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CONTROVERSY

Dermatofibrosarcoma protuberans: Wide local excision vs. Mohs micrographic surgery

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Summary *Background:* Dermatofibrosarcoma protuberans (DFSP) is an uncommon tumor of the skin with high rates of local recurrence. It is debated whether Mohs micrographic surgery (MMS) involves lower recurrence rates than wide local excision (WLE). Recent preliminary reports indicate more consistently favorable cure rates with MMS. We report comparative observational data on 41 patients who underwent MMS and 38 who underwent WLE. Their data were then pooled with those available in the medical literature to obtain more precise estimates of recurrence rates with MMS and WLE.
Methods: The records of 79 patients with DFSP who underwent WLE (n = 38) or MMS (n = 41) in 1990–2005 were reviewed retrospectively. The primary endpoint was tumor recurrence rate. The PubMed database was searched for DFSP case series treated with WLE or MMS, and the recurrence proportions reported for the two separate procedures were pooled.
Results: Five of the 38 WLE patients (follow-up = 4.8 years) had recurrences (13.2%, 95% CI 4.4–28.1%) as opposed to none (95% CI 0–8.6%) of the 41 MMS patients (follow-up = 5.4 years). Pooling of these data with those from the literature yielded 6/463 recurrences for MMS (1.3%, 95% CI 0.5–2.8%) and 288/1394 recurrences for WLE (20.7%, 95% CI 18.6–22.9%). The relative risk of recurrence for WLE vs. MMS patients was 15.9 (95% CI 7.2–35.5).
Conclusions: Significantly lower recurrence rates were recorded in our patients subjected to MMS compared with those treated with WLE. The pooled data also indicated a clear advantage

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of MMS. There is inconclusive evidence for any advantage of MMS in non-primary cases, while MMS was most effective in treating head and neck tumors. These data may be useful to guide clinicians in the choice of the more appropriate surgical treatment for DFSP patients.

Introduction

Dermatofibrosarcoma protuberans (DFSP), a rare, low-grade mesenchymal tumor of the skin, originates in the dermis and accounts for less than 0.1% of all malignancies and for ca. 1.8% of soft tissue sarcomas.[1] The entity was first described by Darier and Ferrand[2] in 1924, but the currently accepted term was coined by Hoffman, when he reported three cases in 1925.[3] Its estimated incidence is 0.8 cases per million a year.[4] Median age at diagnosis is 20–50 years; however, all age groups are affected and congenital cases have also been described. The disease is characterized by a progressive, locally infiltrative behavior. If left untreated, the tumor grows slowly, invading surrounding tissue as well as neurovascular bundles. The tumor rarely metastasizes. In a literature review of 913 cases, Rutgers et al.[5] found only 11 patients (ca. 1%) with regional lymph node metastases and 37 (ca. 4%) with suspected distant metastases. The main site of distant recurrence was the lung, via hematogenous spread (34 of 37 patients). In nearly all cases, metastases were preceded by multiple local recurrences.[6]

Approximately 85–90% of all DFSPs are low-grade lesions. The remaining 10–15% contain a high-grade fibrosarcomatous component that accounts for $\geqslant$5% of the tumor volume. These are regarded as intermediate-grade lesions (known as FS-DFSP) and involve a significantly higher rate of local recurrence and a shorter local recurrence-free survival. FS-DFSP carries an increased risk of distant metastases.[7]

The tumor most commonly involves the trunk (50–60%) and upper limbs (25%), but all body regions can be affected; head and neck sites account for 10–15% of DFSP cases.[8] A slight male predominance has been suggested.[9] Clinically, these neoplasms usually present as a raised, indurated, asymptomatic plaque or nodule that may be any combination of blue, red, brown or flesh color[10] arising on previously healthy skin or, occasionally, in areas of repeated trauma, in vaccination sites, irradiated skin or scars. It may be misdiagnosed as a keloid.[11] The microscopic appearance of DFSP is of monomorphous spindle cells arranged in a storiform pattern embedded in a sparse to moderately dense fibrous stroma, occasionally involving subcutaneous fat.[4,12]

A defining characteristic of DFSP is aberrant overexpression of platelet-derived growth-factor β (PDGFB), which activates platelet-derived growth-factor receptor β and its tyrosine kinases through an autocrine mechanism that results in cell growth and proliferation. PDGFB overexpression is the result of a fusion gene consisting of collagen Type Iα1 (COL1A1) and PDGFB-chain genes from the rearrangement of chromosomes 17 and 22, leading to a supernumerary ring [*r*(17;22)] or to reciprocal translocation [t(17;22)].[13,14]

Diagnostic markers include in most instances CD34 antigen (which, albeit non-specific, is still the most valuable immunohistochemical marker) and specific fusion of the COL1A1 and the PDGF genes.[15,16] Interestingly, ring chromosomes are mainly observed in adult patients, while the t(17;22) translocation is more often found in pediatric cases.[16] Immunostaining for factor XIIIa and CD34 may be required to differentiate dermatofibroma from DFSP, respectively.[17] Wide excision with histologically negative margins is the cornerstone of treatment; nonetheless, recurrence rates are relatively high, especially for head and neck lesions.[8,18] Published series of patients with DFSP describe rates as high as 60% after standard surgical excision,[19,20] while local recurrence rates for wide local excision (WLE) at trunk sites range from 0% to 27% in recent studies,[21,22] with higher rates being reported in earlier studies.[10,23] The optimal width of excision around the primary tumor has never been defined prospectively. Retrospective investigations commonly report excisions with 1–3 cm of normal-appearing skin. Rates of recurrence of 50–75%, are described for head and neck sites.[24,25]

Although wider excision margins are associated with higher rates of local control, they may result in unnecessary removal of normal skin. In 1978, Mohs described seven patients with DFSP subjected to micrographic surgery (MMS),[26] reporting no local recurrences. The favorable results led to further evaluation of MMS. Recurrence rates in these patients now range from 0% to 6.6%, with variable follow-up durations.[27]

We compared two DFSP case series treated with WLE or MMS, and pooled our data with those available in the literature to obtain more reliable estimates of recurrence rates with the two treatments and to guide in the choice of the optimal surgical treatment.

Materials and methods

The medical records of 81 consecutive patients with DFSP treated at three institutions (Department of Dermatology, Catholic University of the Sacred Heart ($n = 5$) and Department of Plastic Surgery, ''La Sapienza'' University ($n = 34$), *Rome, Italy*, and Department of Dermatology, Johann Wolfgang Goethe University ($n = 42$), *Frankfurt am Main, Germany)* between February 1990 and December 2005 were reviewed. Approval for the current study was obtained from the respective Review Boards. Patients were treated with WLE (Italy) or with MMS (Germany) according to the current surgical approach in the different centers.

The diagnosis of DFSP was confirmed histologically prior to surgical excision by an incisional biopsy with standard hematoxylin and eosin stain as well as immunohistochemical markers (CD34, XIIIa factor, vimentin, S100). Oral and written informed consent was obtained before the operation. Age at onset, lesion site, number of any prior excisions and excisional margins, number of micrographic stages, type of surgical repair, number of local recurrences, duration of follow-up, pre-operative size of visible tumor, WLE margins, and size of post-operative defect were recorded where available in the patient's chart. Patients lost to