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CASE REPORT

Musculoskeletal Metastasis from Primary Rectal Cancer: Series of Two Cases of a Very Rare Occurrence with a Short Literature Review

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Introduction

As per Globacan 2012, colorectal cancer is the fourth most common cancer afflicting the worldwide population. It is estimated that around 50–60% of all colorectal malignancies will develop metastasis [1, 2] with the liver and lung being the most common sites for such metastasis. Less commonly involved sites include the peritoneum, and rarely involvement of bone, brain, and spleen is seen [3]. Metastatic cancer deposits in skeletal muscles are extremely rare from the gastrointestinal tract and despite a rigorous search of published literature, only 16 case reports of skeletal metastasis from colorectal cancers were found with only five of them originating from the rectum [4]. The management is not clearly defined in such a scenario and the prognosis remains guarded.

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Case Report

Case 1

A 24-year-old male presented to this hospital with complaints of bleeding per rectum for the past 2 months. He gave history of having undergone a hemorrhoidectomy 3 months previously for similar complaints. His symptoms had subsided for about a month but had resurfaced after that. There was also an associated weight loss (about 5 kg) and loss of appetite. He also gave history of a diffuse swelling involving the left thigh for the past 2 months associated with a dull throbbing pain. As per the patient, the thigh swelling was fairly static in terms of size and gave him a feeling of stiffness in his left thigh. There was no family history of any similar complaints. On per rectal examination there was a growth involving the rectal mucosa circumferentially starting at around 6 cm from the anal verge, with restricted mobility. There were no palpable inguinal or femoral lymph nodes. The examination of the left thigh revealed a 6 cm × 7 cm × 4 cm swelling in the lateral and dorsal aspect reaching up to the left buttock. It was hard, non-tender, and fixed to the underlying tissue.

On colonoscopy, a friable, circumferentially infiltrative mucosal lesion was seen causing a stricture in the lower rectum at 8 cm from anal verge. Biopsy from this rectal lesion showed predominantly infiltrating neoplastic cells singly scattered in a glandular architecture. These cells were intermediate to large in size with abundant clear to pale eosinophilic cytoplasm containing intercellular mucin, pleomorphic, hyper chromatic nuclei pushed to periphery with some cells showing distinct nucleoli. The histological appearance was of a poorly differentiated adenocarcinoma rectum with signet ring morphology (Fig. 1a).

The patient underwent a contrast-enhanced magnetic resonance imaging (MRI) of the pelvis and thighs which revealed rectal wall thickening with diffuse enhancement, perirectal fat

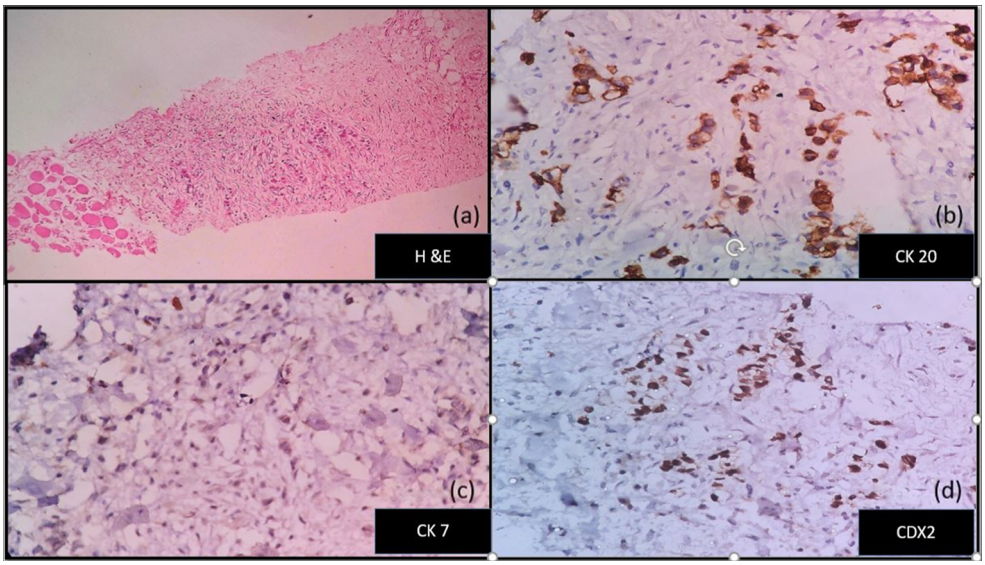

Fig. 1 **a** Adenocarcinoma rectum with signet ring cells. **b**, **c**, and **d**—IHC of neoplastic cells from thigh lesion positive for CK 20, CK 7, & CDX 2

