Recurrent dermatofibrosarcoma protuberans treated with neoadjuvant imatinib mesylate followed by Mohs micrographic surgery

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INTRODUCTION

Dermatofibrosarcoma protuberans (DFSP) is an uncommon, soft tissue sarcoma of mesenchymal origin characterized by its slow, infiltrative growth pattern and high risk of local recurrence after standard surgical excision. We describe a young man with a recurrent dermatofibrosarcoma protuberans after wide local excision treated with neoadjuvant imatinib mesylate and Mohs micrographic surgery, which revealed transformed tumor histology.

CASE REPORT

A 34-year-old white man with no significant medical history initially presented to an outside dermatologist 4 years prior with an enlarging occipital mass. A biopsy found an atypical spindle cell neoplasm with hypercellularity and abnormal mitotic activity. Immunohistochemical stains were positive for CD34, SMMS-1, and BCL2, which are findings consistent with DFSP. A wide local excision was performed, which found a positive deep margin but free lateral margins. The patient went on to have further resection of the galea and periosteum and burring of the calvarium followed by a rotation flap. The periosteum and galea did not reveal tumor in the examined sections. At the time of surgery, magnetic resonance imaging of the brain showed no evidence of residual tumor, and for the next 2 years, annual imaging and physical examination found no evidence of recurrent disease.

Abbreviation used:

DFSP: Dermatofibrosarcoma protuberans

Three years after the patient's resection, he presented with a 3-month history of a rapidly enlarging nodule on the occipital scalp underlying his surgical scars. On physical examination, the patient was a healthy-appearing man with a 4.4- × 3.0-cm firm, tender, subcutaneous nodule without overlying skin changes except for well-healed surgical scars (Fig 1). Full skin examination found no other lesions of concern, and there was no lymphadenopathy. A punch biopsy found a spindle cell neoplasm with hypercellularity and infiltration of the subcutaneous adipose tissue surrounding adipocytes. Higher-power magnification found a proliferation of mildly atypical, elongated fibroblastlike cells with hyperchromatic nuclei in a parallel arrangement (Fig 2). Immunohistochemistry was positive for CD34, consistent with recurrent DFSP. Magnetic resonance imaging of the brain confirmed a 1.1- × 2.8- × 3.0-cm right paracentral soft tissue mass at the level of the torcula that extended from the skin surface to the outer calvarium.

Considering the patient's young age, size of the tumor, and history of recurrence, the decision was made to treat with neoadjuvant imatinib mesylate,

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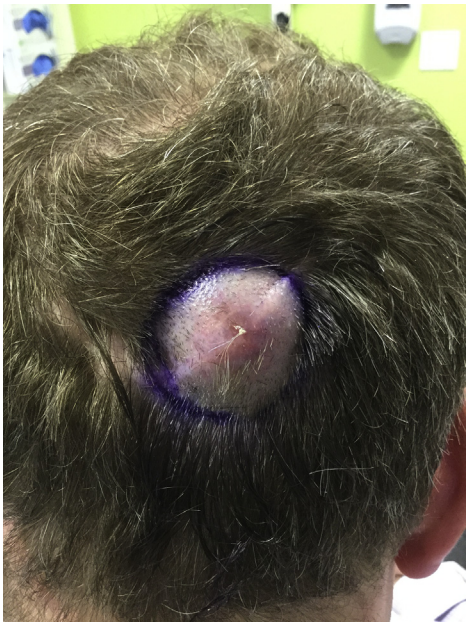

Fig 1. Recurrent DFSP presenting as a 4.4- × 3.0-cm firm, tender, subcutaneous nodule with no overlying skin changes.

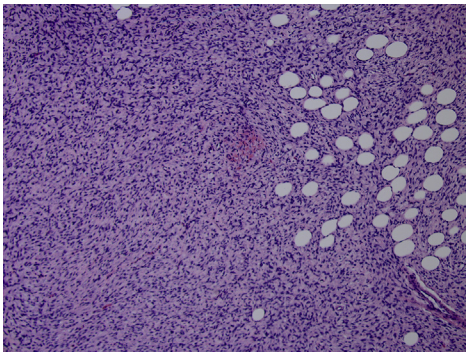

Fig 2. Recurrent DFSP histopathologic examination on high power showed atypical spindle cell neoplasm with hypercellularity.

600 mg daily, before the surgical resection. While on imatinib, the patient experienced mild nausea, fatigue, and rash, all of which resolved. The lesion measured 4.4 × 3.0 cm on clinical examination before treatment, and 3.0 × 2.6 cm 6 weeks after initiating imatinib therapy (Fig 3). At that time, the tumor was completely extirpated with 5 stages of Mohs micrographic surgery to the level of bare bone. Histologically, the tumor was a sparsely cellular spindle cell neoplasm infiltrating the dermis and subcutis (Fig 4). The final defect size was 11.0 × 8.6 cm. The bone was burred to allow for application of a dermal skin substitute with a plan for delayed definitive reconstruction. To decrease the likelihood of local recurrence, the patient was started on adjuvant imatinib, 400 mg daily, with a plan for a 1-year course and close monitoring.

