

Cutaneous sarcoidosis possibly associated with aromatase inhibitors and tamoxifen



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INTRODUCTION

Sarcoidosis is a granulomatous disease characterized by the presence of noncaseating granulomas in multiple organs. Cutaneous sarcoidosis lesions present with a variety of morphologies such as nodules and scars. We report a case of pulmonary and cutaneous sarcoidosis arising during treatment with aromatase inhibitors and tamoxifen.

CASE REPORT

A Japanese woman in her 40s was diagnosed with left breast cancer (cT2N0M0, stage IIA) about 1 year before her first visit. After preoperative chemotherapy, left partial mastectomy was performed. Subsequently, postoperative hormonal therapy with aromatase inhibitors and tamoxifen in combination with radiation therapy was initiated. Aromatase inhibitors were started with exemestane and changed to letrozole and finally to anastrozole. One month after initiating the postoperative therapy, the patient noticed skin symptoms both on her knees and on the cosmetic permanent makeup of her eyebrows which she had had in her 20s. The lesions were stable for the following 6 months, then the patient was referred to our clinic. Clinical evaluation revealed palpable nodules on both eyebrows and 1 centimeter-sized erythematous nodules with scale on both knees (Fig 1, A–C). Laboratory evaluation (complete blood cell count, blood biochemistry, blood immunology) showed no abnormalities except

Abbreviation used:

BHL: bilateral hilar lymphadenopathy

for elevated serum levels of angiotensin converting enzyme (36.0 IU/L; normal, 7.7–29.4) and soluble interleukin 2 receptor (711 U/mL; normal, 121–613). Skin biopsy taken from the nodule on the right knee revealed noncaseating epithelioid cell granulomas with Langhans giant cells and lymphocytes (Fig 1, D and E). No significant infiltrative or mass shadows were observed in the lung field before postoperative hormonal therapy and radiation therapy (Fig 2, A). Chest radiograph taken after the skin biopsy showed bilateral hilar lymphadenopathy (BHL) (Fig 2, B). No ocular, cardiac, or neurological lesions were identified. Based on these findings, the patient was diagnosed with sarcoidosis possibly induced by postoperative therapy; therefore, this regimen was discontinued. Subsequently, the skin symptoms gradually improved with topical corticosteroid over the next 6 months. The BHL gradually reduced without any treatment (Fig 2, C).

DISCUSSION

Several factors have been considered in the pathogenesis of sarcoidosis, such as Th1 and Th17 immune responses.^{1,2} Meanwhile, previous studies have reported an association between drug

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and with the understanding that this information may be publicly available.

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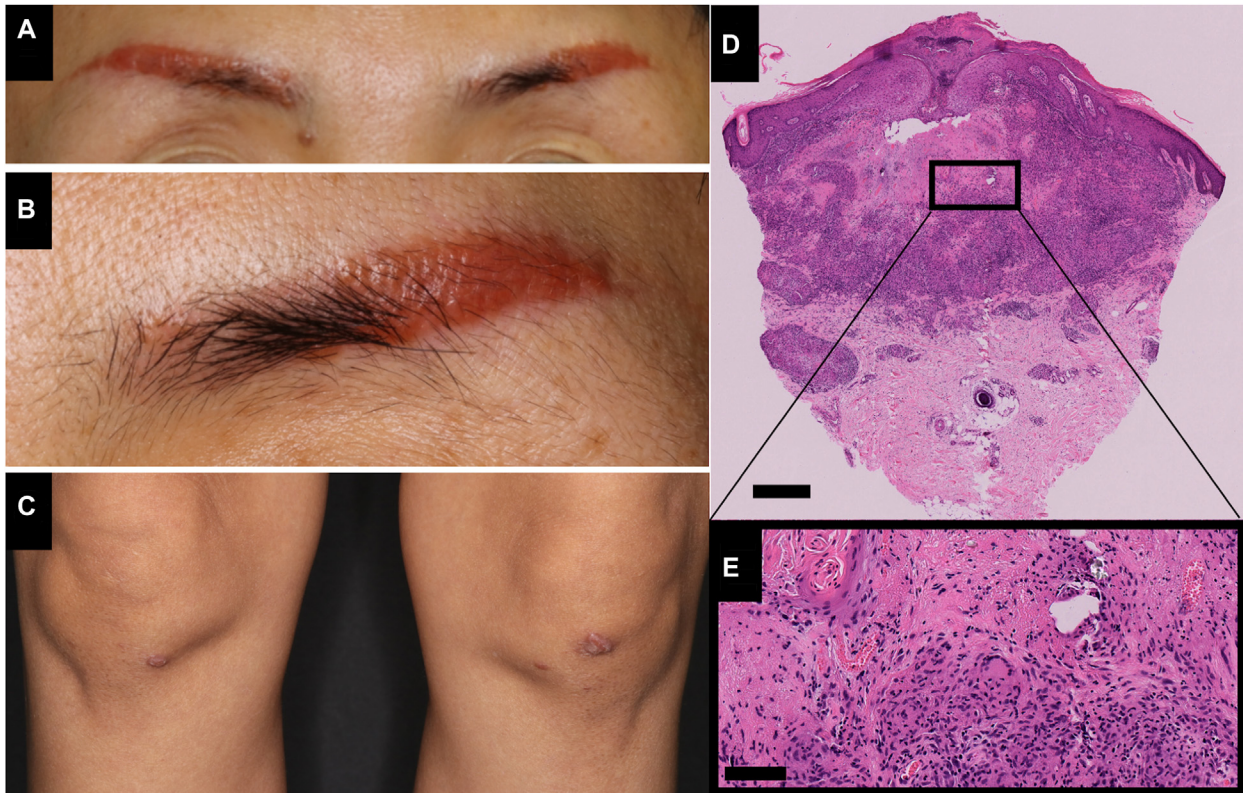


