Treatment of Malignant Fibrous Histiocytoma and Atypical Fibrous Xanthomas with Micrographic Surgery

MARC D. BROWN, M.D. • NEIL A. SWANSON, M.D.

HONORABLE MENTION

Abstract. Fibrous tumors of the soft tissue are usually benign, but some fibrous neoplasms such as dermatofibrosarcoma protuberans (DFSP), atypical fibroxanthoma (AFX), and malignant fibrohistiocytoma (MFH) can be very destructive locally with a high recurrence rate after local excision. On occasion, they can metastasize. Previous reports have confirmed the high success rate of Mohs micrographic surgery for the treatment of DFSP, but data have been lacking on the potential benefit of this surgical approach for MFH and AFX tumors. Over the past 6 years, we have treated 17 patients with MFH (20 tumors) and 5 patients with AFX with Mohs micrographic surgery. A retrospective analysis of the surgical results is presented. To date (average 3-year follow-up), all patients contacted are tumor free with only one recurrence; no patient has developed metastatic disease. Our results to date are very encouraging; they lend support to Mohs micrographic surgery as a desired surgical approach for these diffiult-to-cure neoplasms. J Dermatol Surg Oncol 1989; 15:1287–1292.

INTRODUCTION

Fibrohistiocytic tumors are a large and heterogeneous group of soft-tissue neoplasms that are similar in their composition to cells resembling fibroblasts and histiocytes. The histogenesis of these tumors is uncertain, but they probably arise from mesenchymal cells that show partial histiocytic and/or fibroblastic differentiation.[1,2] The more malignant of these tumors retain some degree of pleuropotentiality.

Fibrohistiocytic tumors can be classified according to their malignant potential. The most common fibrohistiocytic neoplasm is the benign dermatofibroma, which has no invasive or malignant characteristics and rarely requires surgical intervention. Dermatofibrosarcoma protuberans (DFSP) is considered a fibrohistiocytic sarcoma of intermediate malignancy. It bears a striking histologic similarity to the benign fibrous histiocytoma, but grows in a more infiltrative fashion, has a more marked tendency for local recurrence, and in rare instances can metastasize.[3,4] For this reason, DFSP was first described in 1924 as a "progressive and recurring dermatofibroma."[5]

The malignant fibrous histiocytoma (MFH) may resemble a DFSP histologically but also shows numerous atypical mitotic figures and marked pleomorphic cellularity. In addition to a high local recurrence rate, there is a significant metastatic rate usually associated with a poor prognosis.[6,7] Prognosis and survival appears in part to be related to tumor depth.

The atypical fibroxanthoma (AFX) is probably the most superficial or limited form of an MFH. Because of its superficial, intradermal location, it pursues a relatively benign course with a low recurrence rate and practically no metastatic potential.[8]

The surgical management of these malignant fibrohistiocytic tumors has been problematic and controversial due to the high recurrence rate, aggressive local infiltration, and metastatic potential.

Marc D. Brown, M.D., and Neil A. Swanson, M.D., Associate Professor of Dermatology, Department of Dermatology, are from the University of Michigan Medical Center, Ann Arbor, Michigan.

Address reprint requests to Marc D. Brown, M.D., Department of Dermatology, University of Rochester, 601 Elmwood Ave., Rochester, NY 14642.

The surgical process of treating DFSP with Mohs micrographic surgery has been well described in previous reports. At least 6 articles have appeared in the literature attesting to a high cure rate in a total of 26 patients.[9–14] In addition, we have treated 13 patients with DFSP using Mohs surgery (unpublished data) with no recurrences. It has been established that Mohs surgery is a preferred surgical modality for DFSP. As Hanke[13] states, "The limitations of standard vertical section histology may contribute to recurrences of DFSP even when wide excisional margins were used. The microscopic extensions of DFSP can be easily traced out with Mohs micrographic surgery. DFSP should be considered a clear cut indication for Mohs micrographic surgery."

However, the treatment of other neoplastic fibrohistiocytic tumors (MFH and AFX) with Mohs surgery has not been as well established. The purpose of this article is to discuss our experience at the University of Michigan in treating MFH and AFX tumors with Mohs micrographic surgery.