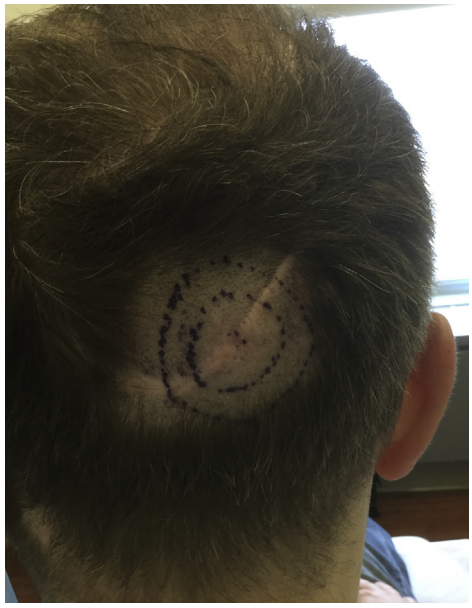

Fig 3. Posttreatment 3.0- × 2.6-cm mass 6 weeks after initiating imatinib therapy.

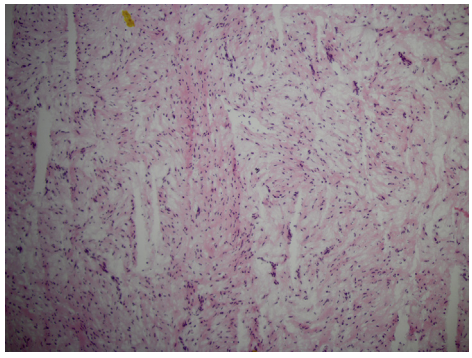

Fig 4. Histopathologic examination on high power of frozen sections of the tumor during Mohs surgery which demonstrates a sparsely cellular spindle cell neoplasm infiltrating the dermis and subcutis.

DISCUSSION

Dermatofibrosarcoma is a rare soft tissue sarcoma of fibroblastic origin that arises in the dermis. All age groups can be affected, including infants, but it is more common in patients in their third to fifth decades of life.[1] DFSP most commonly presents on the trunk, proximal extremities, and the head and neck.[2] DFSP is usually slow growing, presenting as skin-colored plaques with nodules appearing later.[3] The histopathologic examination of DFSP is characterized by uniform cells with spindle-shaped nuclei in a whorled pattern, low mitotic activity, and infiltration into subcutaneous adipose tissue with

possible infiltration of the dermis by tentaclelike projections of neoplastic cells.[4] DFSP has low metastatic potential but a high rate of local recurrence.[5]

DFSP is characterized by the recurrent translocation t(17;22), which results in the fusion of the platelet-derived growth factor-β (*PDGFb*) gene with the type 1 collagen gene (*COL1A1*).[6] This translocation results in constitutive upregulation of *PDGFb* expression, which activates the Ras MAPK and PI3K-AKT-mTOR pathways leading to cell growth and differentiation.[5] DFSP consistently expresses CD34, which has a sensitivity of 84% to 100% for DFSP.[4]

Wide local excision for DFSP yields a recurrence rate of 30.8% compared with 3% in patients who underwent Mohs micrographic surgery; thus, Mohs surgery has become the preferred treatment option for DFSP.[7] The discovery of the PDGF translocation in DFSP has led to the use of imatinib, a c-kit and PDGF-R inhibitor for unresectable tumors and in the neoadjuvant setting to reduce tumor size.[8] Analysis of 24 patients treated with imatinib in 2 phase II trials by the Southwest Oncology Group and the European Organisation for Research and Treatment of Cancer[9] found 46% partial response during the median follow-up of 2.6 years. Median time to progression was 1.7 years. As a result of these trials, imatinib was approved as first-line therapy for patients with metastatic or inoperable DFSP. Considering the patient's relapse in the setting of extensive prior surgeries, we chose neoadjuvant therapy with imatinib before Mohs micrographic surgery. There was evidence of clinical response with a decrease in palpable tumor. Notably on frozen sections, imatinib alters the histologic appearance of DFSP. Treated tumors are paucicellular and have abundant stromal collagen, as we observed on Mohs frozen sections in this case.[10] Clinical trials in this rare malignancy and outcomes of neoadjuvant use of imatinib for recurrent and treated DFSP are limited. In addition, earlier studies have not discussed the use of Mohs micrographic surgery as the treatment of choice after neoadjuvant imatinib.

We report a case of recurrent DFSP that was treated with neoadjuvant imatinib followed by Mohs micrographic surgery and adjuvant imatinib. There is need for prospective randomized trials to evaluate the use of imatinib in the neoadjuvant and adjuvant settings.

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