stranding, and a few perirectal nodes. There was diffuse heterogeneous enhancement with areas of central necrosis involving the left piriformis, left gluteus minimus and medius, left obturator internus and left sartorius muscle with surrounding edema suggestive of a differential diagnosis of an inflammatory neoplastic process versus myonecrosis (Fig. 2). An 18 FDG PET CT for the patient corroborated with the MRI scan showing two distinct metabolic lesions. There was thickening of the rectal wall circumferentially with increased metabolic activity (SUV_{max} − 3.5). Diffuse swelling with patchy areas of increased FDG uptake was also seen in the left thigh and buttock region involving the above mentioned muscles (SUV_{max} − 5.77) (Fig. 3).

Initially several biopsies from the thigh mass showed only necroinflammatory tissue. However, due to a high degree of suspicion of a possible neoplastic origin, the lesion was further investigated. Deeper biopsies from the lesion were taken under anesthesia and they revealed fibroskeletal tissue infiltrated by singly scattered neoplastic cells. The cells were intermediate to large in size with abundant clear to pale, eosinophilic cytoplasm and pleomorphic, hyperchromatic nuclei pushed to the periphery. The immunohistochemistry (IHC) showed tumor cells positive for CK20 and CDX2 and negative for CK7, favoring deposits of adenocarcinoma in a known case of carcinoma rectum (Fig. 1b, c, d).

With the above clinico-radiological picture, the patient was diagnosed as a case of adenocarcinoma rectum with metastasis to the left thigh & buttock muscles. Due to extensive involvement of the soft tissue and muscles of the thigh, surgical resection could not be considered. He was treated with palliative radiotherapy to the pelvis and left thigh mass to a dose of 30 Gy in 10 fractions and was started on palliative

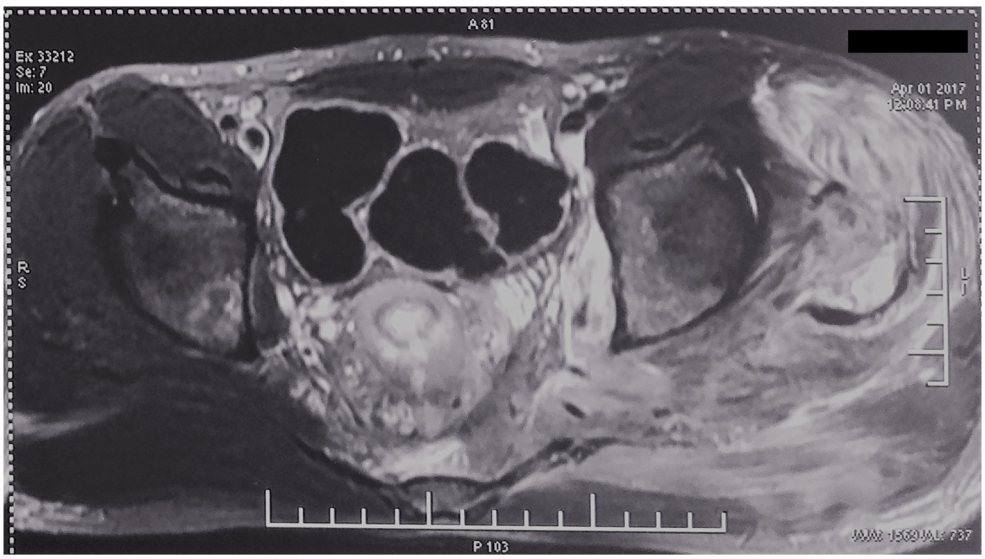

Fig. 2 MRI showing circumferential thickening with enhancement of rectal wall associated with diffuse swelling & heterogenous enhancement of left thigh

