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Colon adenocarcinoma first presenting as shoulder pain. Case report

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ABSTRACT

Bone metastases of colorectal cancer (CRC) are uncommon and usually occur in the context of a widespread disease. A 77-year-old woman presented with increasing pain in the right shoulder which had started 5 months earlier. On examination, a hard mass arising from the right scapula was found. There were no other abnormal findings on body Computerized Tomography (CT). A biopsy confirmed a metastatic adenocarcinoma. Further colonoscopy revealed a colonic obstructive tumour. Both solitary metastasis and the primary tumour were treated, and patient maintains a progression-free status. This is an unusual form of presentation for a colon cancer. With this report we aimed to discuss the unique clinical and pathological features of this colonic cancer and call attention of the physicians' community for this atypical presentation. Isolated bone metastasis in CRC is a rare entity and there are only a few similar cases reported in the literature.

1. Introduction

The CRC is one of the main causes of cancer death in high-income countries. It is historically recognized that CRC has a determined pattern of dissemination. The liver is the most affected organ in 60% of the cases, followed by abdominal lymph nodes and lungs [4]. In contrast, metastases in other organs such as adrenals, brain, bones or skin, are less frequent and commonly occur in the context of a widespread disease with multifocal affection, or a relapse after a primary treatment.

The incidence of bone metastases is reported to be around 5%–23% [3–5,7]. The predisposition for this uncommon metastatic site may be attributed to the pattern of blood flow (connected to the location of the primary CRC) or to molecular protein signals. Most of the patients develop these metastases through the course of the disease, accompanied by extra-bone lesions; however, solitary bone metastases rarely take place at the initial diagnosis [4].

We present an unusual case of right shoulder pain as the first symptom of a primary colonic tumour.

This work has been reported in line with the SCARE criteria [11].

2. Presentation of the case

A 77-year-old woman, smoker, with no significant medical history, consulted the orthopaedic department for atraumatic right shoulder pain with articular crack. The initial x-Ray showed degenerative changes. In the following weeks she experienced worsening of symptoms, deformity and functional inability. The CT revealed a 7-centimetre mass of soft tissue consistence, emerging from the right scapula (Fig. 1). The first suspected diagnosis was a multiple myeloma, but a biopsy revealed metastatic adenocarcinoma, suggesting a colonic medullary subtype.

A colonoscopy was performed, showing an ulcerative mass of the descendent colon (Fig. 2). The carbohydrate antigen (CA) 19.9 and carcinoembryonic antigen (CEA) levels were 631 U/mL (<37) and 0,8 ng/mL (<5) respectively. Other tumour markers were within normal ranges. No other metastases were found.

Because of severe pain, the patient received palliative radiotherapy (5 sessions, 20 Gy), and was then treated with 5 chemotherapy cycles, consisting of Capecitabine (1000 mg/m2/12 h during 14 days), Oxaliplatin (85 mg/m2/every 3 weeks) and Bevacizumab (7,5 mg/Kg/every 3 weeks). Due to weight loss Capecitabine doses were reduced on the 3rd cycle, and the patient could not complete the 6th cycle due to severe diarrhoea. She went through maintenance therapy with Capecitabine and Bevacizumab for 6 months. It

Abbreviations: CT, computerized tomography; CRC, colorectal cancer; CA, carbohydrate antigen; CEA, carcinoembryonic antigen; Gy, Gray (SI unit); AJCC/UICC, American Joint Committee on Cancer/Union for International Cancer Control; MLH-1, multL homolog 1; PMS-2, PMS1 homolog 2; OS, overall survival; PET, positron emission tomography; MSI, microsatellite instability.

