DERMATOFIBROSARCOMA PROTUBERANS

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Abstract

Background. Dermatofibrosarcoma protuberans (DFSP) is a locally aggressive soft tissue sarcoma in which recurrences are common. It usually affects middle-aged individuals with the most common location being the trunk. Sex distribution varies among published series. Mohs surgery is the treatment of choice. Immunostaining for CD34 facilitates the diagnosis of DFSP and aids in indicating the surgical margins of the tumor; however, the sensitivity of this marker is variable.

Materials and Methods. This is a retrospective review of 16 cases of DFSP treated with Mohs surgery at Duke University Medical Center between 1981 and 1994. Clinical and histologic features are analyzed. Immunohistochemical stains for CD34 were performed in one case.

Results. Twelve of the 16 patients were women with four younger than 20 years. The most common location was the trunk. No recurrences following Mohs surgery have been documented. The average number of stages during Mohs surgery was 3.3. Surgical wounds were repaired by complex layered closure in 11 cases. Stains for CD34 were negative on the initial biopsy, but were positive on frozen sections.

Conclusions. Both sexes and all age groups are affected by DFSP. Mohs surgery is the treatment of choice and offers a significant improvement in cure rates with the cosmetic advantage of smaller postoperative wounds. Immunostains for CD34 appear to be an important adjunct to facilitate tumor removal, but the variable expression of CD34 antigen by DFSP tumors can lead to variable staining patterns.

Mohs surgery is well suited for the treatment of DFSP. The precise margin control made possible by this technique enables the removal of microscopic extensions of tumor while preserving normal tissue. It eliminates the guesswork inherent in excising the tumor by arbitrary margin guidelines. Immunohistochemical staining for CD34 helps in establishing the diagnosis of DFSP and the extent of tumor within surrounding tissue.

We report a series of 16 cases of DFSP treated with Mohs surgery at a tertiary referral medical center. Clinical and histologic characteristics are presented and compared with previously published data.

Results

Clinical Findings

The patients age ranged from 13 to 72 years, with an average of 34 years. Of the 16 patients, 12 were women (75%) and 4 men (25%), with a women to men ratio of 3:1.

Tumors were located on the trunk in 5 patients (back 1, chest 1, buttocks 1, breast 1, abdomen 1); shoulder in 4; forehead in 3; lower extremities in 3 (calf 1, knee 1, leg 1); and genitalia in 1 (Table 1).

The size of tumors varied from 0.5 cm to 14 cm (Fig. 1). The number of stages during Mohs surgery ranged from 1 to 5, with an average of 3.3 (Fig. 2). Complex layered closures were done in 11 cases, split thickness grafts in two, full-thickness grafts in one, a local flap in one, and second intention healing occurred in one.
Table 1. Clinical Data on the 16 Patients Studied

| Age  | Sex | Location of Tumor | MMS Stages | Sections | Repair |
|------|-----|-------------------|------------|----------|--------|
| 19   | F   | Shoulder          | 5          | 10       | CLC    |
| 34   | F   | Shoulder          | 4          | 14       | CLC    |
| 72   | M   | Forehead          | 4          | 6        | CLC    |
| 18   | F   | Forehead          | 4          | 13       | STSG   |
| 23   | M   | Forehead          | 4          | 7        | CLC    |
| 18   | F   | Back              | 2          | 2        | CLC    |
| 26   | F   | Shoulder          | 4          | 14       | CLC    |
| 52   | F   | Buttock           | 5          | 23       | CLC    |
| 36   | F   | Chest             | 3          | 22       | CLC    |
| 51   | F   | Leg               | 4          | 12       | 2nd INT. |
| 62   | F   | Vulva             | 3          | 24       | FLAP   |
| 21   | F   | Calf              | 2          | 8        | CLC    |
| 37   | M   | Knee              | 1          | 21       | STSG   |
| 13   | F   | Breast            | 4          | 24       | FTSG   |
| 37   | F   | Shoulder          | 2          | 4        | CLC    |
| 28   | M   | Abdomen           | 2          | 4        | CLC    |

CLC = complex layered closure, STSG = split thickness skin graft, 2nd INT. = second intention healing, FTSG = full thickness skin graft.

