Sarcoidosis with Multiorgan Involvement and Cutaneous Manifestations after Colonic Adenocarcinoma Resection

Abstract

Sarcoidosis is a systemic chronic granulomatous disease. It mostly involves the lungs and hilar lymph nodes and produces epithelioid granulomas. Granulomatous (sarcoid) reaction is known to be associated with malignancies; however, it is uncommonly seen with colon carcinomas. Furthermore, systemic sarcoidosis following cancer diagnosis is less commonly seen. To the best of our knowledge, cutaneous sarcoidosis related with an underlying colon carcinoma has not been reported previously in the literature. In this report, we present a very rare case with sarcoidosis development after resection of sigmoid adenocarcinoma, presenting with multiorgan involvement including the skin, eye, joints, and lymph nodes. 18F-fluorodeoxyglucose-positron emission tomography/computed tomography (18F-FDG-PET/CT) images showed the skin, lung, spleen, mediastinal, and hilar lymph node involvement. Histopathological examination of skin lesions demonstrated granulomatous dermatitis. This case demonstrates that sarcoidosis can cause intensely FDG-avid lesions on 18F-FDG-PET/CT scans, mimicking metastasis in colon cancer patients. Histopathological evaluation is essential for confirming the diagnosis. 18F-FDG-PET/CT scan provides important information for evaluation of disease extension, progression, and clinical follow-up.

Keywords: *Colonic adenocarcinoma, granulomatous dermatitis, sarcoidosis*

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Introduction

Sarcoidosis is a systemic chronic granulomatous disease. It mostly involves the lungs and hilar lymph nodes and produces epithelioid granulomas. Epithelioid granulomas are seen in various conditions, such as autoimmune diseases, infections, toxic-related reactions, and drug reactions. Even though granulomatous reaction is also known to be associated with underlying malignancies with average frequency of 4.4% in carcinomas, it is relatively less commonly associated with colon carcinoma, and there are only few cases reported.[1-7]

Case Report

A 60-year-old male with surgically resected sigmoid colon adenocarcinoma (Grade 3, Stage 3B-T4N1M0) was started on adjuvant chemotherapy consisting of folinic acid, 5-fluorouracil, and oxaliplatin (FOLFOX), for 12 cycles. 1 year after the operation, computed tomography (CT) scan revealed new metastatic liver nodules [Figure 1b]. The patient received multiagent chemotherapy consisting of folinic acid, FOLFIRI, and cetuximab, for 24 cycles. Follow-up positron emission tomography/CT (PET/CT) scan showed multiple fluorodeoxyglucose (FDG)-avid liver lesions (maximum standardized uptake value [SUV max]: 9.8) [Figure 1c]. Subsequently, he received additional chemotherapy consisting of capecitabine for six cycles and FOLFOX and bevacizumab for six cycles.

Three years after the operation, he started having joint pain, skin lesions, and visual problems. He went through cataract surgery. Physical examination revealed erythematous lesions with central keratosis on both the legs and an indurated lesion on the left arm [Figure 2]. 18F-FDG-PET/CT scan showed multiple FDG-avid (SUV max: 6.7) cutaneous and subcutaneous lesions on both the lower extremities and left upper extremity [Figure 1a and e-g]. Other findings included mild FDG uptake (SUV max: 2.9) in multiple mediastinal lymph nodes [Figure 1d], increased reticular density with ground-glass opacity in the subpleural regions of both the lungs and enlarged spleen with diffusely

