

INTRODUCTION

Colorectal cancer is one of the most common cancers afflicting adults in the United States. Approximately twenty percent of patients with colorectal cancer present with metastases at the time of diagnosis, and an even greater number present with metastases further down the road. The most common sites for colorectal cancer metastases are the liver, lungs, brain, and bones. Bone metastasis in colorectal cancer is a rare late manifestation that occurs in only 4-6% of patients. Bone metastasis is nearly always preceded by other organ metastases, such as the liver or lungs. There has been only a handful of documented cases involving colorectal cancer directly metastasizing to bone without other overt organ involvement. The following case is a unique presentation of colorectal cancer metastasizing directly, and only, to a patient's right tibia.

CASE S13-519 (SS)

CHIEF COMPLAINT & PAST MEDICAL HISTORY

In January 2013, a 64 years old white male presented with chief complaints of right tibia and ankle pain as well as open wounds in his right lower leg for the last couple of months.

The patient's past medical history was significant for poorly differentiated infiltrating adenocarcinoma of the rectosigmoid colon (PT3C/D), status post partial colectomy in 2007; metastatic adenocarcinoma to the right distal tibia, consistent with a colon primary (CEA, CK20, CDX2 positive; CK7, TTF-1 negative), in 2009, status post prophylactic rodding in 2011; and metastatic adenocarcinoma to right groin lymph nodes consistent with a colon primary, status post excision in 2010. Additional PMH included hypertension, hypercholesterolemia, status post appendectomy in 1961, history of detached retina in 1990, and status post left ankle fracture in 1998. Other than the metastasis to the right tibia, no additional colorectal cancer metastases were diagnosed in the patient.

The patient was doing relatively well until Fall 2012. At this time, the patient complained of increasing lower leg pain and was ambulating with the assistance of canes. New open wounds were present along the anterior surface of the right lower leg. Radiology showed a continuing extensive osteolytic lesion involving the mid and distal right tibial shaft, with no overt pathological fractures. In addition to this pre-existing lesion, there were two new lucencies noted in the distal femoral condyle and proximal tibial shaft, consistent with possible metastases, as well as two foci in the right pelvis on PET/CT imaging, consistent with possible metastases.

In January 2013, the patient returned with increasing pain, lower right leg swelling, and additional open wounds on the distal tibial surface. At this time, a decision was made to perform a right above-the-knee amputation.

RADIOLOGY



Figure 1: X-rays of right lower leg and total body PET/CT scan.

RADIOGRAPHIC IMPRESSIONS

- aggressive, predominately osteolytic lesion involving the mid- to distal tibial shaft with aggressive periosteal reaction
- fixating intramedullary rod present, with no pathological fracture observed
- degenerative changes in right ankle joint; diffuse osteopenia in distal tibia, right hindfoot
- suspicious lucencies within distal femoral condyle, proximal tibial shaft worrisome for lytic osseous metastatic disease
- 2 probable metastases in right pelvis
- increased BM activity consistent with Neulasta treatment

