

Sarcoidosis Simulating Metastatic Lymphadenopathy after Chemotherapy in a Patient with Breast Cancer: A Case Report and Brief Literature Review

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Sarcoidosis may occur in association with malignancies, particularly testicular cancer and lymphoma. They may also occur following chemotherapy. To our knowledge, studies regarding sarcoidosis occurring after chemotherapy have been reported rarely in Korea. Here we report a case of sarcoidosis simulating metastatic lymphadenopathy in a breast cancer patient treated with chemotherapy. It is suggesting that sarcoidosis must be part of the differential diagnosis when a cancer patient develops lymphadenopathy.

Index words: Breast; Neoplasms; Sarcoidosis; Chemotherapy

Introduction

Previous literature indicates that enlarged hilar and mediastinal lymph nodes due to sarcoidosis may develop in cancer patients (1–5). They occur either synchronously or metachronously, and may also occur after chemotherapy. An association between sarcoidosis and cancer makes the cancer patients with lymphadenopathy a diagnostic dilemma. Malignant involvement of the lymph nodes is common, but benign diagnoses are possible and must be considered (1). Here, we describe a 52-year-old woman with breast cancer treated

with operation and chemotherapy and associated sarcoidosis in the hilar and mediastinal lymph nodes that was initially thought to be metastatic disease.

Case Report

A 52-year-old woman was admitted with left breast pain for 10 days. She had no respiratory symptoms and physical examination revealed no remarkable findings. Laboratory examinations were almost within normal range. Tumor markers (CEA, CA15-3, and CA125) were all negative. 14 months earlier, she had a left modified radical mastectomy due to breast cancer (invasive ductal carcinoma). She was treated with 4-cycles of Adriamycin-Endoxan chemotherapy, 4-cycles of Anzatax chemotherapy, and a 6-week course of radiotherapy. 6 months after chemoradiotherapy, she complained of left breast pain. Initially rib pathology such

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as trauma, metastasis was suspected. Rib series showed normal and bone scan showed focal hot uptake at left 2nd anterior rib. A subsequent contrast-enhanced chest computed tomography (CT) using mediastinal window setting (Sensation 16, Siemens Medical Solutions, Forchheim, Germany) showed symmetric bilateral hilar and mediastinal lymphadenopathy (Figs. 1a, b). Contrast-enhanced chest CT using the lung window setting showed minimally perilymphatic distributed micronodules in right upper lobe and right middle lobe (Fig. 1c). Additionally, radiation pneumonitis with fibrosis was seen in the left upper lobe. There was no evidence of rib destruction. These findings were suggestive of sarcoidosis rather than metastasis. However, metastatic lymphadenopathy with focally lymphangitic metastases could not be excluded completely. So she had a mediastinoscopic biopsy of enlarged lymph node to obtain a tissue diagnosis, and histological examination showed multiple non-necrotizing granulomas, consistent with sarcoidosis (Fig. 1d). Special stains for fungi and acid-fast bacilli were negative. Serum angiotensin-converting enzyme (ACE) level was not assayed. Oral corticosteroid therapy (prednisolon 30mg/day) was started. Follow-up ^{18}F -fluorodeoxyglucose (^{18}F -FDG) positron emission tomography (PET)/CT was performed in 15 months. Non-enhanced axial CT images of ^{18}F -FDG PET/CT showed no enlarged intrathoracic lymph nodes (Fig. 1e). The pulmonary parenchymal lesion also disappeared.

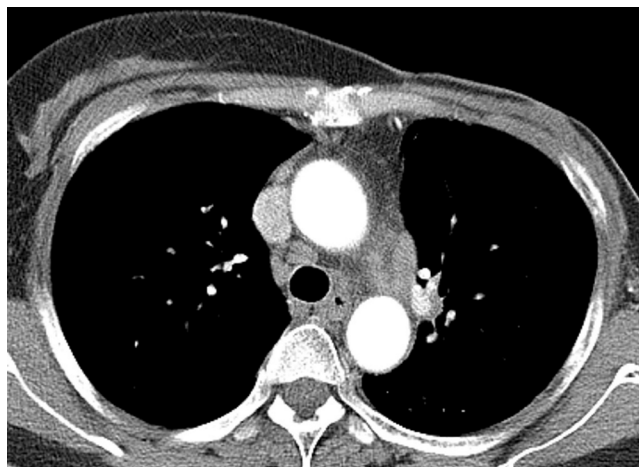
Discussion

Sarcoidosis is a multisystem granulomatous inflammatory disease of unknown etiology characterized by non-caseating granulomas, and it frequently presents with mediastinal and hilar lymphadenopathy, pulmonary infiltration and ocular and skin lesion.

