



A Case Study on ^{18}F -FDG PET/CT Imaging Value in Colorectal Cancer with Subcutaneous, Breast, Kidney, and Muscle Metastases

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Authors' contributions

This work was carried out in collaboration among all authors. Authors ENI and NK wrote the manuscript. Authors BBO and SC reviewed the manuscript. Authors MKD provided radiological consultation. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Aim: To describe an unusual case of colorectal cancer with metastases to various extra-abdominal sites, including subcutaneous tissues as an extremely rare clinical event with ^{18}F -fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F -FDG-PET/CT) findings.

Presentation of Case: We report a case of 51-year-old female patient with metastases of BRAF V600E mutant colorectal adenocarcinoma to the subcutaneous tissue, left kidney, left breast, lower back, anterior abdominal wall, and gluteal region, which was detected by whole body ^{18}F -FDG-PET/CT. Histopathological examination of excisional specimen of a lumbar subcutaneous nodular mass revealed an adenocarcinoma metastasis with RAS wild type, BRAF V600E mutation. The patient was treated with 12 cycles of FOLFOXIRI combined with bevacizumab regimen for 6

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months. Follow-up ^{18}F -FDG-PET/CT after the end of therapy revealed complete metabolic response.

Discussion: Subcutaneous metastasis of colorectal cancer with BRAF V600E mutation is a rare but important phenomenon and has poor prognosis. Triplet chemotherapy plus bevacizumab is the treatment of choice due to its aggressive type of tumor. ^{18}F -FDG-PET/CT is a very effective imaging modality to demonstrate all malignant masses before treatment and to evaluate treatment response. **Conclusion:** It is essential to be familiar with the rare association of colorectal cancer and breast, kidney, muscle, and subcutaneous metastases to improve diagnostic accuracy and patient management. ^{18}F -FDG-PET/CT imaging is very effective to demonstrate all malignant masses before treatment and to exclude the coexistence of another possible primary tumors via treatment results.

Keywords: *Atypical rectal cancer metastases; BRAF V600E mutation; PET/CT; triplet chemotherapy plus bevacizumab.*

1. INTRODUCTION

Approximately, 4% of colorectal cancer patients have cutaneous and subcutaneous metastases [1]. The presence of them generally signifies disseminated disease [2]. Their most frequent location is the abdominal or perineal skin [3]. ^{18}F -FDG PET/CT is the most important imaging modality for the initial diagnosis, staging, and follow-up of colorectal cancer [1,4,5]. Metastatic colorectal cancer patients with subcutaneous metastases who have BRAF V600E mutations were rare and reported to be associated with poor prognosis [6,7]. FOLFOXIRI plus bevacizumab as an appropriate choice for the first-line treatment of patients with metastatic colorectal cancer [8].

In this paper, we present a rare case of a 51-year-old woman with multiple subcutaneous metastases from BRAF V600E mutant colorectal cancer and treated with FOLFOXIRI plus bevacizumab regimen for 6 months. ^{18}F -FDG PET/CT examination after the patient had undergone adjuvant chemotherapy showed complete clinical and radiological response of all the tumors. We conclude that the optimal evaluation and treatment of colorectal cancer with subcutaneous metastases may result in a good prognosis.

2. PRESENTATION OF CASE REPORT

A 53-year-old female patient presented with tenesmus, rectal bleeding, and anal pain for 6 months. Colonoscopy revealed an ulcerated and infiltrating type-2 tumor, occupying the full circumference in a segment of 10 cm long, located at 6-7 cm from the anal margin. A biopsy from the rectum was taken and confirmed a colorectal adenocarcinoma. On physical examination, a mobile palpable 1 cm mass in the upper-inner quadrant of her left breast and

