

## Isolated Metastases in the Elbow as the First Presentation of Metastatic Colorectal Cancer – A Case Report and Overview of Literature

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### Abstract

**Introduction:** Colon adenocarcinoma frequently metastasizes to the liver and lung. Distant metastasis to skeletal muscle and subcutaneous tissues arising from colorectal cancer are rarely reported in the literature. Treatment options include radiotherapy, chemotherapy and surgical excision, with no standard treatment.

**Case presentation:** A 64 years old male presented with painful mass in the left elbow (8.5x5.5 cm). The incisional biopsy of the tumor showed poorly differentiated carcinoma, with no clear differentiation between epitheloid sarcoma or low differentiated carcinoma metastasis. PET CT showed pathological metabolic activity in the left elbow and in the right part of the abdomen. Colonoscopy was performed, showing an ulcerated obliterating adenocarcinoma of the sigmoid colon. Hemicolectomy followed. The histological comparison of the both tumors, showed the same characteristics. Molecular analysis showed biomarkers non mutated status. The radiotherapy of the elbow was applied, and he started with combination of doublet chemotherapy and EGFR inhibitor. After three cycles, complete remission was achieved, remaining present. Due to complete regression surgical resection was not necessary.

**Conclusion:** We have reported an extremely rare case of isolated skeletal muscle metastasis as first presentation of metastatic colon adenocarcinoma. PET CT can be helpful to localize the primary site of the metastatic deposits. Immunostaining and pathohistological comparison of the primary carcinoma and the metastasis should be incorporated to reach the final diagnosis whenever possible.

Since skeletal muscle metastases are considerably rare and the therapy is not standardized, treatments of these patients should be individualized and must depend on the clinical settings and biomarkers status.

**Keywords:** Colon adenocarcinoma; Radiotherapy; Chemotherapy; Isolated skeletal muscle metastasis; EGFR inhibitor

### Introduction

Colorectal Cancer (CRC) is one of the most common cancers and the second leading cause of cancer-related death worldwide [1]. Distant metastases from colon cancer spread most frequently to the liver (20-70%) and the lung (10-20%) [2]. Distant metastasis to skeletal muscle and subcutaneous tissues arising from colorectal cancer are rarely reported in the literature. We report a case with isolated skeletal muscle metastasis in the left elbow as a first presentation of metastatic adenocarcinoma of the colon, with complete response after the treatment in respect to the patient's biomarkers status. In addition we provide an overview of the literature.

### Case Report

A 64 years old male was presented at a multidisciplinary case conference at the Oncology Institute Ljubljana in April 2014. The patient had limited function of the arm and paresthesia in the fingers of the left hand because of a painful mass in the left elbow (8.5x5.5 cm). He reported a loss of appetite because of the pain, and, in consequence, a weight loss of 10 kg in the last four months. He reported a defecation rate decrease (once in two days). He had neither blood stools, nor painful defecation, nor pain in the abdomen. He was in very good PS WHO (0-1), with normal liver and kidney function, and normal values of CEA and Ca 19-9. In 2009 he had a myocardial infarction followed by a karvedilol and acetylsalicylic acid treatment. At his presentation his cardiac function was good (Cycloergometry-achieved 71% of planned stress, with no ischemia or stenocardia).

MRI showed an aggressive infiltrative tumor mass with necrotic zones in the ulnar part of the forearm, which was infiltrating the structures in the cubital canal (Figure 1). The incisional biopsy of the tumor showed poorly differentiated carcinoma. No clear differentiation

between epitheloid sarcoma or low differentiated carcinoma metastasis could be made, not even after a Immunohistochemistry (IHC) analysis for broad specter of biomarkers for different tumors.

The treatment strategy for sarcoma with Hyperthermic Isolated Limb Perfusion (HILP) with melphalan was initially selected. Before starting the treatment, a PET CT was performed which showed pathological metabolic activity in the elbow (SUV 22,2) and in the right part of the abdomen (SUV 21,1). Colonoscopy followed showing an ulcerated obliterating mass in the sigmoid colon. A subsequent right hemicolectomy revealed a large ulcerated mass (8 x 4 cm) with histological picture of low differentiated intestinal adenocarcinoma. An IHC comparison of the primary tumor and metastasis in the left elbow tissue showed the same poorly differentiated component in the both, presented as negative staining for cytokeratin 7 and cytokeratin 20. Molecular analysis showed unmutated biomarkers status (KRAS, NRAS, BRAF).