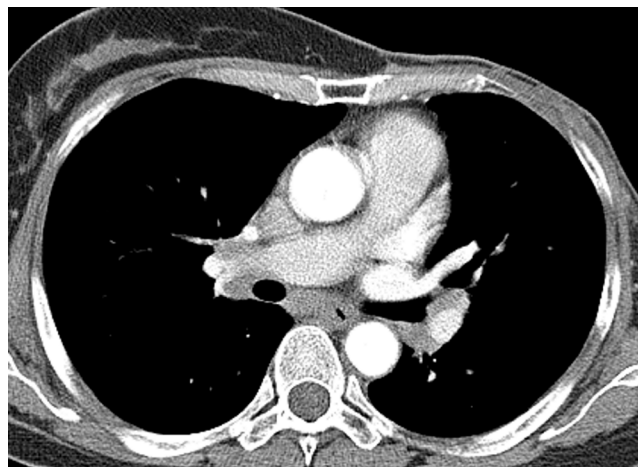
Sarcoidosis has been reported to occur in patients preceding, concurrent with, or after the diagnosis

of cancer (2, 3). Several epidemiologic studies have asserted an increased incidence of sarcoidosis in cancer patients, but others have not confirmed this association (2-4). Shigemitsu examined 1153 patients with sarcoidosis, found increased incidence of cancer, and proposed the term sarcoid-cancer syndrome that would encompass sarcoid-like reaction and multisystem sarcoidosis occurring in patient with cancer and various lymphomas, which may occur at any time in relation to the course of any cancer (2). Hunt et al examined in 41 cases of biopsy-proven sarcoidosis (1). Twenty-one cases of sarcoidosis developed after a diagnosis of cancer. The average time that diagnosed between cancer diagnosis and sarcoidosis diagnosis was 3 years. No primary cancer type was predominant. Multiple different chemotherapeutics were used, with no single regimen predominating. Sarcoidosis due to chemotherapeutic treatments has been reported in hematologic malignancies (6, 7) and also described after treatment for solid tumors including radiation and chemotherapy for testicular cancer and interferon for renal cell cancer (8, 9). Alpha interferon appears to be the most common agent that causes sarcoidosis in patients treated for malignancies (2, 10). In present case, multiple different chemotherapeutics such as 4-cycles of Adriamycin-Endoxan chemotherapy and 4-cycles of Anzatax chemotherapy were used.

An association between sarcoidosis and cancer remains a vexed issue. The causal relationship is an unknown. It is unclear whether the chronic inflammation and possible decreased immune surveillance associated with sarcoidosis may predispose patients to cancer (1). Conversely, the host immune response to cancer or cancer therapy may predispose to sarcoidosis, perhaps by acting as a type of auto-Kveim reagent (1, 5). In two non-Hodgkin's lymphoma patients, Kornacker et al have suggested that sarcoidosis may have been triggered by immunologic aberrations induced by antineoplastic therapy or as a consequence of an