MATERIALS AND METHODS

Over the past 6 years, we have treated a total of 22 patients with 25 neoplastic fibrohistiocytic tumors using Mohs micrographic surgery. All patients were treated in an outpatient setting in the Cutaneous Surgery and Oncology Unit. Local anesthesia, usually 1% lidocaine with epinephrine, was used for all patients. Standard horizontal frozen sections were prepared in the usual manner after appropriate mapping and staining of the excised tissue. The diagnosis of these fibrohistiocytic tumors preoperatively and tumor-free margins postoperatively were confirmed by our dermatopathologist. In no instance was there any disagreement between our reading of these tumors on frozen section and what the dermatopathologist interpreted on permanent sections.

There were 20 MFH tumors seen in 17 patients and 5 AFX tumors seen in 5 patients. Eight patients were female and 14 patients were male. The average age was 50 years with a range between 14 and 84 years of age. The location of these tumors was widespread, although there seemed to be a unique predilection for the head and neck area. Eight tumors were located on the face, specifically, 5 on the nose. There were 5 lesions on the scalp, 6 on the trunk, 2 on the ear, 1 on the arm, 1 in the mouth, and 1 on the buttock. Twelve of these tumors were considered primary and 11 were recurrent tumors, having been treated elsewhere with non-Mohs surgical procedures, and 2 were incomplete excisions. The 5 patients with AFX required an average of only one stage and four sections for clearing of the tumor. However, the patients with MFH required an average of 2½ stages and 16 sections. The preoperative size of these tumors averaged 3.0 × 2.3 cm with an average postoperative defect size of 4.8 × 3.5 cm. Most defects were repaired at the time of Mohs surgery after tumor-free margins were documented: 8 defects by primary layered closure, 4 with flaps, 1 with a full-thickness skin graft, and 2 by granulation. The largest defects required closure by referral to facial plastic surgeons. All patients were generally pleased with their final cosmetic result. Figures 1–5 document a clinical and histologic example.

RESULTS

The follow-up period on these patients has been an average of 3 years. We reviewed their progress and outcome by review of hospital and clinic records, as well as by telephone survey. The majority of patients were seen on a regular basis every 6 months in our surgical follow-up clinic. Of the 22 patients who were treated, we have been able to contact 19 (approximately 85%). Two patients have died of other causes unrelated to their fibrohistiocytic tumors. There has been recurrence of two tumors. One patient subsequently underwent a second Mohs micrographic procedure and continues to be tumor free for a 5-year period. The other patient had a local recurrence and a cutaneous metastatic lesion on the scalp. The patient presumably died of cardiovascular failure; it was uncertain whether there was visceral metastatic disease. Therefore, of the patients contacted, 94% were tumor free. Only one patient, described above, had probable metastatic disease.

DISCUSSION

Malignant fibrous histiocytoma is the most common soft-tissue sarcoma of late adult life.[6] Many tumors previously described as pleomorphic variants of liposarcoma, fibrosarcoma, or rhabdosarcoma were probably mislabeled examples of MFH. The tumor typically appears between the ages of 50 and 70 years.[1,2] The average age in our patient population was 50 years. Malignant fibrohistiocytoma is slightly more common in males, and Caucasians are affected more commonly than blacks or Orientals. Clinically, the tumor presents as a painless, enlarg-

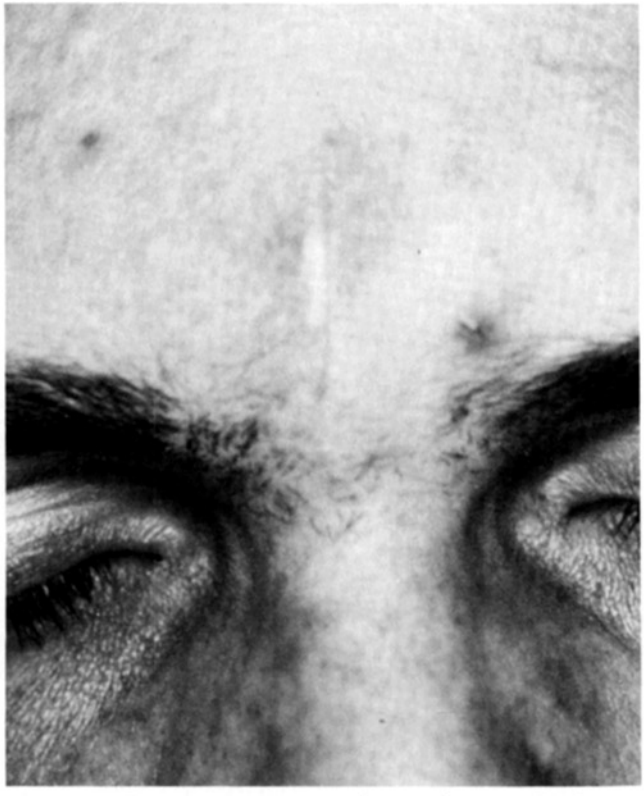

FIGURE 1. Preoperative surgical site of incompletely excised MFH.