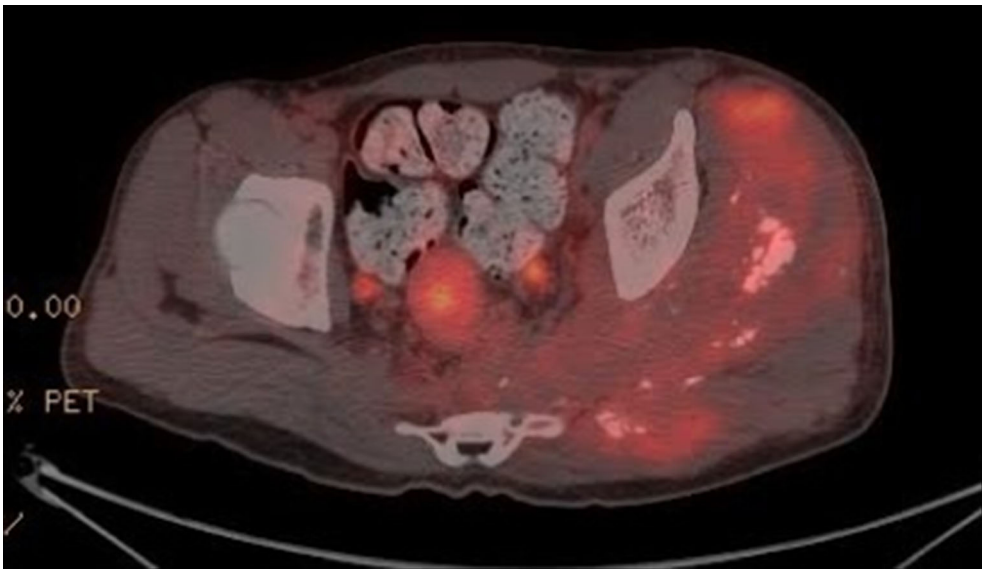

Fig. 3 FDG PET CT showing FDG avid mass in rectum and left thigh

chemotherapy with tablet Capecitabine. However, after the first cycle the patient developed symptoms of acute intestinal obstruction and underwent a diversion colostomy. Intraoperatively there were multiple peritoneal deposits with ascites indicative of progressive disease. His condition deteriorated and he was considered unfit for any further chemotherapy and was placed on best supportive care. He succumbed to his disease 6 months after his diagnosis.

Case 2

A 50-year-old female presented to our hospital with history of swelling in the right upper thigh for a period of 3 months. Her symptoms had rapidly progressed in the past 2 months in the form of pain, swelling, and unquantified weight loss associated with loss of appetite. On clinical examination, there was 5 cm × 6 cm swelling involving the medial compartment of her left thigh proximally. It was hard in consistency with restricted mobility. The patient underwent a detailed evaluation with the clinical suspicion of a sarcoma. A contrast-enhanced magnetic resonance imaging of the pelvis showed a well-circumscribed heterogeneous signal intensity mass lesion measuring 5.3 cm × 7.6 cm × 12 cm epicentered in the medial compartment of the proximal part of right thigh (Fig. 4). It was involving the adductor group of muscles, obturator internus, externus, and pectineus muscles with edematous changes. An 18 FDG PET scan showed metabolically active lesion in the thigh (SUV_{max} − 12.5), with multiple bilateral scattered lung nodules (SUV_{max} − 8.45) and increased uptake in the sigmoid colon (SUV_{max} − 14.5) and left ischium (SUV_{max} − 5.92) (Fig. 5).

She underwent a trucut biopsy from the soft tissue mass, which showed tumor cells lining malignant glands, which on IHC were positive for CK 20, CDX2, CA 19.9, and negative for CA 125, GCDFP, ER, PR, HER-2neu, and TTF-1 (Fig. 6). The final diagnosis was metastatic adenocarcinoma favoring a primary from gastrointestinal tract. With this input, the patient underwent a colonoscopy that revealed an ulceroproliferative growth 11 cm from the anal verge. Biopsy from this growth showed neoplastic glands infiltrating the sub-epithelium, suggestive of a moderately differentiated adenocarcinoma.

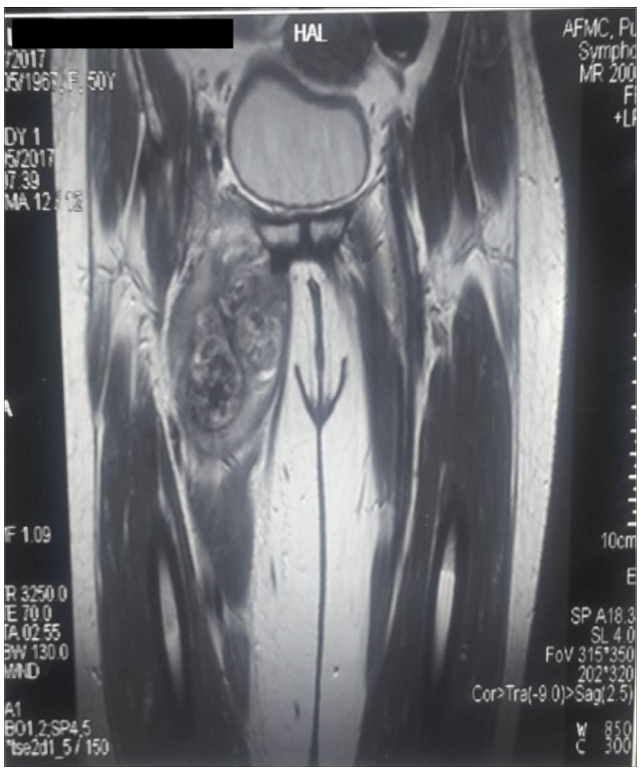

Fig. 4 MRI showing well circumscribed lesion with heterogenous signal intensity in medial compartment of left thigh