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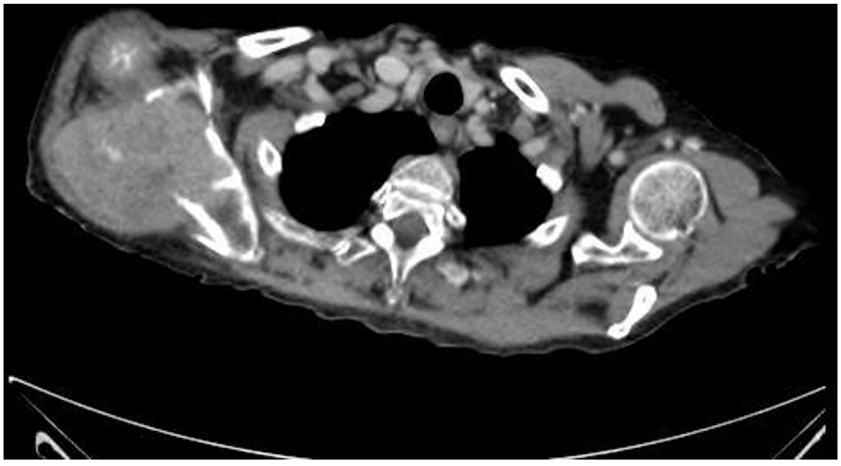

Fig. 1. Right scapula mass.

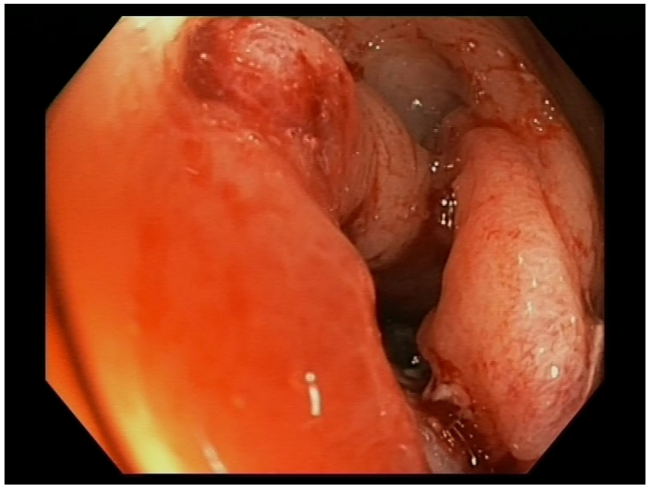

Fig. 2. Primary tumour, descendent colon.

was interrupted after patient request, and by then the disease was stable.

A year later, CT revealed regression of the bone metastasis and no other signs of disseminated disease. The patient presented enlargement of the colonic tumour, so a laparoscopic right hemicolectomy was performed. The histologic findings showed a pT4a pN1a (1 affected lymph node amongst 8 examined, AJCC/UICC, 8th edition), poorly differentiated adenocarcinoma (G3), without perineural or lymph-vascular invasion. The immunohistochemistry of the DNA repair proteins showed absence of MLH-1 and PMS-2 proteins, and the same findings were confirmed in the bone's sample (Figs. 3 and 4). RAS-protein oncogene was mutated.

More than three years after the diagnosis she remains clinically stable, with no new lesions on CT (last visit was on March 27th, 2020) and normal tumour markers.

3. Discussion

Bone metastases are uncommon in CRC. Once detected they are usually multiple and occur late in the course of the disease, commonly indicating a bad prognosis, with a median survival of 5–7 months [5]. In contrast, it had been noticed that patients with isolated bone metastases have a significantly better prognosis than those with multiple skeletal or visceral metastases [6] and should probably be considered separately.

Osseous metastases usually involve the axial skeleton and the long bones. Some authors ascribe the higher incidence of skeletal metastases to the invasion of deep pelvic veins and dissemination via the paravertebral plexus of Batson, with the rectosigmoid colon being the primary site [6,8], although there are a few cases of long bone metastases from rectum cancer described in the literature [9]. This could be justified due to the connection with the iliofemoral veins. The second most common source of bone metastases is the cecum [8]. In radiological imaging they are frequently lytic, normally creating reactive changes within the bone and adjacent soft tissue, being more likely to simulate a primary bone lesion [8]. Mixed and osteoblastic lesions are less prevalent [3].

