeal joint of the ring finger under intravenous sedation with local anesthetic. Findings of the final pathology report were most consistent with poorly differentiated carcinoma, favoring squamous cell origin. There was extensive necrosis involving the distal phalanx and deep soft tissue resection margins. Immunohistochemical analysis revealed the presence of keratins and epithelial membrane antigen (Figure 4). S100 and vimentin staining was negative, indicating cells of mesenchymal origin.

The patient experienced pain relief shortly after the amputation. He died from his primary disease approximately one week postoperatively in the hospice setting. No autopsy was performed.

CASE 2

A 56-year-old man with poorly differentiated, stage IIa (tumor-node-



Figure 1. Metastatic lesion on the distal phalanx of the ring finger, showing bony destruction and a pathologic fracture. Such metastases occur rarely and are most frequently associated with bronchogenic carcinoma.

metastasis stage T1, N1, M0) adenocarcinoma of the lung presented to the urgent care center with pain and swelling in his right ring finger. He had undergone a lobectomy approximately one year earlier and had been deemed inappropriate for postoperative chemotherapy due to multiple medical issues, including perioperative complications involving a previous colovesicular fistula repair.

His medical history was also significant for hepatitis C, hypertension, anxiety, and diverticulitis. His active

medications included metoprolol, diphenhydramine, and chlorpromazine. He had no history of hand trauma and no systemic symptoms of infection.

Upon examination by the urgent care team, he had a tender swelling and ecchymoses over the proximal phalanx. Radiographs revealed destructive changes involving the distal aspect of the proximal phalanx (Figure 5). A tagged white blood cell scan showed increased uptake at the site of the lytic lesion.



Figure 2. Anteroposterior (A) and lateral (B) radiographs of the left ring finger of the first patient, showing significant soft tissue swelling and a lytic lesion involving the distal phalanx with significant cortical destruction and a pathologic fracture.

The patient was admitted to the internal medicine service, and the admitting team performed a bedside bone aspirate. Intravenous antibiotics were administered with the presumptive diagnosis of osteomyelitis. Cultures of the aspirate sample were negative, however, and his serum white blood cell count was within normal limits. He was discharged with oral antibiotics and pain medication and referred to the Orthopaedic Hand Clinic.

The clinic team first evaluated the patient approximately two weeks after his discharge. An open biopsy performed at this time yielded results consistent with adenocarcinoma. The patient underwent a palliative amputation at the metacarpophalangeal joint under regional anesthesia. In-

traoperatively, the surgeons observed extensive bony destruction from the lesion (Figure 6). All intraoperative cultures were without growth.

Findings of the final pathology report were most consistent with moderately differentiated adenocarcinoma, along with necrosis and hemorrhage involving the soft tissue and bone (Figure 7). A mucin stain was positive, confirming the diagnosis of adenocarcinoma.

As in the first case, the patient experienced near immediate pain relief following amputation. At his two-week postoperative visit, his sutures were removed and his incision was well healed. He died at home from his primary disease approximately three and a half months after his amputation.

EPIDEMIOLOGY AND PATHOPHYSIOLOGY

Most reports indicate that hand metastases comprise less than 0.2% of all bony metastatic lesions.¹⁻³ Of these, bronchogenic carcinoma is the most common primary malignancy, accounting for over 40% of cases.^{2,4} The terminal phalanges are the bones most frequently involved, and most cases involve a single lesion.^{2,3} Carpal or metacarpal involvement comprises approximately 20% of cases.⁵

Though the exact mechanism is unknown, several studies have examined how bronchogenic carcinoma spreads to the hand. In 1889, Paget proposed that bones must be hematopoietically active in order to be adequate hosts of tumor cells.⁶ Since red marrow is scarce in the bones of the hand in adults, the rarity with which hand metastases occur supports this “seed and soil” theory.

Nevertheless, one explanation for why cancer occasionally metastasizes to the hand involves repeated trauma



Figure 3. Anteroposterior (A) and lateral (B) radiographs of the left ring finger of the first patient, taken one week later, demonstrating progressive bony destruction of the distal phalanx. Though the lesion has progressed, there is no periosteal reaction or new bone formation.