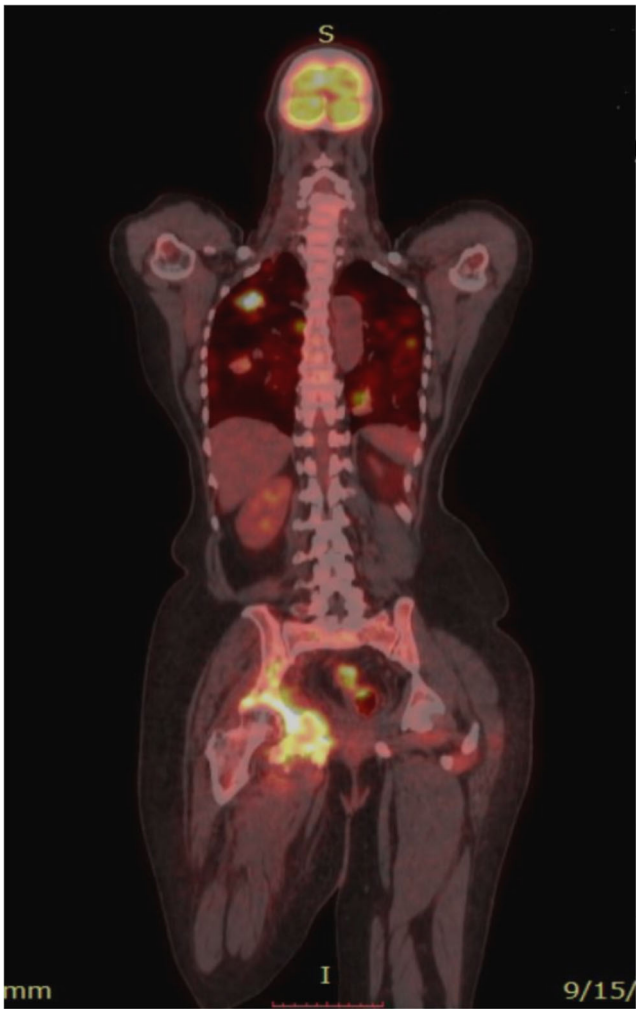

Fig. 5 FDG PET scan showing metabolically active lesions in Rt thigh, rectum, and both lungs

The patient was diagnosed as a case of metastatic carcinoma rectum and underwent palliative radiotherapy to the right thigh to a dose of 30 Gy in 10 fractions and had 50% relief in pain and reduction in the size of the tumor as well. She was started on palliative chemotherapy with capecitabine and oxaliplatin and received 6 cycles. Response evaluation with a PET CT scan revealed stable disease with regression in the thigh and rectal lesions. Patient refused further chemotherapy and is presently on 3-month surveillance. She has stable disease at 9 months from her diagnosis.

Discussion

Colorectal cancers remain one of the leading causes of death globally [5], and almost half of them develop distant metastases. Most patients with metastatic CRC have incurable disease. In this group of patients, median survival has improved from less than 10 months with best supportive care to 14 months with fluoropyrimidine treatment [6, 7] and to more than 2 years with a combination of various cytotoxic [8, 9] and biologic agents [10, 11].

The common pattern of metastasis involves the liver and lung and then other organs. Various theories of metastasis include hematogeneous, lymphatic, or peritoneal spread along with direct extension of the tumor [3]. The spine can be involved because of Batson's plexus and other metastatic bony sites are skull, femur, and pelvis [12–14]. There is some evidence to prove than synchronous metastasis has poorer prognosis as compared to metachronous metastasis (especially involving liver metastasis) [15].

Oligometastatic disease is a recent concept associated with rectal malignancies [16] and the treatment varies from potentially curative resection or local therapy to palliative care.