The case hereby reported represents an unusual metastatic colonic cancer presented as a solitary bone lesion, mimicking an articular disease. In this patient both the time of presentation and the metastatic site were unusual. To our knowledge, there is only one case in the literature reporting a solitary scapula metastasis [7].

A retrospective study with 10 patients with CRC presented as bone metastases reported by Babu et al. [4], tried to rule out some common features among those cases, but only in three of them the bone metastases were solitary. They detected that the most affected bones were vertebras and pelvis. The median overall survival (OS) in the group was 5,5 months. However, the authors identified that the higher OS corresponded to those patients with bone-only involvement. All the patients were younger than 50 years, and the OS was also increased in those who had received chemotherapy, had a low CEA (<100) and absence of liver disease [4].

Kawamura et al. [2] aimed to identify the prognostic factors and characteristics associated with survival in 104 CRC patients with bone metastases. The spine was the most common site, mostly in left-sided CRC, followed by pelvis, whereas right-sided CRC was correlated with long bone metastases. Liver metastases were associated with spinal metastases, and >1 extra-bone metastases were linked to a poorer prognosis, as well as multiple bone metastases, high levels of CEA, osteolytic lesions, hypercalcemia and pathologic fracture. The median survival time was 5 months. Nine patients with no extra-bone metastases, showed better survival. Radiotherapy was associated with improved OS, fact that is consistent with our case.

Kanthan et al. [9] concluded that patients with bone-only metastases had a superior 5-year-survival comparing to those with bone and visceral metastases. Roth et al. [10] performed a retrospective study where bone metastases didn't appear alone, suggesting that in the rest of the studies extra-bone metastases were misread, since they claim that PET and TC should be performed in all patients. Our patient didn't go through a PET scan.

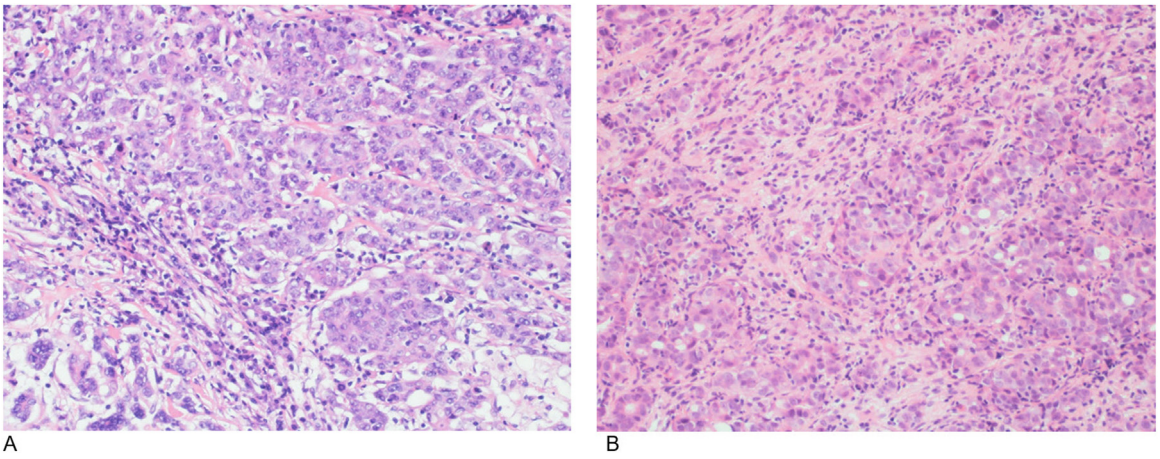

Fig. 3. A. Right Scapula Mass histology: fibrotic tissue infiltrated by a carcinoma, described as probably colorectal (medullar) or hepatic; B. Colonic Primary histology: colon adenocarcinoma, Grade 3.