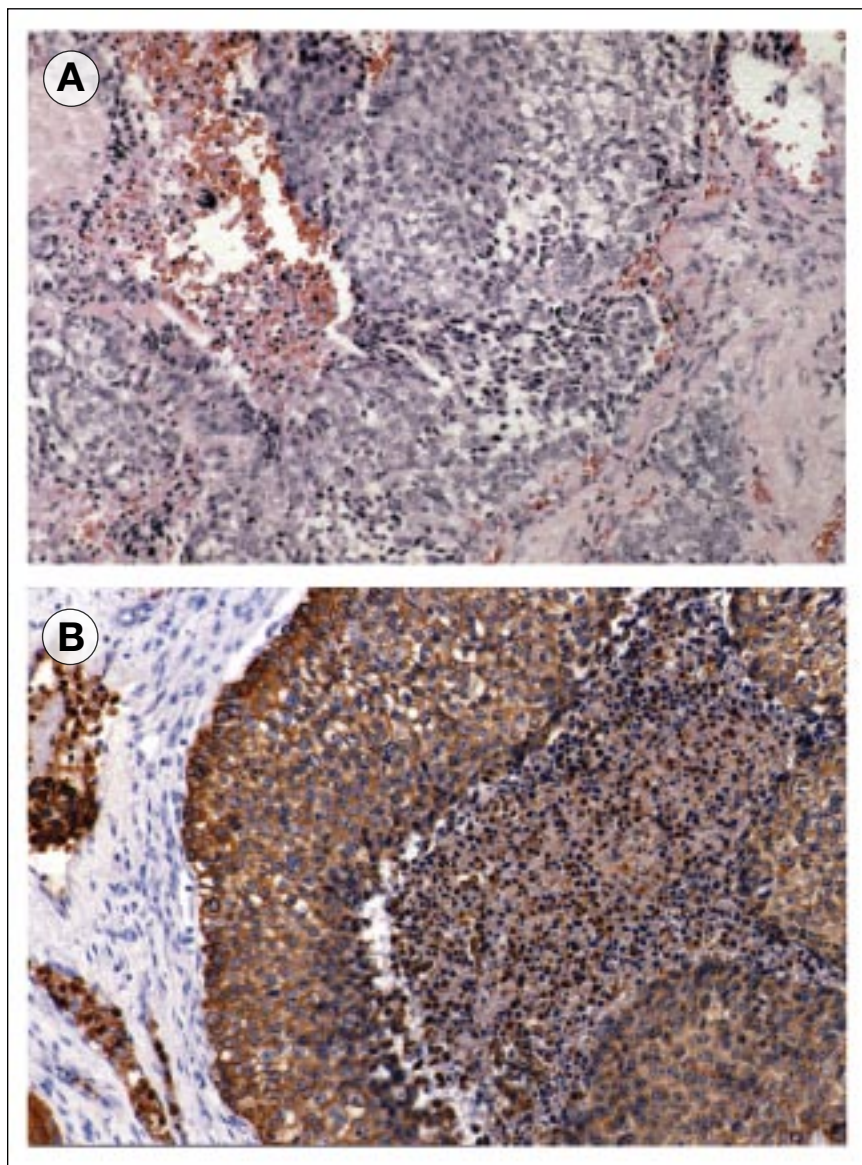


Figure 4. Histopathologic images (magnification, 20x) from the first patient. (A) Hematoxylin and eosin staining reveals pleomorphic nuclei, a finding that suggests poorly differentiated carcinoma, most likely of squamous cell origin, with extensive necrosis. (B) Treatment of the specimen with monoclonal antikeratin antibody AE1 is positive (brown-stained areas), confirming the diagnosis of squamous cell carcinoma.

to the digits. In this proposed mechanism, the fingers become suitable “soil” by reducing local resistance to tumor seeding.⁷ Another theory relies on the anatomy of the pulmonary vasculature, positing that tumor erosion into the pulmonary vein allows tumor

emboli direct access to the systemic circulation without being filtered by the lung or liver. This would allow for artery-carried tumor cells to seed the appendicular skeleton. The role of prostaglandins as chemotactic factors and the unique bone microenviron-

ments as a milieu for tumor cell proliferation also has been examined.^{8,9}

Although bronchogenic carcinoma is the most common primary tumor to establish metastases in the hand, numerous studies have described instances of other primary cancers seeding the hand. As such, practitioners should not rule out metastatic disease based solely on the fact that the primary malignancy has a nonbronchogenic identity.