### Treatment

The pain was successfully treated with opioid patch of fentanyl 100 ug, and 5-10 gtt of Morphine oral solution for breakthrough pain immediately after presentation. In June 2014 the patient started with

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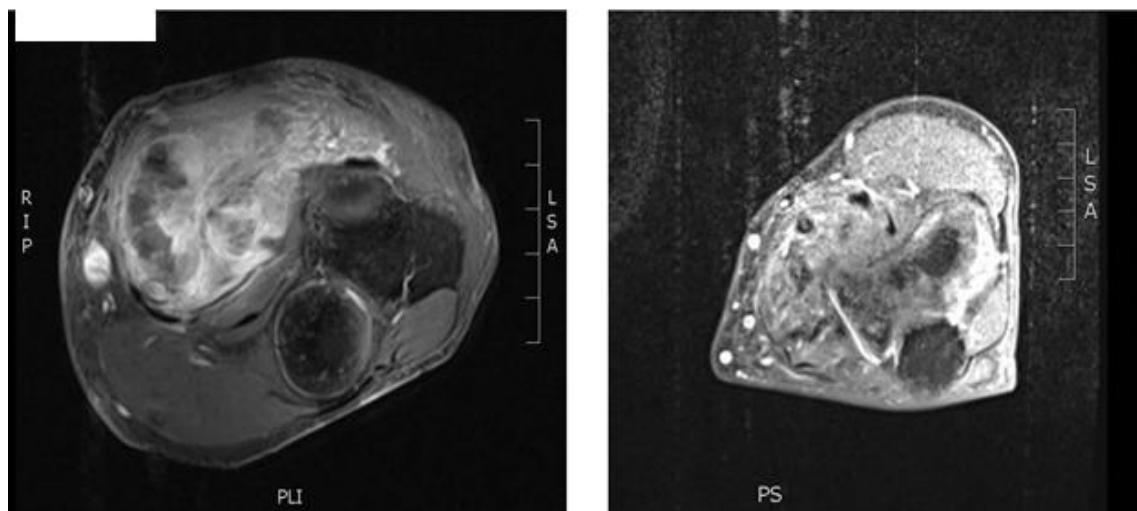


Figure 1: MRI of the tumor mass in the left elbow before (1a) and the complete remission after three cycles FOLFOX with Cetuximab.

chemotherapy doublet scheme FOLFOX (Oxaliplatin 100mg/m<sup>2</sup>, 5-FU bolus and 5-FU 1000 mg/ml in 46 h infusion) and EGFR inhibitor Cetuximab (initially 400 mg/m<sup>2</sup> followed by weekly infusions of 250 mg/m<sup>2</sup>) due to his pan RAS unmutated status of the primary tumor. In the same time palliative Radiotherapy (RT) with 20 Gy (4x5Gy) to the tumor mass was applied. After the first application of FOLFOX with Cetuximab, and RT, there was noticeable shrinkage of the tumor mass, from 8.5 × 6 cm to 5 × 5 cm, and relief of the pain and neurological symptoms. As result, the fentanyl dose was decreased to 25 ug/h. After two cycles of FOLFOX with Cetuximab, the patient regained finger movement.

In September 2014, after three cycles of treatment, MRI showed complete regression of the tumor mass (image 1b).

As of this writing the patient had received six cycles of FOLFOX and Cetuximab. He is remaining in complete remission and in very good condition, and, on own request, continues with regular follow-ups only, without Cetuximab maintenance therapy.

## Discussion

Distant metastases from colon cancer spread most frequently to the liver (20-70%) and the lung (10-20%) [2]. Skeletal muscle metastases are usually late manifestation of the disease and are therefore associated with poor patient prognosis with average survival of 5-12 months after diagnosis [3]. They are often presented as painful masses [4]. The differential diagnosis for a solitary soft tissue lesion includes sarcoma, benign soft tissue neoplasm, hematoma, and infection [3,5]. Incisional biopsy is needed for a differentiation between a primary soft tissue sarcoma and metastatic carcinoma [6]. In our case PET-CT was crucial to discover the primary malignancy in the sigmoid colon. Hystopathological comparison of the tumor mass excised from the elbow with the removed adenocarcinoma tissue of the colon provided the basis for the final diagnosis.

As mentioned, metastases are typical for an advanced disease, which was not the case with our patient. Symptoms of the secondary deposit in the skeletal muscle were presented before the diagnosis of the colon adenocarcinoma was made. The primary lesion was only discovered because of the mass in the elbow. The resected colon adenocarcinoma had pT3N0 (0/32) characteristics. As lymphangiocarcinomatosis was

present, the patient was defined as 'high-risk' stage II patient with very good 5-year survival prognosis of 60-80% after surgery [7]. However, he presented with solitary skeletal muscle metastasis in the elbow. The remission after 3 cycles of chemotherapy and Cetuximab combined with palliative radiotherapy was remarkable [8-11].