another nontender and mobile 1 cm subcutaneous nodule in the left lumbar region were detected. Pelvic magnetic resonance imaging revealed the malignant colorectal tumor with transmural penetration and perirectal fat invasion. Staging ^{18}F -FDG PET/CT was performed and showed hypermetabolic masses in the colorectal area, right gluteal muscle, left subcutaneous fat of the anterior abdominal wall, upper pole of left kidney and left breast. Hypermetabolic nodules with a diameter of 9 mm (SUV max: 4.85) in the upper inner part of the left breast, and 1,5 cm (SUV max:16,26) hypermetabolic nodules at the level of the right 9th rib posterolaterally under the skin of the thorax. (Fig. 1 a-e). Clinical stage is T3NxM1. Histopathology of the excisional biopsy of the lumbar subcutaneous mass suggested that the primary tumor was colorectal adenocarcinoma, and the others were metastatic (Fig. 2). On immunohistochemical stains, CK20 was positive, whereas CK7, TTF, synaptophysin and chromogranin were negative. The molecular testing of KRAS, NRAS, BRAF mutations and MSS/MSI status were analyzed using real-time PCR. KRAS and NRAS were wild type and MSS were negative. BRAFV600E mutation was found positive. After 12 cycles of FOLFOXIRI plus bevacizumab, follow-up ^{18}F -FDG PET/CT revealed complete metabolic response to all the tumors, including subcutaneous metastatic nodular lesions (Fig. 1 f-j). No new metastases were observed. The patient was consulted in multidisciplinary oncology committee and maintenance therapy with capecitabine and bevacizumab, and a short course of local colorectal radiotherapy that was pelvic 5x5 GY were applied. The last examination in July 2021, PET/CT revealed that still had a complete response radiologically. Moreover, bevacizumab continues as maintenance therapy for the patient.

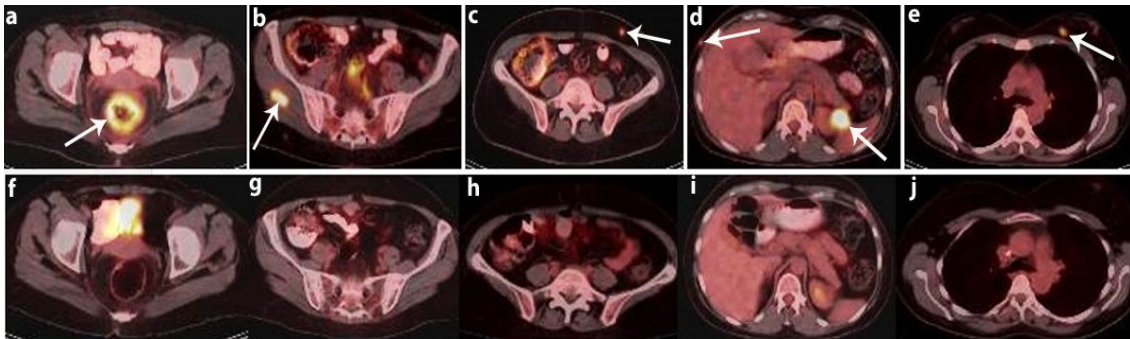


Fig. 1. (a-e) Axial fused ^{18}F -FDG PET/CT images in a 51-year-old female patient obtained for initial evaluation show hypermetabolic masses in the rectal wall (a), right gluteal muscle (b), left subcutaneous fat of the anterior abdominal wall (c), upper pole of left kidney (d) and left breast (e). (f-j) Axial fused ^{18}F -FDG PET/CT images after patient had undergone chemotherapy for colorectal cancer show lack of tracer uptake within the tumors, which confirms favorable metabolic response to therapy

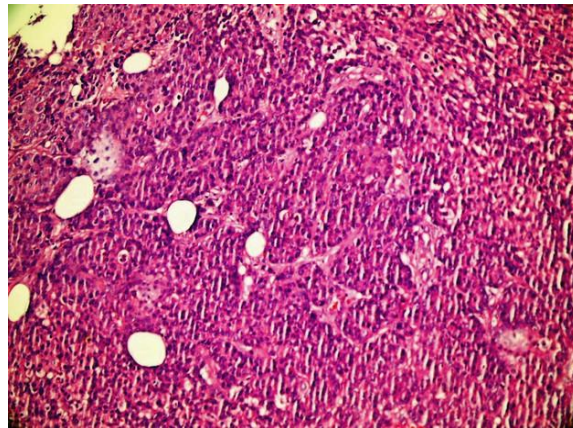


Fig. 2. Microscopic findings

In the examination of the sections, neoplastic infiltration consisting of large, pleomorphic atypical cells with vesicular nuclei forming cribriform structures and adenoid structures of different diameters are observed. Many atypical mitotic figures are seen