In a minority of cases, hand metastasis is the first manifestation of malignancy. In one case series from the Mayo Clinic, hand metastasis was the presenting symptom of an underlying cancer for only two of the 18 patients.¹⁰ A global review of medical literature further supported this observation.¹¹ The finding that most metastatic lesions are discovered after diagnosis of the primary neoplasm suggests dissemination and distal



Figure 5. Anteroposterior (A) and oblique (B) radiographs of the right ring finger of the second patient, demonstrating a pathologic fracture of the proximal phalanx through a lytic lesion. There is significant soft tissue swelling and no appreciable periosteal reaction or new bone formation.

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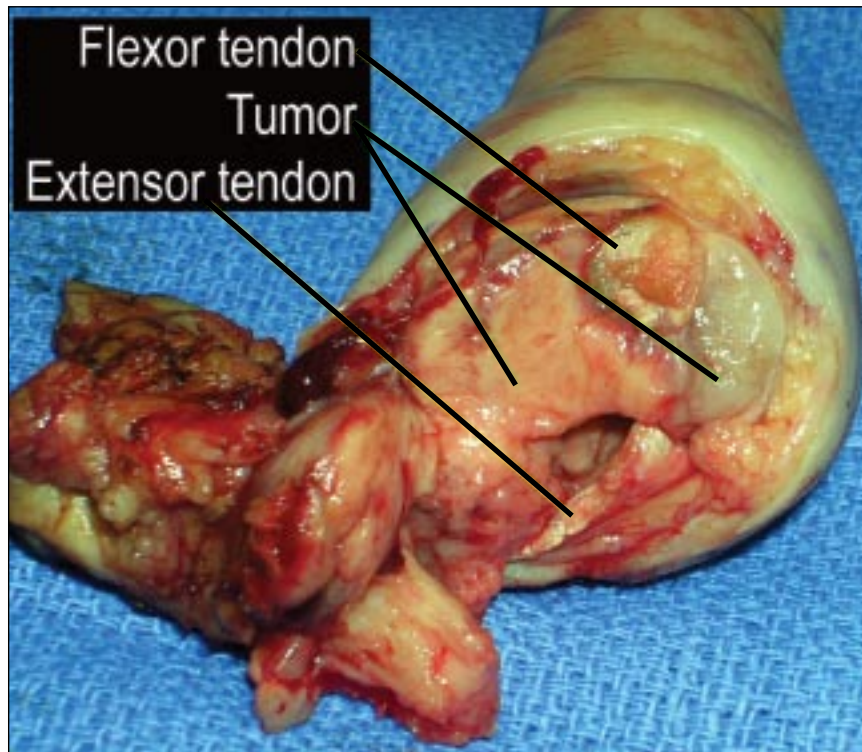


Figure 6. Intraoperative specimen from the second patient, showing extensive tumor destruction of the finger with no bone remaining at this level.

seeding of tumor cells is a late event in the natural history of the disease.

PRESENTATION AND DIAGNOSIS

Clinically, patients often present with a red, painful, swollen digit. Lesions can ulcerate and erode the skin. Radiographs display irregular lytic lesions with minimal periosteal reaction or reactive bone. Pathologic fractures can be seen, and lesions rarely cross joints. Pain may precede radiographic changes.¹² Clinically and radiographically, these lesions can be easily mistaken for other diseases.

Both cases in this report were initially misdiagnosed and treated as infections. Similar cases have been reported in the literature. Though unlikely to affect prognosis, misdiagnosis subjects patients to unnecessary procedures and potentially harmful antibiotics and delays treatment that

can ease pain. In cases in which the diagnosis is uncertain, a biopsy may be necessary to make an accurate diagnosis.¹³

TREATMENT AND PROGNOSIS

Treatment goals may vary depending on the patient's overall health or prognosis. For most patients with lung cancer, the primary goal is pain control.

Both nonoperative and operative modalities have shown efficacy in palliation. Radiation has been shown to relieve pain and, in curative doses, allow recalcification of lytic lesions.^{1,14} Operative palliation often entails amputation. In both of the cases presented here, the patients underwent uneventful, successful, palliative amputations and were spared a general anesthetic by the use of sedation and regional and local analgesia.

In a 1957 case report describing metastasis of pulmonary carcinoma to the hand, Greene concluded that, "because patients with phalangeal metastasis survive for so short a time, it is doubtful that any reconstructive hand surgery should be done."¹⁵ Despite great advances in the care of cancer patients since that time, the prognosis following a diagnosis of distal metastasis remains poor.