Initially, DFSP presents as a plaque of cutaneous thickening that develops later into a multinodular tumor. Ulceration and necrosis are rare. The tumors can grow abruptly and become tender in 10 to 25% of cases. Characteristically, DFSP is fixed to the skin, but movable over deeper structures. The tumors can be flesh-colored, violaceous, or reddish-brown. Their size varies from a few millimeters to more than 20 cm. The clinical course is characterized by persistent but indolent growth. Metastases are rare, with most series reporting an incidence of 2 to 6%. Approximately 75% of patients with metastases have hematogenous spread to the lungs, the remaining 25% have lymphatic spread to regional lymph nodes. Metastases to the brain, bone, and heart have also been documented, but are rare.

Histologically, DFSP is a dermal tumor composed mainly of spindle cells in storiform or cartwheel pattern. “Honeycomb” entrapment of fat is characteristic. Mitoses are rare. Approximately 5% of cases have significant amounts of pigmented dendritic cells, the so-called Bednar tumor. Myxoid changes are more commonly seen in recurrent lesions but may also occur in primary tumors.

A DFSP frequently infiltrates dermis and subcutis diffusely, with microscopic extensions that may project 3 cm or more away from the primary mass. Underlying fascia may be invaded. These characteristics may explain the high recurrence rates seen after conventional surgical excision. The presence of sarcomatous areas and increased number of mitoses (> 5 per 10HPF) may indicate a poor prognosis.

The clinical and histologic differential diagnosis includes keloid and hypertrophic scars, dermatofibroma (DF), malignant fibrous histiocytoma (MFH), and atypical fibroxanthoma (AFX) (Table 2).

Dermatofibroma presents as a small, slightly elevated nodule, with a pigmented (brown) surface. Women are affected more often than men and the legs are the most common location. The lesions are usually firm, asymptomatic, and are associated with a history of trauma. Usually, DF is composed of a mixed popula-

Histologic Findings

Most biopsies showed dermal tumors composed of spindle cells in a classic storiform pattern, with mild pleomorphism and rare mitoses. “Honeycomb” entrapment of fat was common (Fig. 3).

Immunostaining for CD34 in one case was reported as negative on paraffin-embedded sections (Fig. 4), but was strongly positive on frozen sections obtained at the time of surgery (Fig. 5).

DISCUSSION

Dermatofibrosarcoma protuberans was first described by Darier and Ferrand in 1924 and was named by Hoffman in 1925. The estimated incidence of DFSP is 0.8 cases per million persons per year, comprising only 0.1% of all malignancies.

The tumor is a low grade sarcoma of the skin with a strong tendency for recurrence, but is of low metastatic potential. Immunohistochemical studies support a fibro-histiocytic derivation. This tumor usually presents in young to middle-aged adults (20 to 50 years) and is rare in childhood or at birth. Men are affected slightly more frequently than women (57% vs. 43%). The most common location is the trunk (62%), followed by the extremities (25%), and the head and neck regions (13%). Antecedent trauma is reported in about 20% of cases.

No evidence of recurrence or metastases has been documented after an average follow-up of 4.4 years.
tion of multinucleated giant cells and spindle cells, arranged in an indistinct storiform pattern, with a mixture of xanthomatous and hemosiderin-laden histiocytes and inflammatory cells. It does not infiltrate subcutaneous tissue.