In patients with non-resectable oligometastatic disease, those with metastatic disease to the liver or lung have a better

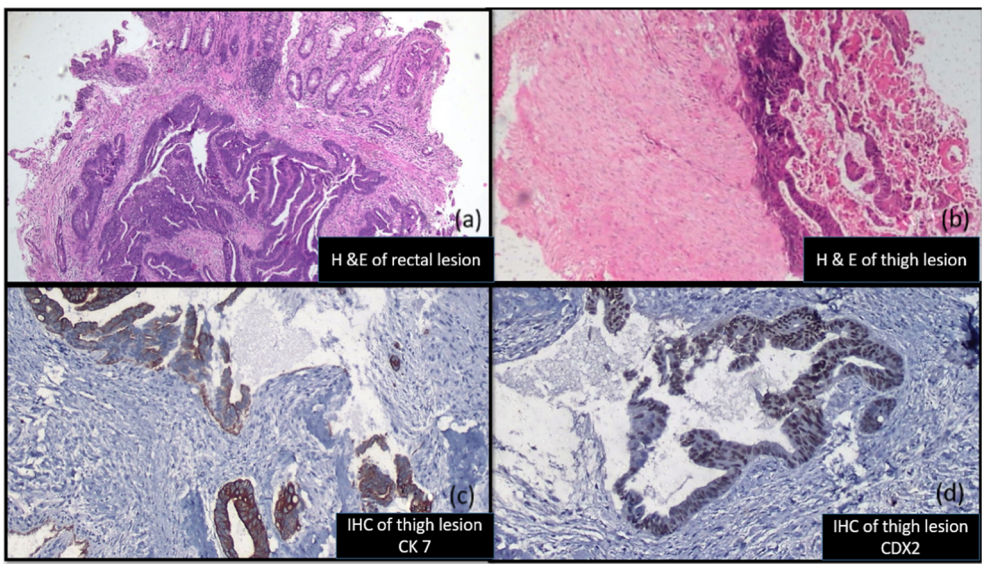

Fig. 6 **a** Adenocarcinoma rectum with malignant glands. **b** Thigh lesion also showing malignant cells with gland formation. **c** and **d** IHC of neoplastic cells from thigh lesion positive for CK 7 & CDX 2

Table 1 Summary of case reports of skeletal muscle metastasis from colorectal primary

S no.	Author	Age/sex	Site of metastasis	Primary location	Treatment	Survival after diagnosis of metastasis
1.	Takada J, et al. [22]	71/M	Iliopsoas	Sigmoid colon	RT + FOLFOX 4+ RESECTION & S-1	5 months
2.	Naik VR, et al. [23]	56/M	Rectus abdominis	Ascending colon	RESECTION+ FOLFOX4	NA
3.	Burgueno Montanes, et al. [24]	60/M	Lateral rectus of orbit	Recto-sigmoid	RT + FOLFOX 4	NA
4.	Hasegawa S, et al. [25]	60/M	Extensor carpi ulnaris	Transverse colon	RESECTION+FOLFOX4	NA
5.	Homan HH, et al. [26]	72/F	Erector spinae	Descending colon	RESECTION+FOLFOX4	NA
6.	Bonjer HJ, et al. [27]	NA	Rectus abdominis	Recto-sigmoid	FOLFOX4	NA
7.	Jaquet P, et al. [28]	NA	Rectus abdominis	NA	RESECTION+FOLFOX4	NA
8.	Tunio MA, et al. [3]	28/M	Gluteus maximus & rectus abdominis	Transverse colon	RT + FOLFOX4	Alive at 12 months

M male, *F* female, *RT* radiotherapy, *NA* not available

prognosis than those with metastases to the peritoneum, brain, or bone [17]. The concept of oligometastaic disease is best explained by the seed and soil theory first propagated by Rutherford. According to it, the seed or cancer cell must find a suitable environment, i.e., soil, for metastasis to occur. There is also a complex role of target microenvironment affecting cancer cell gene expression, behavior, and response to treatment [18–21].

Metastases to skeletal muscle from a colorectal primary is extremely rare and only eight such cases have been reported in literature (Table 1). Of these, only two cases had a recto-sigmoid primary with the others cases having a colonic primary. Hence, it was an extremely rare coincidence to encounter two such patients in our hospital within a few months of each other. The secondary site varied from muscles of the back and abdomen to muscles of the orbit and hand. The management in these reports has varied from extremely aggressive treatment with combined surgery, radiotherapy and chemotherapy to palliative chemotherapy alone. The prognosis can be expected to be poor in such cases with the reported survival ranging from 5 to 12 months. With such a small but varied set of cases, it is difficult to define a management strategy.

In the first case, despite a single site of metastasis, the patient could not be treated radically due to the large deposit in the thigh and rapidly progressing disease with worsening of general condition. In the second case, the patient was asymptomatic for the primary rectal malignancy and presented as a swelling in the thigh. She is alive and stable at 9 months from diagnosis.

This series highlights two different cases with two different presentations of an extremely rare site of metastasis in carcinoma rectum.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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