The mean survival has been reported to be three to six months from the time of diagnosis of acrometastasis.^{3,16} In the Mayo Clinic series, while mean survival was somewhat longer (14 months) for the entire group, the five patients with bronchogenic carcinoma had a mean survival of only five months.¹⁰

The cases presented in this report are no exceptions. Both patients had progression of disease despite intervention and died shortly after their metastasis was diagnosed.

SUMMARY

Despite the rarity of distant skeletal metastasis, it is an event with considerable prognostic value. Metastasis is most commonly misdiagnosed as infection, though gout, primary malignancies, vascular lesions, and rheumatoid disease also can mask a metastatic lesion. These patients may not be ideal operative candidates, but a biopsy, often open, may be needed to avoid a misdiagnosis. Practitioners should maintain a high index of suspicion for metastasis when evaluating extremity pain in any patient with known cancer. In the VA health system, where patients are generally older and sicker than those in the general population, a heightened awareness of this unique clinical presentation is particularly important. ●

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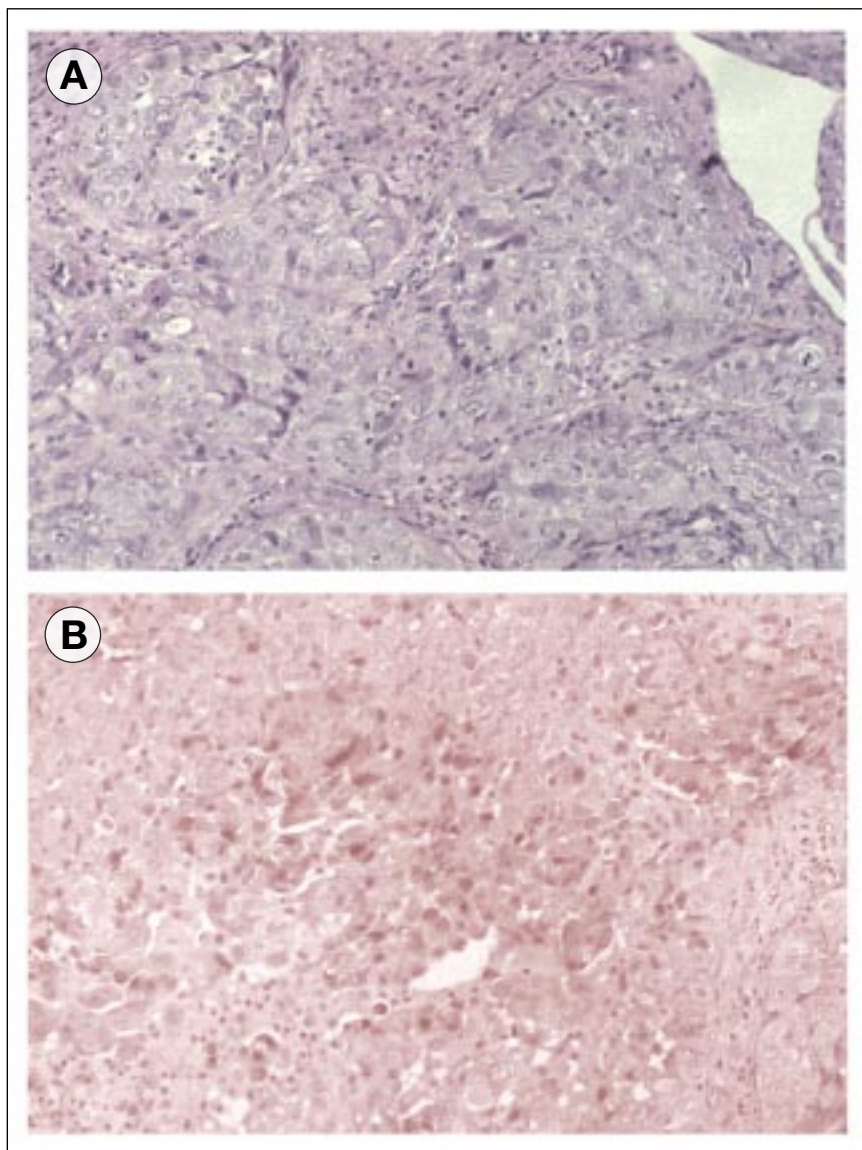


Figure 7. Histopathologic images (magnification, 20x) from the second patient. (A) Hematoxylin and eosin staining reveals a glandular arrangement of tumor cells most consistent with moderately differentiated adenocarcinoma. (B) Mucin staining is positive (pink-stained central areas), confirming the diagnosis of adenocarcinoma.

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