Dermatofibrosarcoma protuberans (DFSP) with fibrosarcomatous changes in a patient with psoriasis treated with adalimumab

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Psoriasis is a Th1/Th17 chronic immune-mediated disease, characterized by increased levels of tumor necrosis factor (TNF)-alfa. TNF-alfa blockers including adalimumab have been widely used to treat immune-mediated diseases such as inflammatory bowel disease, psoriasis, rheumatoid arthritis, and psoriatic arthritis. TNF-alfa plays a central role in the inflammation and cellular immune response and TNF inhibitors have all been associated with malignancy and infection, especially when used in combination with other immune suppressants. 1 Here we describe a patient with psoriasis treated with adalimumab who developed dermatofibrosarcoma protuberans (DFSP) with fibrosarcomatous change.

CASE REPORT

A 34-year-old Caucasian man with a history of psoriasis was treated with adalimumab injections, subcutaneous 40 mg every 2 weeks for the past 2 years. The patient was born and raised in New Jersey. He was overweight with a body mass index of 29 but otherwise healthy. His medical history was significant only for psoriasis and removal of an atypical nevus about a decade earlier. HIV antibody serology was negative.

During therapy with adalimumab the patient did not take any other oral medications. He used topical agents including clobetasol propionate spray, lactic acid cream, and hydrocortisone cream for psoriatic lesions.

Two years after starting treatment with adalimumab the patient presented to his dermatologist with a mass on the left upper aspect of his back. The mass was first noted by the patient the year before, but the patient noticed rapid growth in the past 2 months. The patient did not recall any trauma or burn to this area.

The physical examination was remarkable for a 3- to 4-cm soft, rubbery, mobile, subcutaneous mass on the upper aspect of the back. The overlying skin was intact and had no scar. The initial excision of this revealed a nonencapsulated but well-defined tumor that extended beyond the expected clinical size. The histopathologic examination revealed a densely cellular nonpigmented spindle cell tumor in the dermis and subcutaneous tissue not associated with the overlying epidermis. The tumor showed some areas of storiform (cartwheel) arrangement (Fig 1) and other areas showed elongated fascicles with a herringbone appearance (Fig 2). Mitoses were easily identified. Large areas of the tumor stained positively

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with CD34 and CD10. Part of the tumor was negative for CD34 stain, and the mitotic count in that area was high with up to 36 mitoses per 10 high power field (HPF). The histologic features were most compatible with DFSP showing fibrosarcomatous change. Adalimumab was discontinued and the tumor was treated with Mohs micrographic surgery, yielding a defect of $9.4 \times 6.7$ cm that was successfully closed with a rhombic flap.

**DISCUSSION**

DFSP is an unusual, infiltrative, locally aggressive cutaneous neoplasm of intermediate malignancy. Most frequently it occurs with a slight predominance in young adult men on the trunk and proximal extremities. It arises from the dermis and invades deeper subcutaneous tissues but, despite its local invasiveness, it rarely metastasizes (5% of cases).\(^3\) Fibrosarcomatous change in DFSP is a form of tumor progression that carries an increased risk of metastases.\(^3\)

The origin of DFSP is unknown.\(^2\) It is not clear whether in our case the development of this tumor was triggered or caused by TNF-alfa blocker therapy or represents an independent event. One might also speculate that the fibrosarcomatous changes may be related to the adalimumab therapy. To our knowledge, despite the intense interest in evaluating the risk of cancer associated with TNF inhibitors, there were no reported cases of DFSP or DSFP with fibrosarcomatous features in patients on TNF-alfa blocker treatment. However, there are reported cases of occurrence of DFSP in immunocompromised patients. A case of locally invasive DFSP has been described in a patient 4 years after a successful kidney transplantation.\(^4\) Occurrence of DFSP in patients with HIV has been reported.\(^1\) An unexpected high incidence of this tumor was observed in children with adenosine deaminase-deficient severe combined immunodeficiency.\(^5\)

Given the rarity of DFSP and its prior association with immune suppression, a single case in a patient treated with a TNF inhibitor may suggest a safety signal. Additional reports will be necessary for further investigation. Patients receiving chronic TNF inhibitors should be carefully monitored for skin malignancies.\(^7\)

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