Malignant fibrohistiocytoma is more prevalent in the 5th and 7th decades of life, although it can occur in children and young adults. A slight predominance of men is reported. Seventy-five percent of lesions arise on the extremities, with approximately 30% occurring on the thigh. The tumor is a high grade sarcoma, usually composed of markedly pleomorphic spindle cells and multinucleated giant cells with frequent atypical mitoses and areas of necrosis. This tumor metastasizes frequently, usually to the lungs, liver, lymph nodes, and bones within 2 years of presentation.

An AFX is considered a pseudosarcoma of the skin with low metastatic potential. It generally affects older individuals of both sexes but can also present in younger persons. The most common locations include sun-exposed areas of the head and neck, but lesions on the trunk and extremities are not rare. Clinically, AFX presents as nodular lesions that frequently ulcerate and can be misdiagnosed as basal cell or squamous cell carcinoma. They vary in size but most lesions are less than 4 cm in diameter. Cytologically, AFX is identical to MFH, but are distinguished by their smaller size, confinement to the dermis, lack of deep subcutaneous involvement, or necrosis. Prognosis is excellent even with conservative therapy.

In addition to routine histologic studies, CD34 immunostaining is a useful diagnostic technique that allows differentiation of these fibrohistiocytic tumors. A DFSP usually stains positive for this marker, whereas keloids, DF, MFH, and AFX are negative.

Treatment of DFSP consists of surgical excision. Radiotherapy has been unsuccessful, and the slow growth rate of the tumor precludes the use of chemotherapy as an effective alternative.

Traditional surgical excision usually fails to treat adequately the microscopic extensions that presumably account for the high recurrence rate associated with DFSP. In most series, recurrence rates of 49 to 53% have been reported, with the majority developing 1 or 2 years after initial therapy. Recurrence rates of 73 to 89% have been documented for DFSP with sarcomatous changes. When surgical margins of 3 cm are used, the recurrence rate drops to 10 to 20%.

Mohs surgery offers the advantage of microscopic control of surgical margins and is currently considered the treatment of choice. No recurrences have been documented with the use of this technique at follow-up periods ranging from 18 months to at least 5 years. Since rare recurrences can occur as late as 20 years after therapy, the follow-up in these studies seems rather short.

The identification of tumor cells in areas of inflammation or scarring is difficult. Immunostains for CD34 help in the diagnosis and in demarcating the surgical margins of DFSP. Reports on the use of this marker have been positive in both paraffin-embedded and frozen sections; however, variability exists and caution is advised when interpreting the results of these stains during Mohs surgery. The percentage of DFSP tumors that stain positive for CD34 ranges from 20 to 100%. Even in CD34-positive cases the staining is not uniform. Some tumor strands are heavily stained, whereas others remain unstained. In addition, within the stained strands there are unstained tumor cells. A markedly variable CD34-staining of the nodular areas as compared with the strongly CD34-positive staining of plaque areas was noted by Kamino et al.

The results of our series agree with those reported previously, regarding the age of patients, the location and size of tumors, histologic findings, and the number of recurrences; however, some significant differences were noted. In contrast with most series reporting that DFSP is rare in childhood, we found four patients under...
20 years old, accounting for 25% of the total cases. All were girls, with ages ranging from 13 to 19 years. The youngest had a DFSP located on the breast and the lesion was probably congenital. According to Rabinowitz et al., there are 27 pediatric cases of DFSP reported in the English literature and only 3 of them were treated with Mohs surgery. The age in these patients ranged from birth to 16 years. Eight cases were congenital and 15 cases developed during the first 10 years of life. Fourteen cases were girls and 6 were boys. In seven cases the sex was not reported. In six cases the tumor was located on the back in four on acral sites, three on proximal extremities, two each on the chest and cheeks, and one each on the abdomen and buttocks. Our youngest patient is the 28th pediatric DFSP case reported in the English literature and the 4th case treated with Mohs surgery. She is also the first case with the tumor located on the breast.

Ours is the first series of DFSP tumors showing a clear predominance in women. The W:M ratio was 3:1. Most series have reported either a slight predominance in men or an equal sex distribution.