GROSS FINDINGS

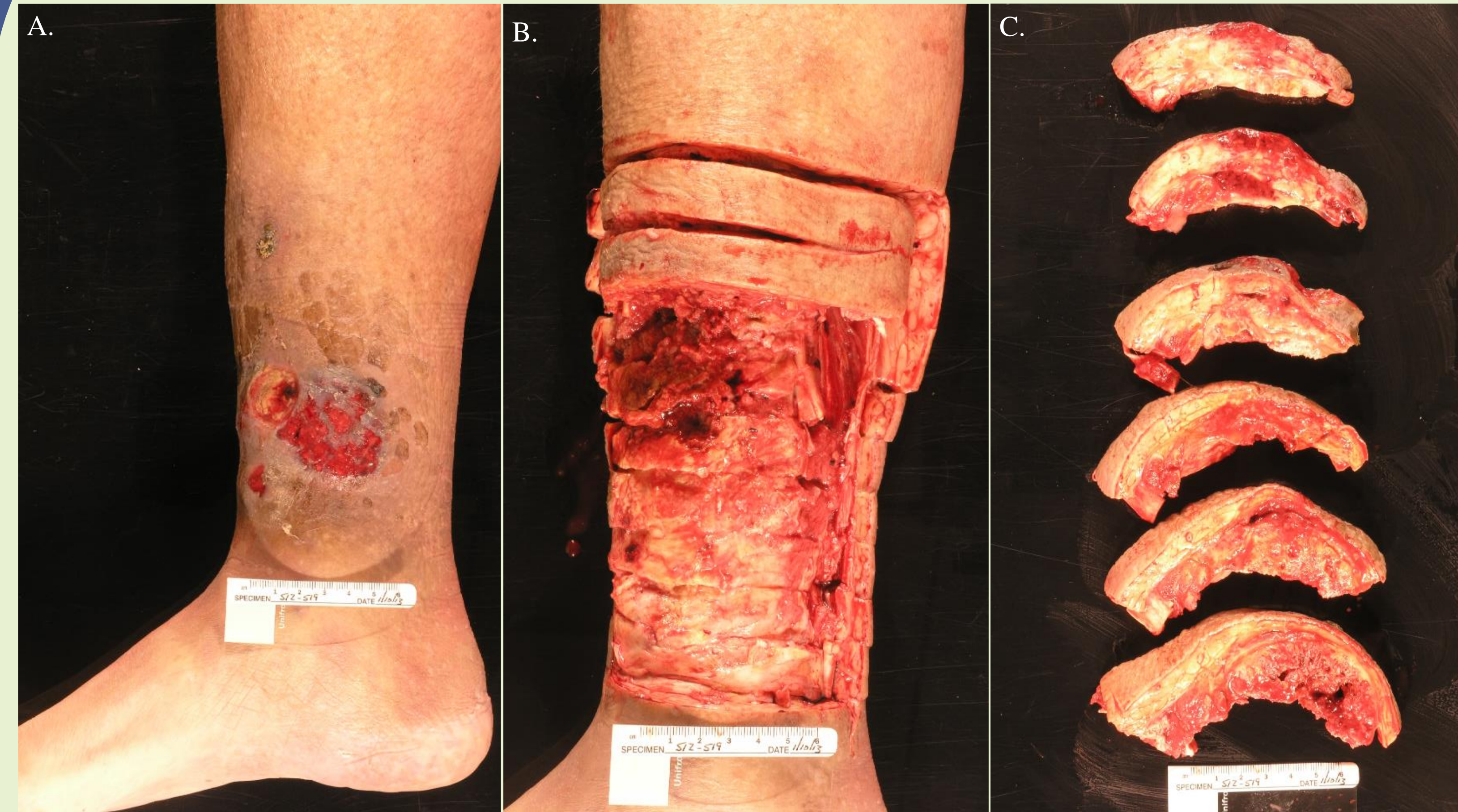


Figure 2: A. Right above-the-knee amputation showing a large indurated area with an ulcerated granular focus along the anterior-medial aspect of the right lower extremity. B. Sectioning reveals an underlying 15.0 cm friable mass eroding through the tibia. C. The distal portion of the mass is more hemorrhagic and extends to the ulcerated skin.

GROSS DESCRIPTION

The specimen is received fresh labeled "Right Leg" and consists of a right above-the-knee amputation 25.5 cm from the heel to the tip of the great toe and 50 cm from the skin and soft tissue resection margin. Extending from the soft tissue margin is a 6 cm unremarkable portion of femur. The proximal half of the skin is wrinkled glistening and gray-white. Along the anterior knee is a 9.5 cm tan-white old scar. The word "yes" is written just below the knee. In the distal half of the anterior tibial region is a 16.0 x 11.0 cm markedly indurated discolored dark brown to gray-purple area. The distal half of this area incorporates a 7.0 x 4.0 cm ulcerated granular red-purple to gray-green area. This overall extends to within 25 cm of the skin/soft tissue resection margin and 32 cm from the osseous resection margin. Sectioning reveals approximately 15.0 x 7.0 x 4.0 cm mass which extends to the medial half of the midline along the anterior tibial and medial surfaces. The mass has a large friable firm focally eroding pink-red osseous component primarily in the proximal two-thirds of the specimen. The distal two-thirds of the mass is slightly more soft hemorrhagic ill-defined and red-purple. The hemorrhagic ill-defined areas extend up to the ulcerated skin area. The proximal osseous component appears to include grossly new bone growth as well as a deep erosion into the tibia where greater than 7 cm of the tibia is essentially eroded away. Cross-sections through the bone are not complete due to the presence of an intramedullary rod. The gross is reviewed with Dr. Adamec. Gross photographs are taken. Representative sections are submitted as follows: A- femoral resection margin following decalcification, B- cutaneous resection margin, C- soft tissue resection margin, D- vascular bundle resection margin, E-L- sections of mass from proximal to distal. Blocks E-H will be submitted following decalcification. SS/jp