Fig 1. Clinical presentation, histopathological and chest radiographic findings of the patient. **A-C**, Clinical pictures. Palpable nodules on both eyebrows with the traces of art makeup (**A** and **B**). Erythematous nodules with scale on both knees (**C**). **D** and **E**, Histological findings. Histopathological examination of a skin biopsy from the nodule on the *right* knee demonstrates noncaseating epithelioid cell granuloma consisted of epithelioid cells, Langhans giant cells, and lymphocytes (hematoxylin-eosin stain; scale bars, 500 μ m, 100 μ m respectively).

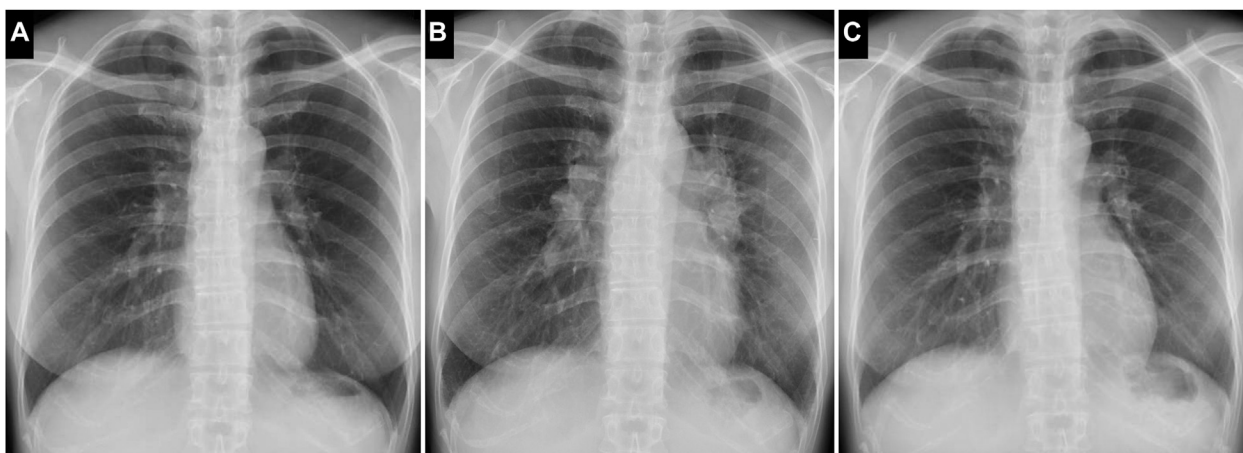


Fig 2. Chest radiograph throughout the time series. **A**, No significant lung lesions were observed before postoperative hormonal therapy and radiation therapy. **B**, Bilateral hilar lymphadenopathy was observed in a chest radiograph taken just after the skin biopsy. **C**, Bilateral hilar lymphadenopathy was gradually reduced after the discontinuation of postoperative therapy.

exposure and sarcoidosis-like skin reactions.^{1,3} Prolonged duration of estrogen exposure has been reported to decrease the incidence of sarcoidosis,

suggesting that estrogen may be protective against sarcoidosis.⁴ Aromatase inhibitors and tamoxifen are used to treat breast cancers: both of them attenuate

estrogen receptor signaling pathways. Therefore, sarcoidal responses in our case might have been triggered by aromatase inhibitors and tamoxifen treatment.

On the other hand, sarcoidosis is also known to develop in association with malignant tumors.^{2,5} In our case, it is possible that sarcoidosis developed in association with breast cancer. Based on the course of BHL presenting after radiotherapy, the patient might develop pulmonary sarcoidosis due to radiation, and then cutaneous sarcoidosis subsequently might appear on the eyebrows and knees. A sarcoidal foreign body reaction was considered given the occurrence within cosmetic permanent makeup but is unlikely in view of the lesions on the knees without any foreign material identified.

Given that we could not find any reports of radiation-induced sarcoidosis and that radiation is rather used as a treatment for pulmonary sarcoidosis, it is unlikely that radiation-induced sarcoidosis developed in our case. Although sarcoidosis may be associated with malignancy itself or radiation in our case, we consider our case as sarcoidosis possibly induced by aromatase inhibitors and tamoxifen in combination with trauma because the patient has been successfully treated for breast cancer and

had no evidence of recurrence or metastasis, and BHL appeared after the initiation of hormone therapy and reduced upon its discontinuation. Clinicians should bear in mind that aromatase inhibitors and tamoxifen might reduce the threshold to induce the development of sarcoidosis.

Conflicts of interest

None disclosed.

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