Prognostic impact of fibrosarcomatous transformation in dermatofibrosarcoma protuberans: A cohort study

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Background: Dermatofibrosarcoma protuberans (DFSP) is a rare, low-grade cutaneous malignancy that sometimes transforms into a high-grade fibrosarcomatous variant (DFSP-FS). Limited data compare clinical features and biological behavior of these 2 entities.

Objective: We sought to compare clinical features and biological behavior of DFSP and DFSP-FS.

Methods: This was a retrospective cohort study of ambulatory patients with DFSP or DFSP-FS treated between January 1955 and March 2012 in the dermatology department of a tertiary care academic medical center.

Results: Of 188 patients, 171 (91%) had DFSP and 17 (9%) had DFSP-FS. Recurrence-free survival differed significantly between the groups over time (P = .002). The 1-year and 5-year recurrence-free survival was 94% and 86%, respectively, for DFSP, vs 86% and 42%, respectively, for DFSP-FS. Metastatic disease occurred in no patients with DFSP and in 18% (3 of 17) with DFSP-FS (P < .001). There were no statistically significant differences in age at diagnosis, sex, race, symptomatology, maximum tumor size, muscle/bone invasion, or duration of tumor before diagnosis.

Limitations: The retrospective nature of study was a limitation.

Conclusions: DFSP-FS exhibits more aggressive behavior than DFSP, with lower recurrence-free survival and greater metastatic potential. Their similar clinical presentation mandates histopathological differentiation for prognosis. (J Am Acad Dermatol 2015;72:419-25.)

Key words: cutaneous signs of disease; dermatofibrosarcoma protuberans; fibrosarcoma; oncogenesis; pathology; surgery.

Dermatofibrosarcoma protuberans (DFSP) is an uncommon, infiltrative tumor of the skin and soft tissue. It comprises 6% of all soft tissue sarcomas and has an estimated annual incidence in the United States of 4.2 to 4.5 per million, with young and middle-aged adults most frequently affected.[1-4] The trunk and proximal extremities are the most commonly involved anatomic sites.[5] Although DFSP has a high rate of local recurrence, cases of metastasis and death are rare.[6] Microscopically, it is characterized by small elongated cells arranged in a storiform pattern extending into the subcutaneous fat to produce a "honeycomb" or "string of pearls" configuration.[7]

Occasionally, DFSP may exhibit high-grade histopathological features, when it is then termed DFSP

Abbreviations used:

CI:	confidence interval
DFSP:	dermatofibrosarcoma protuberans
DFSP-FS:	dermatofibrosarcoma protuberans with fibrosarcomatous change
FS:	fibrosarcomatous
MMS:	Mohs micrographic surgery
WLE:	wide local excision

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"with fibrosarcomatous (FS) change" (DFSP-FS). This tumor has been associated with a high recurrence rate and potential for metastasis.[8] In contrast to DFSP, DFSP-FS has cellular atypia, a fascicular or "herringbone" growth pattern, and more than 10 mitoses per 10 high-power fields involving more than 5% of tumor tissue.[7] Although recent studies have attempted to better characterize this variant, its clinical difference from classic DFSP has not been well defined. Relevant studies to date have shown conflicting results and are limited by low statistical power because of the rarity of these tumors.

The purpose of this large retrospective review was to identify relevant differences between DFSP and DFSP-FS in terms of predefined clinical features, recurrence-free survival, and rate of metastasis in all patients with DFSP or DFSP-FS evaluated at our institution over the past 57 years.

CAPSULE SUMMARY

- Dermatofibrosarcoma protuberans is a rare, low-grade cutaneous malignancy that sometimes transforms into a high-grade fibrosarcomatous variant.
- Dermatofibrosarcoma protuberans transformed into a high-grade fibrosarcomatous variant exhibits more aggressive behavior than dermatofibrosarcoma protuberans, with lower recurrence-free survival and greater metastatic potential.
- Their similar clinical presentation mandates histopathological differentiation for assessment of prognosis.

METHODS

After approval by the institutional review board, we conducted a retrospective cohort study of patients given the diagnosis of DFSP or DFSP-FS. Patients were identified by entering the terms "dermatofibrosarcoma protuberans" and "DFSP" into a searchable diagnosis database. Data were collected from the medical records of ambulatory patients seen at our dermatology department between January 1955 and March 2012.

All biopsy specimens were reviewed by board-certified dermatopathologists or soft tissue pathologists at our medical center at the time of patient presentation and diagnosed using established criteria. Cases were categorized as either DFSP or DFSP-FS on the basis of pathology records extracted by the study authors. Data extraction was not performed in duplicate. In addition to tumor subtype, the following clinical data were obtained by chart review: age at diagnosis, sex, and race; history of tobacco exposure, skin cancer, pregnancy, and trauma; and tumor symptomatology, maximum tumor size (centimeters), anatomic location of tumor, treatment type (wide local excision [WLE] or Mohs micrographic surgery [MMS]), margin status after initial excision (positive or negative), surgical closure type, duration of tumor before diagnosis, metastases, muscle or bone involvement, duration between diagnosis and surgical treatment, date of recurrence, and date of last follow-up. History of trauma was defined as significant injury (heat/chemical/radiation, incisional, or blunt force) to a soft tissue site preceding tumor development, as reported by the patient at time of presentation. To evaluate potential differences in tumor frequency among races, we classified all patients as one of the following, as defined by the investigators: white, black, Native American, or other.

All data requiring patient follow-up were obtained through review of the medical records for patients who had at least 1 follow-up visit with a dermatologist at our institution after tumor removal. End of follow-up was defined as a patient's last recorded visit to our institution at the time of data collection. Recurrence was defined as clinically evident tumor regrowth at the original tumor site with biopsy confirmation. All patients without clinically evident tumor regrowth were considered not to have recurrence.

Statistical analysis

Continuous features of patients with or without FS changes were summarized with means (SDs), medians, and ranges. Categorical features were summarized with frequency counts and percentages. Age at diagnosis was compared using a 2-sample t test. Duration of tumor and postoperative maximum size of tumor were compared using the Wilcoxon rank sum test. Race, tumor location, closure type, metastases, muscle or bone involvement, magnetic resonance imaging result, history of skin cancer, tobacco exposure, prior trauma, and pregnancy were compared using the Fisher exact test. The remaining categorical features summarized in Table I were compared using the χ^2 test. The Kaplan-Meier method was used to estimate recurrence-free survival. Log rank tests were used to compare recurrence-free survival between the patient groups. Duration of follow-up was defined as the time between the date of treatment and the date of recurrence or last follow-up. SAS software (SAS Institute Inc, Cary, NC) was used to perform statistical