HISTOLOGY

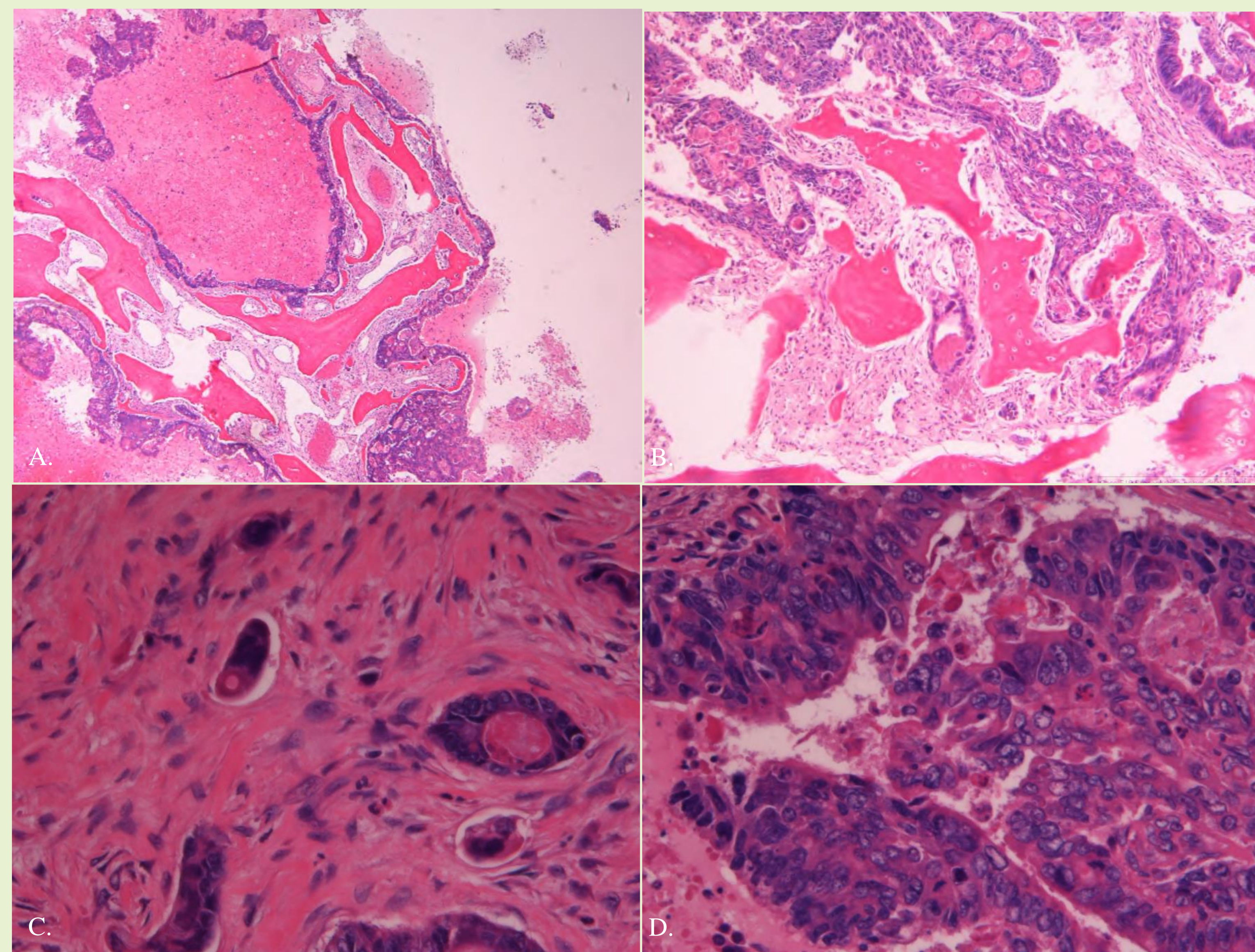


Figure 3: A. Lamellar bone interspersed with poorly differentiated infiltrating adenocarcinoma. B. Lymphovascular invasion. C. Higher magnification of the glandular component reveals "dirty necrosis" and ugly-looking cells with elongated hyperchromatic nuclei.

