#### Case report

# Colorectal Cancer with Uncommon Metastatic Spread

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#### Abstract

The prevalence of bone metastases from colorectal cancer (CRC) is quite low and the presence of isolated osseous metastases at the time of diagnosis or the onset of bone metastases without other organ involvement during follow-up is even lower. Here, we present an interesting case of diffuse skeletal metastases from CRC in which both the atypical presentation of the metastatic spread and the presence of infective comorbidities created some troubles in getting the final diagnosis.

Keywords: Bone metastasis, colorectal cancer, comorbidity, positron emission tomography-computed tomography

## **Introduction**

A 50-year-old woman presented to the emergency room for sudden worsening of abdominal pain and difficulty in evacuation. She underwent abdominal ultrasound (US) and X-ray scans that suggested a bowel obstruction. A right hemicolectomy with lymphoadenectomy (22 perivisceral nodes) was necessary for the presence of a neoplastic lesion of the transverse colon causing severe lumen stenosis. Final diagnosis was "signet ring cell carcinoma" G3 sec. World Health Organization, with angiolymphatic invasion, involvement of perineural spaces and no tumor-infiltrating lymphocytes, pT3N1b, stage C2 (Dukes mod. Astler and Coller), KRAS wild-type (codons 12 and 13), and BRAF V600E wild-type.<sup>[1]</sup>

Hepatic US and chest X-ray were negative for distant metastases.<sup>[2]</sup> Fifty days after surgery, the first cycle of adjuvant treatment (FOLFOX 4) was performed.<sup>[2,3]</sup> Due to the appearance of diffuse erythema with pimple-like lesions and fever, chemotherapy was stopped after the fourth cycle and patient was re-hospitalized.

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The patient had a temperature constantly higher than 38°C. The erythema, at first located just at the trunk, spread to the limbs, coupled with a moderate itch.

The main clinical problem, anyway, was the onset during hospitalization of worsening back pain, nonsteroidal anti-inflammatory drugs-resistant, and associated with extreme weakness.

A spine X-ray showed cuneal deformation of D12, L1, and L2. A bone scan, then, revealed the presence of diffuse skeletal lesions, highly suspicious for metastatic disease [Figure 1].

In order to re-stage the disease, the patient underwent a CT scan that confirmed the diffuse skeletal involvement and revealed the presence of multiple and bilateral lung lesions, compatible with metastases. A positron emission tomography-computed tomography (PET/CT) with 18F-fluorodeoxiglucose (FDG) showed high FDG uptake in the pulmonary and skeletal lesions [Figure 2a].

The patient was discharged with a final diagnosis of skeletal and lung metastases from colon cancer and diffuse erythema of uncertain nature (reaction to chemotherapy?) partially responsive to antimicrobial, steroidal, and antihistaminic treatments.

#### Address for correspondence:

Dr. Lorenzo Stefano Maffioli, Department of Nuclear Medicine, AO "Ospedale Civile di Legnano," Via Papa Giovanni Paolo II, 20025 Legnano, Milan, Italy. E-mail: lorenzo.maffioli@ao-legnano.it Chemotherapy with FOLFIRI plus bevacizumab and zoledronate was established.<sup>[2,3]</sup> Before beginning chemotherapy, anyway, a CT angiography (performed for suspect acute pulmonary embolism) showed an important reduction of the known bilateral parenchymal lesions.

A new PET/CT revealed the resolution of almost all lung lesions, while the presence of multiple skeletal lesions with high tracer uptake was confirmed [Figure 2b].

No chemotherapy had been administered between the two PET/CT scans but several antimicrobials, suggesting the infective nature of lung lesions (blood culture positive for *Klebsiella pneumoniae*, probably related to central venous catheter infection).



Figure 1: Spine X-ray (left panel) showing cuneal deformation of D12, L1, and L2. In the bone scan (right panel), multiple lesions involving both axial and appendicular skeleton can be seen



**Figure 2b:** Fluorodeoxyglucose positron emission tomography-computed tomography, the second study: Maximum intensity projection image and fused axial images. Resolution of the previously described lesions, along with the appearance of bilateral pleural effusion, can be seen in the lungs (upper panel and lower left panel). Diffuse and intense uptake of the tracer, even higher than previously seen, is confirmed in all skeletal lesions (lower right panel)

Meanwhile, a dermatologist found an infective origin also for the erythema: It was a rather aggressive form of scabies, probably related to the drug-induced immunosuppression.

The infective nature of both skin and lung lesions, associated with the uncommon involvement of the skeleton in colon cancer, called into question also the metastatic nature of skeletal disease, although imaging investigations were almost pathognomonic. To exclude an unusual presentation of a primary bone pathology or infection, a bone marrow biopsy was performed: The result confirmed the presence of metastases from colon adenocarcinoma [Figure 3]. The patient died few weeks later, 6 months after surgery.

## **Discussion**

The prevalence of bone metastases from colorectal cancer (CRC) is quite low. Before the introduction of modern chemotherapy, bone metastases were reported in 10–24% of patients with advanced CRC, based on clinical and autopsy records while a more recent analysis of 252 CRC patients showed that only 5.5% had bone metastases at primary diagnosis.<sup>[4-7]</sup> In addition, the presence of isolated osseous metastases at the time of diagnosis or the onset of bone metastases without other organ involvement during follow-up is extremely



Figure 2a: Fluorodeoxyglucose positron emission tomography-computed tomography, the first study: Maximum intensity projection image and fused axial images. Intense uptake of the tracer can be seen in lung lesions, mainly located in the right lung (upper panel and lower left panel), and in all skeletal lesions, for example in the pelvis (lower right panel)



Figure 3: Metastatic signet ring cell carcinoma on a bone marrow biopsy (EE, 20HPF) (CAM 5.2, 20 HPF)

rare.<sup>[8]</sup> In a recent multicenter study of 264 patients with CRC involving bone, the presence of diffuse skeletal involvement was not described in any patient.<sup>[9]</sup>

In this scenario, our case looks interesting since it highlights how the diagnostic process could be influenced by the expected diagnosis and previous findings. First, the presence of diffuse skeletal involvement in a CRC patient with no other metastatic sites induced us to believe in the secondary nature of the lung lesions. Then, the resolution of these lesions with no chemotherapy and the identification of a rare infective comorbidity (scabies) instilled doubts about the effective skeletal metastatic involvement and led to an unnecessary biopsy.

The prognosis of this patient would surely not have been better even without these diagnostic troubles. Nonetheless, this case teaches us something: In local-advanced CRC (T3/T4), the presence of bone metastases, even without other organs involvement and even in a diffuse uncommon form, should always be considered.

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