On histologic examination our findings confirm previous experiences. All of our patients had dermal tumors composed of spindle cells in storiform pattern, with finger-like projections extending to subcutaneous tissue. Entrapment of fat was common and mitoses rare. We did not find any case showing pigmented dendritic cells (Bednar tumors) or myxoid variants that are reported with a frequency of 5% and 15%, respectively.

We performed CD34 immunostaining only in one case. Whereas immunostains were negative on paraffin-embedded sections from the initial punch biopsy, they were strongly positive on frozen sections during Mohs surgery. This variability in CD34-staining has been well documented and the results of these stains on frozen sections during Mohs surgery must be interpreted with caution. To avoid false negative results we recommend, that biopsies be obtained from plaque areas and include fatty tissue. Excisional or wedge biopsies are preferable.

Due to significant subclinical involvement, the final extent of a DFSP tumor may be several times the clinically apparent lesion. In our patients the preoperative size of tumors varied from 0.5 cm to 14 cm and the postoperative size ranged from 1.8 to 19 cm. The number of stages during Mohs surgery ranged from 1 to 5, with an average of 3.3. The total number of sections ranged from 2 to 24 with an average of 13. The tumors were only 53% larger in average than the clinical lesions, suggesting that early diagnosis and treatment with Mohs surgery can lead to smaller surgical defects and simpler, more esthetic repairs.

A DFSP is best treated with Mohs surgery. Mohs himself reported five cases treated with the fixed-tissue technique and two with the fresh-tissue technique without recurrence after 5 years. Mikhail et al. treated two cases without recurrences after 5 years. Robinson, Hobbs, had similar experiences. We did not find any recurrence after an average follow up of 4.4 years. These findings compare very favorably with traditional surgical excision since recurrence rates of at least 10% have been reported even when using 3 cm surgical margins. Certain, follow-up over the ensuing years will help confirm the long-term benefits of Mohs surgery.

Another significant advantage of Mohs surgery is tissue conservation. Surgical treatment using 3 cm margins creates large wounds, difficult to repair. Repair then requires skin grafting techniques or healing by second intention, at times with poor cosmetic outcomes. In our series, the lesions in 11 of the 16 patients were repaired with complex layered closures, including two on the forehead and one on the calf with excellent cosmetic results. One lesion located on the mons pubis and vulva was repaired with a local flap. Only three cases required grafts: split-thickness in 2 (knee and breast), and full-thickness in one (forehead).
Table 2. Characteristics of Dermatofibroma, Malignant Fibrohistiocytoma, and Atypical Fibroxanthoma

| Dermatofibroma                                                                 | Malignant Fibrohistiocytoma                                                                 | Atypical Fibroxanthoma                                                                 |
|--------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| Multinucleated giant cells                                                      | High-grade sarcoma                                                                           | Pseudosarcoma                                                                           |
| ("Monster cells")                                                              | Pleomorphic spindle cells                                                                     | Pleomorphic spindle cells                                                                 |
| Spindle cells                                                                   | Atypical mitoses                                                                             | Confinement to dermis                                                                    |
| Storiform pattern                                                               | Necrosis                                                                                    | Lack of necrosis                                                                         |
| Xanthomatous histiocytes                                                        | + subcutaneous tissue                                                                        |                                                                                         |
| Hemosiderin-laden phagocytes                                                    | + infiltration of fascia                                                                      |                                                                                         |
| Inflammatory cells                                                              |                                              |                                                                                         |
| Lack of subcutaneous infiltration                                              |                                              |                                                                                         |

CONCLUSIONS

The tumor DFSP must be considered in the differential diagnosis of indurated skin lesions in both adults and children. It affects both sexes equally and any difference in sex distribution reflects the small number of patients in each series. The use of Mohs surgery has several advantages over conventional surgery, including the cosmetic advantage because most patients with DFSP tumors are young adults.

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