FINAL DIAGNOSIS

- metastatic ADC, consistent with a metastasis from the patient's prior colon primary
- lymphovascular invasion identified
- associated abscess formation and necrosis
- resection margins negative for ADC

DISCUSSION

The most frequent sites for colorectal cancer metastases, in order of frequency, are the liver, lungs, brain, and bones. Organ involvement is largely attributable to the pattern of blood and lymph flow. The majority of the venous drainage from the colon enters the portal system, making the liver the most common site for colorectal cancer metastasis. An exception to this is adenocarcinoma of the rectum, which does not drain into the portal circulation and instead drains into the iliac veins. As a result, the majority of rectal cancer metastases circumvent the liver and first present elsewhere.

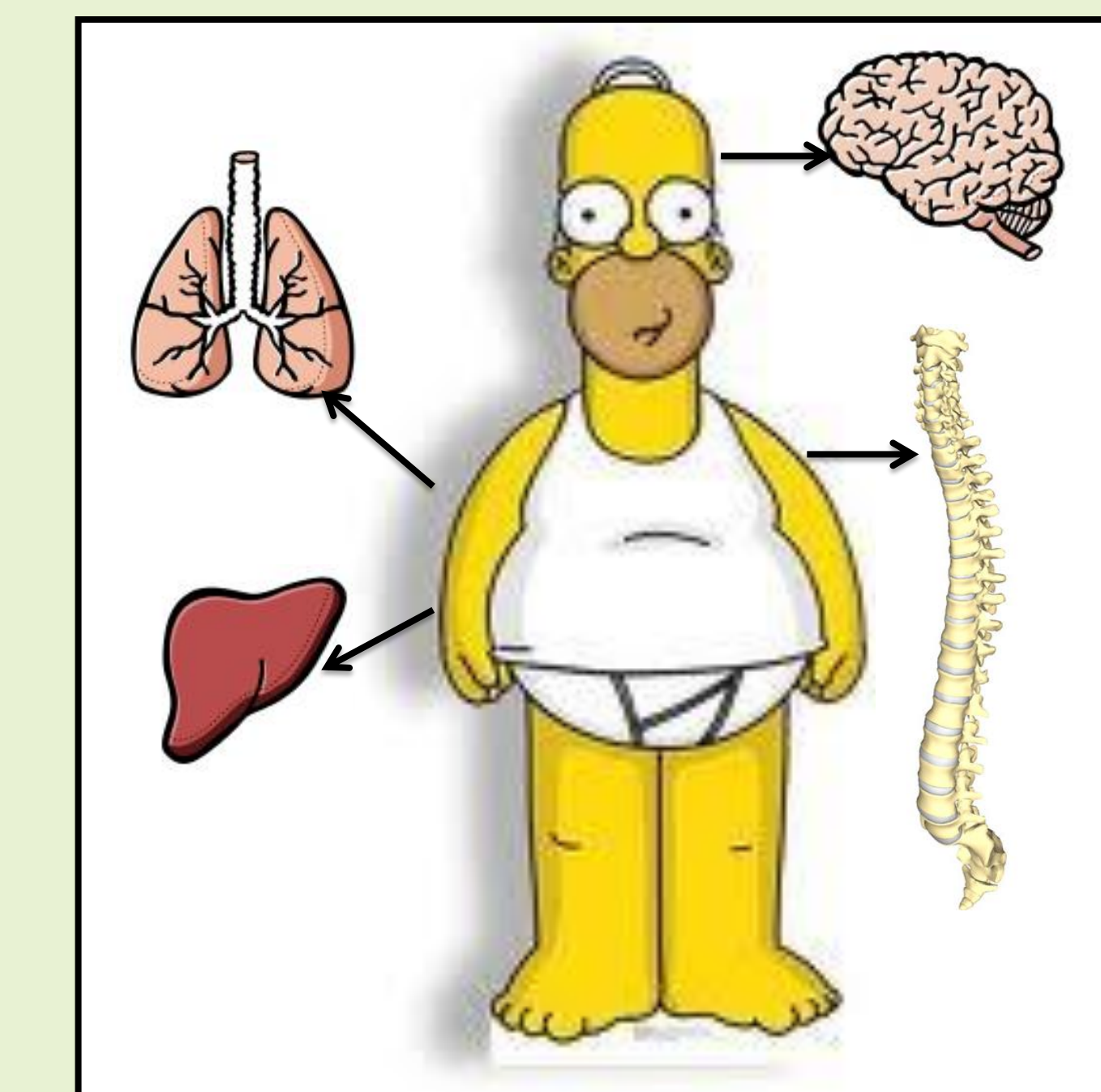


Figure 4: Sites of colorectal cancer metastases.

The spread of cancer is also influenced by the intrinsic properties of the tumor cells and the microcosm of an organ. Many factors make bone an ideal metastatic niche, including extensive lymphovascular drainage; sluggish vascular supply through the metaphyses of long bones, allowing adequate time for tumor cells to move in and out of bone marrow; a high rate of angiogenesis; and stromal cells that support the differentiation and proliferation of cancer cells through specific signaling pathways, especially those involving VCAM-1, MMP-2, and syndecan-1.

Most research indicates that colorectal cancer cannot bypass major organs and metastasize directly to bone; in order for bone metastases to occur, there must first be prior organ involvement. Numerous studies have shown that patients do not have bone metastases without at least lung or liver involvement. While this appears to be the general consensus, there have been several documented cases where colorectal cancer metastasized directly to bone in the absence of other organ metastases. How or why this happened in these cases remains unknown.