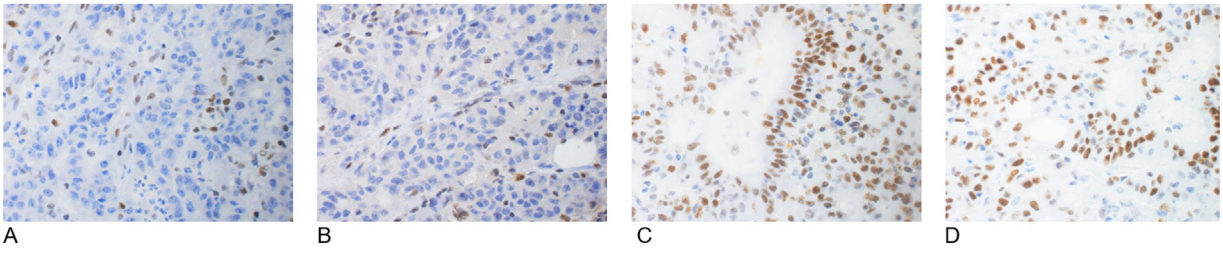

Fig. 4. A and B. Loss of MLH-1 and PMS-2 expression. C and D. Retained MSH-2 and MSH-6 expression.

Amongst histological subtypes of CRC, medullary carcinoma appears in women, right-sided and poorly differentiated tumours, with numerous intramural infiltrating lymphocytes. However, it is well delimited, probably justifying its less aggressive behaviour. This subtype of carcinomas doesn't usually originate lymph node metastases and is strongly associated with loss of DNA repair proteins [1]. In our case, the bone biopsy immunochemistry suggested a medullary type, although the analysis of the primary tumour could not corroborate those findings. The bone metastasis' sample was substantially small, which could have been a limitation factor when comparing both tissues.

Microsatellite instability (MSI) plays a role in the pathogenesis of 10–15% of the CCRs. Some are hereditary mutations (for example, Lynch Syndrome), but 80% are sporadic. MSI-high tumours usually have an advanced T stage at presentation, although they show lymph node metastases less frequently. They are known to be less aggressive, with a better overall survival, when compared with microsatellite stability colon cancers. This fact could justify the benign response in our patient, with a stage IV adenocarcinoma, alive without active disease for more than 3 years follow up.

The histological analysis remains crucial in these cases, when trying to figure out its association, if exist, with the tumours' behaviour. Several characteristics of our case fit with the medullar type tumours' behaviour, particularly the loss of MLH-1 and PMS-2 DNA repair proteins (Fig. 4) and the favourable outcome, although no relationship between these characteristics and bone metastases pattern of dissemination is known.

As an uncomplicated primary tumour, the initial management in our patient was focused on the treatment of the metastatic lesion. Due to severe pain, radiotherapy and up-front chemotherapy were administered for treatment of the disseminated disease. A posterior colonic resection was necessary due to an enlargement of the primary tumour. Our patient, who was diagnosed with a colonic adenocarcinoma with DNA mismatch repair deficiency and a solitary bone metastasis, is still alive after 3 years of follow up with no evidence of disease.

4. Conclusion

It is important to consider CRC on differential diagnosis in patients with bone metastases from adenocarcinoma with unknown primary despite its rare occurrence, even in the absence of other lesions. Considering this underexplored condition, we believe that this report can be useful for surgeons, oncologists and pathologists. More studies should be performed, aiming to learn more about these tumours' behaviour.

Declaration of Competing Interest

There are no conflicts of interest to declare.

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Ethical approval

As a case report, this work did not require ethical approval from ethics committee.

Consent

Informed written consent was obtained from the patient for publication of this report and any accompanying images.

Author contribution

Isabel FL, Manuel DA and Laura JA were attending doctors for the patient.

Isabel FL and Manuel DA preformed the surgical operation. José BM prepared the pathological report and provided pathological images.

All authors were involved in drafting and revising the manuscript, and all authors read and approved the final manuscript.

Registration of research studies

1. Name of the registry: Not applicable.
2. Unique identifying number or registration ID: Not applicable.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): Not applicable.

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