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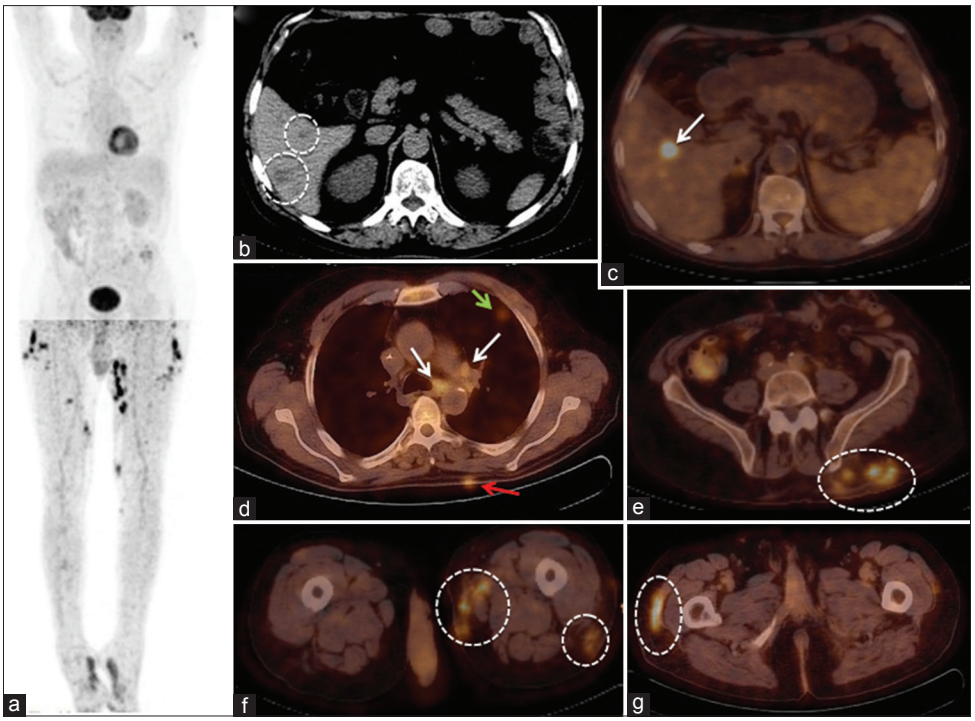

Figure 1: (a) Fluorodeoxyglucose-positron emission tomography maximum intensity projection image demonstrates multiple fluorodeoxyglucose - avid foci over the cutaneous and subcutaneous tissues. (b) Computed tomography image reveals multiple hypodense hepatic lesions (circles). Axial fluorodeoxyglucose-positron emission tomography/computed tomography images demonstrate fluorodeoxyglucose - avid lesions in (c) liver (maximum standardized uptake value: 9.8) (arrow), (d) multiple lymph nodes in the mediastinum and hilum (maximum standardized uptake value: 2.9) (white arrows), peripheral left lung (green arrow), cutaneous left paraspinal region (red arrow), (e) cutaneous tissue over the left posterior pelvic region (oval), (f) soft tissue over the left leg (circles), and (g) subcutaneous tissue of the right thigh (maximum standardized uptake value: 6.7) (oval)

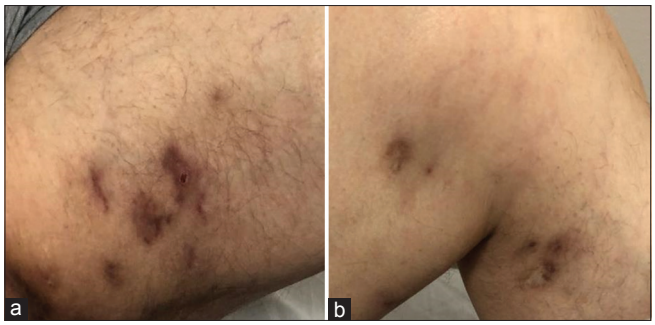

Figure 2: (a) Erythematous lesions on the left medial thigh, (b) Lesions on the medial region of the left knee and upper calf

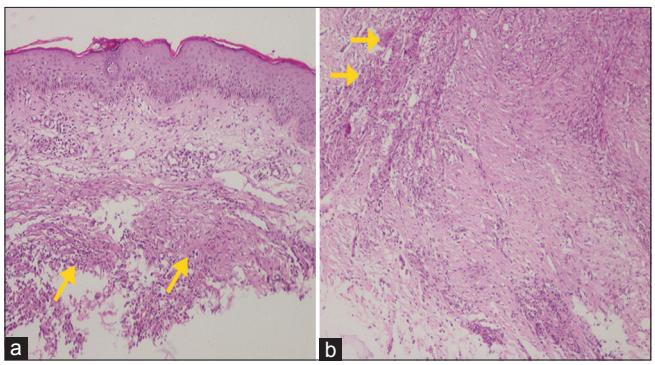

Figure 3: (a) Normal epidermis at the surface and granuloma formation (arrows) at the dermis. No necrosis was seen in granulomas (H and E, ×100), (b) Granulomas formed in the deep dermis. Multinucleated giant cells are found on the left upper corner (arrows) (H and E, ×100)