Skeletal muscle metastasis is a rare entity, especially when it comes to isolated skeletal muscle metastasis of colorectal adenocarcinoma. There are few cases reported in the literature. In order to shed more light on this issue, we used Pubmed and Researchgate as information base in search for similar cases (published in english). In the table below we present an overview of the reported cases of isolated skeletal muscle metastasis originating from colorectal adenocarcinoma from 1987 to 2013 (Table 1). In most of these cases the metastasis were found only after the primary cancer was diagnosed and treated. The information of the primary cancer stage was included in only two cases [12-14]. Of ten cases summarized in the table only one, reported by Chang et al. [15,16], was similar to our case. The patient presented with the metastasis to the muscle as initial manifestation of colon adenocarcinoma. After the broad excision of the muscle metastasis and palliative transverse-sigmoid colocolonostomy was performed, the patient refused further treatment and developed brain metastases. Excision of the mass was possible in almost all described cases, usually followed by radiotherapy or chemotherapy (Table 1). In only two cases the treatment did not include surgical removal of the mass [10,15]. The overall treatment strategy [3,8-16] was unclear as there is no standard treatment for isolated muscle metastasis of colorectal adenocarcinoma. Most of the authors didn't include data regarding survival after diagnosis and treatment [3,8,9,12,15,16]. The variability and the lack of published data prevents a conclusion about the connection between initial carcinoma stage, time of metastatic presentation, treatment used and prognosis.

In our case, the EGFR inhibitor Cetuximab was successfully included, as the biomarkers indicated sensitivity of the tumor. There was a complete remission of the muscle metastasis after combination of radiotherapy, chemotherapy and the EGFR inhibitor. Therefore surgical removal was not needed. The patient continues to lead a quality life thank to immediate pain treatment and avoidance of excision or

Author	Age	Primary location	Site	Treatment of metastasis	Survival after diagnosis of skeletal metastasis
Glockner et al. [3]	44 years female	Colon	Gluteal region	NA	NA
Torosian et al. [8]	68 years female	Colon	Thigh	Resection	NA
Lampenfeld et al. [9]	75 years female	Rectum	Gluteal region	Resection + RT + fluorouracil	NA
Omnia et al. [10]	45 years male	NA	Rectus abdominis	FOLFOX + RT + FOLFIRI	Alive at 8 months
Ünsal et al. [11]	31 years male	Recto-sigmoid	Proximal half portion of the forearm, infiltrating the medulla of the radius	RT + 5-FU+ calcium folinate + resection + irinotecan	Alive at 15 months
Naik et al. [12]	56 years male	Colon	Rectus abdominis	Resection	NA
Lee et al. [13]	42 years male	Sigmoid colon	Diaphragm	Resection+ FOLFIRI	Alive at 7 months
Iusco et al. [14]	73 years female	NA	Capsulated mass adjacent to the soleus muscle.	Resection + RT	Alive at 24 months
Salar, et.al. [15]	67 years female	Rectum	Piriformis muscle	Chemotherapy + RT	NA
Chang et al. [16]	42 years male	Descending colon	Tibialis anterior	Resection	NA
<b>Present case</b>	64 years male	Sigmoid colon	Elbow region	FOLFOX + RT + Cetuximab	Alive at 18 months

**Table 1:** Cases of colorectal adenocarcinoma with isolated skeletal muscle metastasis reported from 1987 to 2013.

limb amputation.

## Conclusion

Although the majority of soft tissue masses are benign, with an incidence 50-100 times higher than malignancies, it is important to consider malignancy in the differential diagnosis when signs including large size, rapid growth, and location in the deep fascia occur. In case of malignancy, metastases should be considered as well as the possibility of an atypical primary neoplasm in some other organ.

In conclusion, we have reported an extremely rare case of isolated skeletal muscle metastasis as first presentation of metastatic adenocarcinoma of the colon. PET CT can be helpful to localize the primary site of the metastatic deposits. Immunostaining and pathohistological comparison of the primary carcinoma and the metastasis should be incorporated to reach the final diagnosis whenever possible.

Since skeletal muscle metastases are considerably rare, and the therapy is not standardized, treatments of these patients should be individualized and must depend on the clinical settings and biomarkers status. In our case, the EGFR inhibitor Cetuximab was successfully included, as the biomarkers indicated sensitivity of the tumor. There was a complete remission of the muscle metastasis after combination of radiotherapy, chemotherapy and the EGFR inhibitor. Therefore surgical removal was not needed. The patient continues to lead a quality life thank to immediate pain treatment and avoidance of excision or limb amputation.

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