3. DISCUSSION

Colorectal cancer is one of the most frequent oncological diseases. The most common site of metastasis for colorectal cancer is the liver. Cancers with subcutaneous metastases are unusual presentations and may result in both direct invasions and distant spread of primary malignancies. The incidence of cutaneous metastasis was 420 of 4,020 metastatic carcinoma patients presented by [9-10]. Among cutaneous metastases from 18 colorectal cancer patients, distant metastases were detected in only 7 patients (38.9%) [10]. Additionally, in distant metastasis, the metastatic nodules are most commonly located at the trunk, pelvis and lumbar regions, or in breast tissue, as in our

case. The incidence of cutaneous metastasis from a primary visceral tumor range from 0.7% to 9% [9,11-14], and those of cutaneous metastases from colorectal cancers are less than 4% [11]. Eventually, very few studies have been reported about subcutaneous metastasis from colorectal cancer, because subcutaneous tissue as the first site of metastasis without other organ involvement is highly rare [2,10,15]. Besides, the mean survival time for patients with soft-tissue metastasis has been reported to be 5.4 months [10,13]. Furthermore, 8-12% of advanced colorectal cancer (aCRC) patients, tumors have the V600E activating mutation in BRAF (BRAF-mutant). Also, BRAF-mutant aCRC confers a markedly worse prognosis independent of associated clinicopathological features [16].

Moreover, the presence of a BRAF V600E mutation in metastatic colorectal cancer can be a key prognostic biomarker for poor outcome [17]. Triplet regimen as FOLFOXIRI combined with bevacizumab appears to be a pragmatic and efficient approach for selected patients, specifically in the context of patients with BRAFV600E mutated aCRC, who mostly do not receive second-line treatments [8,16,18]. The patient in our case received triplet chemotherapy plus bevacizumab due to its aggressive type of tumor with BRAF mutation. Another example by Camci et al. revealed that subcutaneous nodules around the right shoulder and the back from patient with colon carcinoma and three courses of second-line chemotherapy (Irinotecan and deGramont regime) and four weekly pamidronate infusion were given in colon carcinoma and they showed that partial remission was determined at the subcutaneous metastases after the third course of therapy [19]. PET-CT imaging is increasingly being used in cancer patients due to the role for staging and assessment of disease burden and in treatment response evaluation in advanced cases. In the presented case, we demonstrated the achievement of a complete metabolic response on ¹⁸F-FDG PET/CT imaging after the treatment. Besides, posttreatment PET/CT imaging findings also excluded the possibility of another primary malignancy, such as kidney or breast. PET/CT seems to be a useful tool in the evaluation of colorectal cancer by metabolically characterizing undetermined lesions suspected to be recurrent disease to identify occult metastatic disease [20]. Since subcutaneous metastasis is a rare situation in colorectal cancer, and metastases would not be detected if PET/CT was not revealed subcutaneous lesion for staging.

4. CONCLUSION

In conclusion, subcutaneous metastases with or without other sites from a BRAF V600E mutated colorectal cancer is an unusual event. When present, the metastases usually signify disseminated disease and poor prognosis. Both physical examination and ¹⁸F-FDG PET/CT imaging for staging are crucial for colorectal cancer patients. We here report this case not only for its rarity but also to demonstrate the complete response of the treatment on ¹⁸F-FDG PET/CT imaging. ¹⁸F-FDG-PET/CT is a very effective imaging modality to demonstrate all malignant masses before treatment and to exclude the coexistence of another possible primary tumors via treatment results. Isolated

cutaneous-subcutaneous metastases from colon cancer detected with FDG-PET/CT have been rarely reported in the literature. Under skin lesions in a case with colon cancer history should always raise suspicion of skin metastasis and should be evaluated further with histopathologic confirmation.

CONSENT

All authors declared that written informed consent was obtained from the patient herself for publication of these case reports and accompanying images. However, identification of the patient is not disclosed anywhere in the article.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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