ORIGINAL ARTICLE

Hormone receptor expression in patients with dermatofibrosarcoma protuberans

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Background: Dermatofibrosarcoma protuberans (DFSP) is a rare cutaneous sarcoma for which the exact etiology is unknown. Case reports exist of DFSP appearing and growing rapidly during pregnancy, suggesting a hormonal role.

Objective: Our goal was to determine the expression of estrogen receptors (ERs) and progesterone receptors (PRs) in patients with DFSP.

Methods: Archived formalin-fixed, paraffin-embedded tissue from patients with DFSP in the past 20 years at a single institution were analyzed for ER and PR using immunohistochemistry. A semiquantitative scoring method was used to evaluate the expression as positive or negative. Analysis was used to determine whether there was an association between receptor positivity and tumor site, age at diagnosis, sex, race, or disease recurrence.

Results: Forty-four patients with DFSP were included in the study. Tumors were 22.7% ER^+/PR^+, 34.1% ER^+/PR^-, 9.1% ER^-/PR^+, and 34.1% ER^-/PR^-. There was no significant association between expression of ER and PR and sex, age at diagnosis, race, or tumor location. Loss of receptor expression was observed in all recurrent tumors.

Limitations: This study is limited by a lack of follow-up and a new scoring system.

Conclusions: The data presented warrant additional study to determine hormone receptor function and the potential efficacy of antihormone therapies for the treatment of patients with DFSP. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2016.07.011.)

Key words: dermatofibrosarcoma protuberans; estrogen receptor; growth factor; growth hormone; histology; histopathology; immunohistochemistry; progesterone receptor; receptor expression; sarcoma.

INTRODUCTION

Dermatofibrosarcoma protuberans (DFSP) is a rare cutaneous sarcoma with an incidence of 4.2 cases per million Americans.[1] The exact etiology of DFSP is unknown, but case reports exist of DFSP lesions appearing[2,3] and growing rapidly[2,4,5] during pregnancy, suggesting a hormonal relationship. Notably, while some small case studies have sought to analyze the presence of estrogen receptors (ERs) and progesterone receptors (PRs) in DFSP lesions,[2,3,6,7] the results were inconsistent and the sample sizes were small. Recent epidemiologic research has shown affected females to be at increased risk of subsequent primary cancers that are sensitive to sex hormones (eg, breast, soft tissue, and melanoma).[8] DFSP patients are also at decreased

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risk of a subsequent primary cancer for which sex hormones are protective (eg, colon cancer).[8-11] Increased exposure to endogenous and exogenous female sex hormones, including estrogen and progesterone, increases the risk of breast cancer and melanoma[12-14] and decreases the risk of colorectal cancer.[11,15] Together, these results suggest an association between female sex hormones and DFSP development and progression; we seek to further characterize this relationship and determine if DFSP lesions display female hormone—sensitive activity by using immunohistochemical staining for ERs and PRs.

CAPSULE SUMMARY

- Reports exist of dermatofibrosarcoma protuberans growing rapidly during pregnancy, suggesting a hormonal role.
- We found no significant association between receptor expression and demographics, but loss of receptor expression was observed in all recurrent tumors.
- Further study is warranted to determine the potential efficacy of antihormone therapies for patients with dermatofibrosarcoma protuberans.

METHODS

Cases

Institutional review board approval was obtained from University Hospitals Case Medical Center and Case Comprehensive Cancer Center before conduction of this study. Cases were selected with an archive search for "dermatofibrosarcoma protuberans" in pathology records over the last 20 years. Electronic medical records for eligible patients were reviewed. Demographic data, including age at diagnosis, sex, race, and tumor location were collected. If patients had recurrent disease, efforts were made to analyze both primary and recurrent tumor samples.

Immunohistochemistry

Archived discarded formalin-fixed, paraffin-embedded tissue slices from case subjects were retrieved and immunohistochemistry was performed. Commercially available antibodies against ER and PR were used for immunohistochemistry. An automated stainer was used, and ER^+/PR^+ breast tumor tissue was used as a positive control for ER and PR immunohistochemistry. Slides were reviewed by a certified dermatopathologist.

We used the Allred semiquantitative scoring method[16] to evaluate the expression levels of ER and PR proteins (Table I). Each slide was microscopically examined and scored according to staining intensity (Intensity Score [IS]: 0, none; 1, weak; 2, intermediate; and 3, strong) and the percentage of immunoreactive cells (Proportion Score [PS]: 0, none; 1, >0-1%; 2, >1-10%; 3, >10-33.3%; 4, >33.3-66.6%; and 5, >66.6-100%). A Total Score (TS) equal to IS plus PS was calculated (0-2, negative; ≥3, positive).

Statistics

Descriptive analysis of the study population was performed. Cases were grouped into 2 sexes (ie, male and female), 3 racial groups (ie, white, black, and unknown), 5 age at diagnosis groups (≤19, 20-39, 40-59, 60-79, and ≥80 years of age), and 6 anatomic tumor sites (ie, trunk, upper limb, lower limb, head, genitals, and unknown).

We used Fisher's exact test to evaluate the association between the expression of ER and PR with a number of factors, including sex, age at diagnosis, race, and tumor location. All data were analyzed using SEER*Stat software (v 8.0.4; National Institutes of Health, Bethesda, MD).[17]

RESULTS

Sixty cases of DFSP were identified from pathology records between 1995 and 2015. Sixteen patients were excluded from the study because histologic slides or tumor blocks were not available. The major characteristics of the cases are reported in Table II. Of the 44 DFSP cases included in this study, 52.3% were female and 47.7% were male. No patients were pregnant at the time of diagnosis. By race, 63.6% were white, 27.3% were black, and 9.1% were unknown. The majority of patients were diagnosed between 20 and 59 years of age (56.8%). Of all cases, 27.3% were on the trunk, 13.6% on the upper limb, 31.8% on the lower limb, 20.5% on the head, 4.5% on the genitals, and 2.3% unknown. Two patients had multifocal disease (defined as multiple primary DFSP tumors in different locations) and 2 patients had recurrent disease. One Bednar tumor, 1 giant cell fibroblastoma, 1 fibrosarcomatous variant DFSP, and 1 congenital DFSP were included in the study. Characteristics of these unique cases are shown in Table III.

Using the Allred scoring method, 56.8% of tumors stained positively for ER and 31.8% stained positively for PR. More specifically, tumors were 22.7% ER^+/PR^+, 34.1% ER^+/PR^-, 9.1% ER^-/PR^+, and 34.1% ER^-/PR^- (Table II). Photographs of characteristic tumor slides are shown in Fig 1. Statistical analysis showed no significant association between expression of ER and PR and sex, age at diagnosis, race, or tumor location.

Two patients had multiple primary DFSPs (ie, multifocal). Three recurrent tumors were available