This case is a unique presentation of metastatic colorectal adenocarcinoma with a metastasis to the right distal tibia in the absence of additional overt organ metastases. It is possible that this patient is part of the very small percentage of cases in which colorectal cancer appears to directly metastasize to bone and circumvent organs such as the liver, lungs, and brain. An alternative possibility is that the patient had additional undetected metastases at the time of his right tibial metastasis, which due to their size or intrinsic properties, were unable to be detected by diagnostic imaging. If the latter is true, these additional metastases continue to exist and remain undetectable as of the patient's most recent x-rays and PET/CT scans.

TREATMENT & PROGNOSIS

Treatment options for bone metastases include surgery, radiation, chemotherapy, endocrine therapy, and bisphosphonates. Treatment improves the quality of life and overall survival of the patient, but it does not target the underlying pathophysiology and therefore does not prevent additional lesions from developing. The average survival of patients with bone metastases is ten months, with an 8.1% 5-year survival rate. According to these statistics, our patient had been doing really well considering that his initial tibial bone metastasis was diagnosed in 2009. Despite this, the presence of new lucencies on radiology indicate probable new bone metastases requiring further treatment and signifying a worsening prognosis.

REFERENCES

- Choi, Seok Jin, et al., *Long-term disease-free survival after surgical resection for multiple bone metastases from colorectal cancer*, World J Clin Oncol, 2001. 2(8): 326-328.
- Fleming, Matthew, et al., *Colorectal Carcinoma: Pathologic Aspects*, Journal of Gastrointestinal Oncology, September 2012. 3(2).
- Kose, F, et al., *Colon Adenocarcinoma and Solitary Tibia Metastasis: Rare Entity*, Journal Gastrointestinal Cane, 2008. 39:146-148.
- Oh, Yoon Kyeong, Hee Chul Park, and Young Sook Kim, *Atypical Bone Metastasis and Radiation Changes in a Colon Cancer: a Case Report and a Review of the Literature*, Jpn J Clin Oncol, 2001. 31(4):168-171.
- Roth, Eira S., et al., *Does colon cancer every metastasize to bone first? A temporal analysis of colorectal cancer progression*, BMC Cancer, 2009. 9:274.
- Santini, D., et al., *Natural history of bone metastasis in colorectal cancer: final results of a large Italian bone metastases study*, Annals of Oncology, 2012.
- Theriault, Rachel L. and Richard L. Theriault, *Biology of Bone Metastases*, Cancer Control, 2012. 19(2): 92-101.
- Image: http://sellerby.com/good_17391_460468302-Homer-Simpson-in-Underwear-Cutout.htm