increased moderate-FDG uptake (SUV max: 3.6) in the splenic parenchyma. He did not have any respiratory symptoms such as dyspnea, cough, or wheezing. Skin biopsy from the arm lesion revealed nonnecrotizing granulomas with multinucleated giant cells and numerous histiocytes [Figure 3]. Consequently, he was diagnosed with granulomatous dermatitis. Ziehl–Neelsen staining and pan-keratin immunohistochemical staining were both found negative. Even though the patient was on maintenance therapy with capecitabine (xeloda) and bevacizumab, follow-up PET/CT scan identified intensely FDG avid multiple hypodense liver lesions compatible with metastatic liver nodules which was confirmed as colonic metastasis after needle biopsy. Percutaneous radiofrequency ablation was performed on the liver for the lesions, and he was started on FOLFIRI and bevacizumab. The patient is still receiving chemotherapy.

Discussion

Granulomatous reaction associated with an underlying malignancy has been observed in several different organs such as regional lymph nodes, stroma of a tumor, or even organs far from primary tumor.[1-8] Granulomatous reaction seen in lymph nodes draining malignant tumors was reported with a wide variety of underlying malignancies such as cervical, breast, lung, skin and vulva cancer, and parotid carcinoma.[8] More rarely, granulomatous reactions

can be seen in the stroma of tumors in various cancers.[8] Either situation has been reported only few times in the presence of colon cancer.[2,4] In addition, in a few cases, granulomatous reaction occurred in the spleen or hilar and/or mediastinal lymph nodes up to 5 years after colonic carcinoma resection.[3,5-7,9,10] However, systemic sarcoidosis with cutaneous involvement following colonic carcinoma diagnosis has not been reported previously, as far as we know. This case report reveals sarcoidosis development with multiorgan involvement including the skin, eye, joints, spleen and lymph nodes, after resection of colonic adenocarcinoma.

There are possible mechanisms of granulomatous reaction following a malignancy which were summarized by Fujii *et al*., as a localized defense reaction to tumor cells themselves, a simple tissue reaction to a tumor embolism in the lymphatic system or capillaries, or an immunological reaction to substances released from the tumors transported along with the lymphatic system.[4] Granulomatous reaction is thought to play an important role in defending against metastatic spread in cancer patients. Sarcoid reaction has been observed in oncologic patients after receiving antineoplastic treatment with interferon, interleukin-2, or various chemotherapeutic agents.[11-13] Shima *et al*. suggested that chemotherapy can give rise to an immunologic reaction of granuloma formation.[7] Capecitabine and FOLFOX were found to be associated with sarcoidosis and/or granulomatous reactions in previous publications, suggesting a possible explanation of mechanism in our case, as well.[14,15]

In the previous studies, approximately 50%–70% of patients with idiopathic sarcoidosis were symptomatic at the time of diagnosis.[16,17] However, according to one study, only 24% of the patients with sarcoidosis following malignancy were symptomatic.[18] Baughman *et al*. reported the most commonly involved organs in sarcoidosis as lungs (95%), skin (15.9%), lymph nodes (15.2%), liver (11.8%), eye (11.5%), erythema nodosum (8.3%) and spleen (6.7%).[19] On the other hand, in patients with metastatic colon cancer, the most common sites of metastasis are the liver (70%), thorax (32%), peritoneum (21%), and nervous system (5%).[20] Splenic and cutaneous metastases are rarely seen.[21,22]

Recently, Stanziola *et al*. reported three cases with surgically resected sigmoid colon cancer that were treated with chemotherapy and developed sarcoidosis afterward.[10] Interestingly, all patients had left-sided colon cancer, specifically sigmoid cancer (which represents 31% of all colon cancers), similar to our case and a previous report of sarcoid-like reaction development after sigmoid cancer resection, which raises suspicion that there may be association between sarcoidosis and specifically sigmoid colon cancer.[7,10,23]

In patients with metastatic cancer, sarcoid lesions may initially be difficult to differentiate. 18F-FDG-PET/CT scan makes it possible to visualize metastatic lesions and/or inflammations by increased radiotracer uptake. Differentiating the etiology of hypermetabolic lesions is important for appropriate management and can be achieved with multidisciplinary approach. Newly emerging atypical lesions or lesions increasing in size and metabolic activity on imaging despite chemotherapy should bring in mind that sarcoidosis may be accompanying cancer. Histopathological evaluation is essential for confirming the diagnosis. Since biopsy cannot be performed separately from each lesion, 18-FDG-PET scan provides important information as a noninvasive diagnostic method for evaluation of disease extension, progression, and clinical follow-up.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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