

Dermatofibrosarcoma protuberans case report: when drug therapy can obviate the need for surgery

A 49-year-old woman had a long standing history of subtle skin thickening and a small subcutaneous nodule involving the skin of the mons pubis. She was evaluated by her primary care physician, and observation was initially recommended. Over the following 14 years, the patient detected slow enlargement of the area of abnormality, without pain, erythema, or skin ulceration. Ultimately, she noted increased nodularity of the region and some subtle changes in skin color. A biopsy was performed, which revealed dermatofibrosarcoma protuberans (DFSP), and she was referred to a subspecialty sarcoma clinic for evaluation.

On physical examination at the time of presentation, there was a diffuse area of erythematous induration involving the mons pubis measuring 10 × 8 cm. Within this area, there were several smaller nodules measuring 5–7 mm. The normal pubic hair pattern was absent (Figure 1A).

The patient was offered radical excision of the lesion, with reconstruction of the area and possible postoperative radiotherapy. As an alternative, she enrolled on a clinical trial using imatinib (Gleevec, 400 mg twice daily). The dose was reduced to 300 mg twice daily secondary to a whole-body rash. Within 10 days of beginning therapy, the patient noted softening of the area and decreased erythema of the region. This dramatic improvement continued with near-complete resolution of all visible abnormalities (Figure 1B). She remains

well, now 51 months on therapy with imatinib. Her Eastern Cooperative Oncology Group (ECOG) performance status is 0.

An uncommon skin tumor

DFSP is an uncommon low-grade tumor of the skin and subcutaneous tissues. DFSP was first described by Darrier and Ferrand in 1924, with the currently accepted term proposed by Hoffman in 1925.^{1,2} Rarely, DFSP may develop a high-grade fibrosarcomatous component.³

The natural history of the disease is characterized by slow, infiltrative growth over years and decades.

Approximately 1%–4% of patients will develop distant metastasis, typically many years after the initial lesion develops.⁴ Distant spread of disease is believed to arise from the high-grade fibrosarcomatous component.⁴ DFSP is not characterized by a clear racial or gender predilection and can occur across the age spectrum, with congenital DFSP being rare.⁵ Grossly, the tumor may have a plaque or nodular appearance, which may be red or skin-colored, with surrounding red or blue discoloration.⁶

DFSP is characterized by a chromosomal translocation between distinct regions of chromosomes 17 and



FIGURE 1 Diffuse area of erythematous induration involving the mons pubis (a). Within 10 days of the patient beginning therapy with imatinib for advanced dermatofibrosarcoma protuberans, a complete clinical response was noted (b).

22, t(12;22), leading to fusion of the collagen 1 alpha 1 (*COL1A1*) gene to the platelet-derived growth factor B (*PDGFB*) gene.^{7,8} The resulting fusion protein COL1A1-PDGFB is processed to yield fully functional PDGFB.⁹ It is thought that this autocrine PDGF receptor stimulation contributes to the development and growth of DFSP.⁹ COL1A1-PDGFB fusion transcripts may be associated with the fibrosarcomatous component of DFSP.⁵

Targeted therapy: a treatment alternative

Standard treatment of DFSP is surgical excision. Local recurrences in up to 60% of cases have been reported when margins are inadequate.¹⁰ However, when margins are clearly negative, the local recurrence rate is significantly lower, with 4% at 10 years reported in one study.¹¹ Some physicians have advocated Mohs' micrographic surgery as the primary means of resection; however, this technique is not routinely available and has not been directly compared with wide surgical excision alone.⁶

When DFSP occurs in an anatomical location not amenable to surgery without significant surgical morbidity, as in the case presented, or in the rare case of metastatic disease, a systemic approach to treatment should be considered. The small molecule tyrosine kinase inhibitor imatinib, which selectively inhibits PDGFR-B, Abl, and Kit kinases, is a rational targeted therapy for this disease.¹²

The first patient reported to be treated with imatinib in this setting was a 25-year-old man with DFSP (initially presented in 1995) who was treated with surgical resection. In 2001, he presented with a paravertebral soft-tissue metastasis that was inoperable. The patient was treated with imatinib (400 mg orally twice daily), with significant clinical improvement

noted within 2 weeks. Magnetic resonance imaging and positron emission tomography showed significant response to therapy at 16 days and 4 months post therapy.¹³

A larger series of eight patients with locally advanced DFSP and two patients with metastatic disease confirmed the activity of imatinib in controlling the condition.¹⁴ In this study, four patients achieved a complete clinical response. Of those with metastatic disease, one patient had a partial response but then experienced disease progression after 7 months. The other patient did not respond. Interestingly, the patient with an initial response had a confirmed chromosomal translocation, t(17;22), whereas the nonresponding patient did not.

In summary, DFSP is an interesting soft-tissue neoplasm of the subcutaneous tissues with a unique chromosomal translocation that drives its growth. Wide surgical excision remains the mainstay of treatment in patients with resectable, localized disease. However, in cases where resection would lead to significant morbidity or functional impairment, or in the rare case of metastatic disease, a trial of imatinib should be considered. This disease represents another example of the benefits of rationally utilized targeted therapies.

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