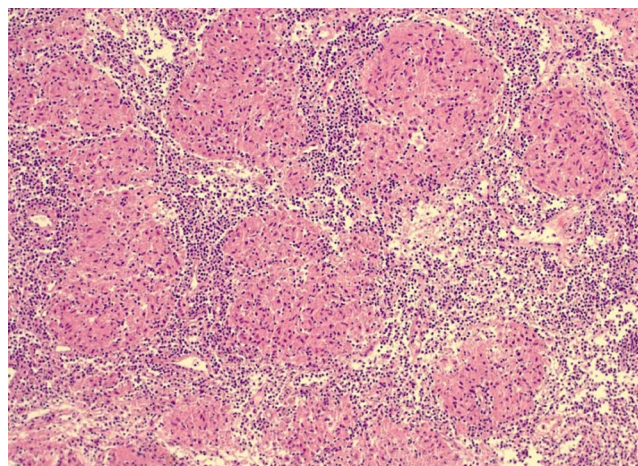
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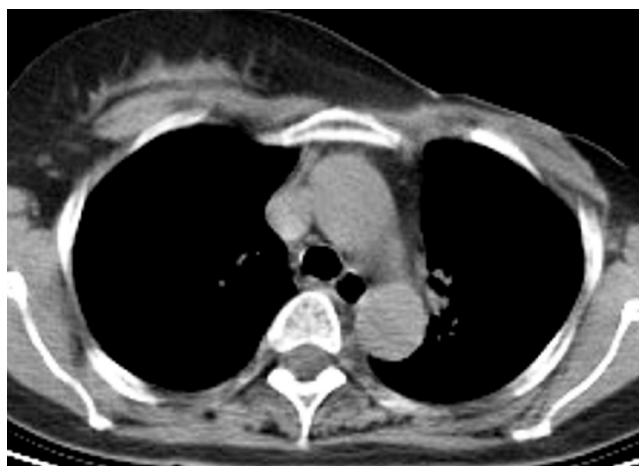
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Fig. 1. Imaging findings of a 52-year-old breast cancer patient treated with chemotherapy.

(a, b) Contrast-enhanced chest CT using mediastinal window setting shows bilateral hilar and mediastinal lymphadenopathy. (c) Contrast-enhanced chest CT using lung window setting shows minimally perilymphatic distributed micronodules in the right middle lobe. (d) Histopathologic examination of mediastinal lymph node shows multiple non-necrotizing granulomas (H & E, $\times 100$). No malignant cells are seen. (e) Follow-up non-enhanced axial CT image of ^{18}F -FDG PET/CT shows no enlarged intrathoracic lymph nodes.

underlying immunologic disturbance associated with the lymphoma (6). Because of this correlation, sarcoidosis must be part of the differential diagnosis when a cancer patient develops lymphadenopathy.

Because the incidence of sarcoidosis, compared with the past is a tendency to increase in Korea, sarcoidosis may appear more frequently in cancer patients with or without treatment. Therefore, an association between sarcoidosis and malignancy makes the cancer patient with bilateral hilar and mediastinal lymphadenopathy a diagnostic dilemma. Although sarcoidosis predominantly occurs in patients with lymphoma, the new onset of sarcoidosis has subsequently been noted in several oncologic patients with solid tumors affecting the cervix, liver, lung, skin, testicles, and uterus (1–5, 10). Clinicians and radiologists should keep in mind the possibility of sarcoidosis and include the differential diagnosis of sarcoidosis when bilateral hilar and mediastinal lymphadenopathy is developed in a cancer patient.

In the present case, despite cause of bilateral hilar and mediastinal lymphadenopathy was thought to be sarcoidosis rather than metastatic lymphadenopathy, we performed mediastinoscopic biopsy because of lack experience in concomitant sarcoidosis and cancer. However, if there was single finding demonstrating enlarged hilar and mediastinal lymph nodes, we propose to need the tissue confirm.

In conclusion, it is clearly important to be aware that there is an increased incidence of sarcoidosis, although rare, that may co-exist with malignancy to avoid misdiagnosis and inappropriate management. In cancer patients with bilateral hilar and mediastinal

lymphadenopathy, sarcoidosis must be considered in the differential diagnosis.

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화학요법치료를 받은 유방암 환자에서 전이성 림프절 종대로 오인된 사르코이드증: 증례보고 및 문헌고찰

노 지 영

차의과학대학교 분당차병원 영상의학과

사르코이드증은 악성종양 특히 고환암, 림프종과 동반되어 보고되었고 화학요법치료 후에서 발생할 수 있다. 암 환자에서 화학요법치료 후 종격동과 폐문 림프절 종대를 일으키는 양성 원인으로 사르코이드증은 한국에서는 드물게 보고되었다. 이에 저자는 유방암 환자에서 화학요법치료 후 발생한 림프절 종대로 나타났던 사르코이드증을 문헌 고찰과 함께 보고하고자 한다.

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