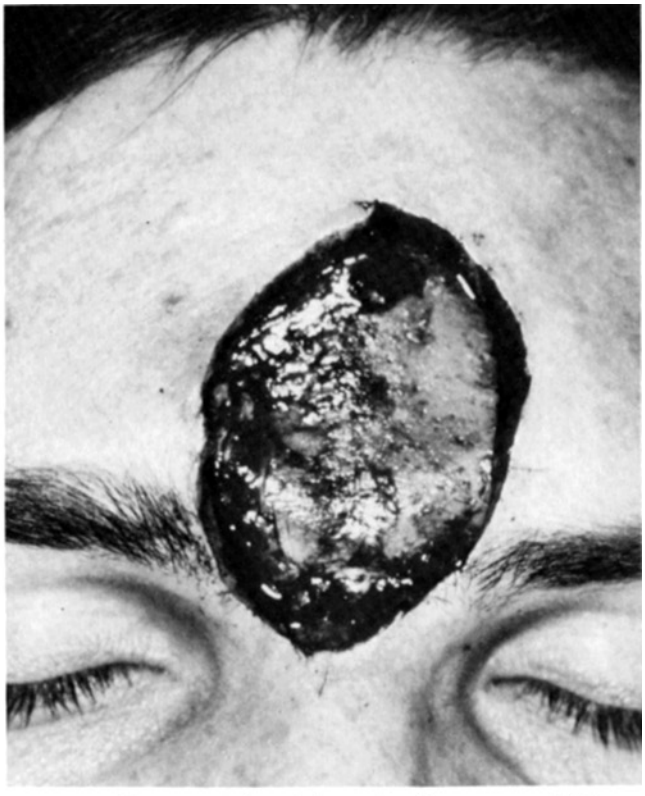

FIGURE 2. Postoperative defect after 5 stages and 35 sections with Mohs surgery.

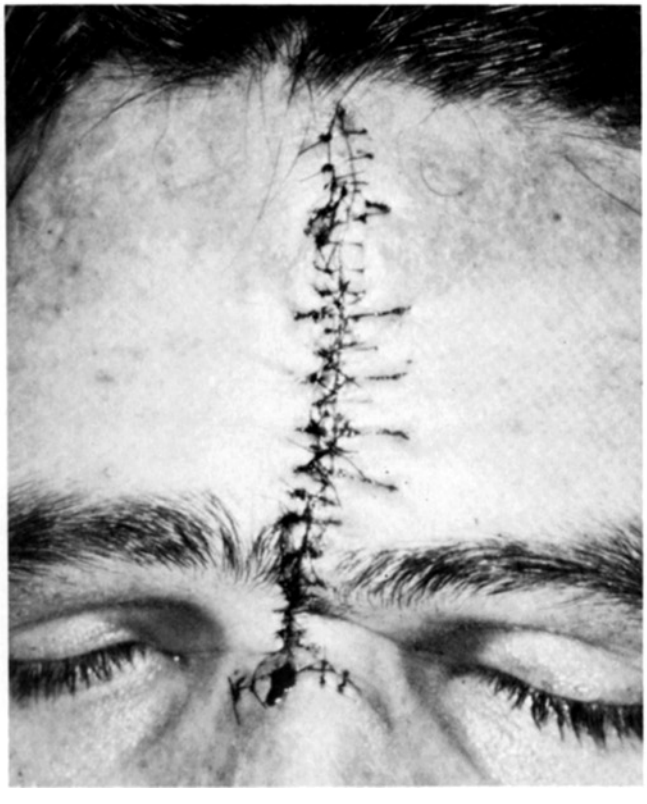

FIGURE 3. Primary closure of defect.

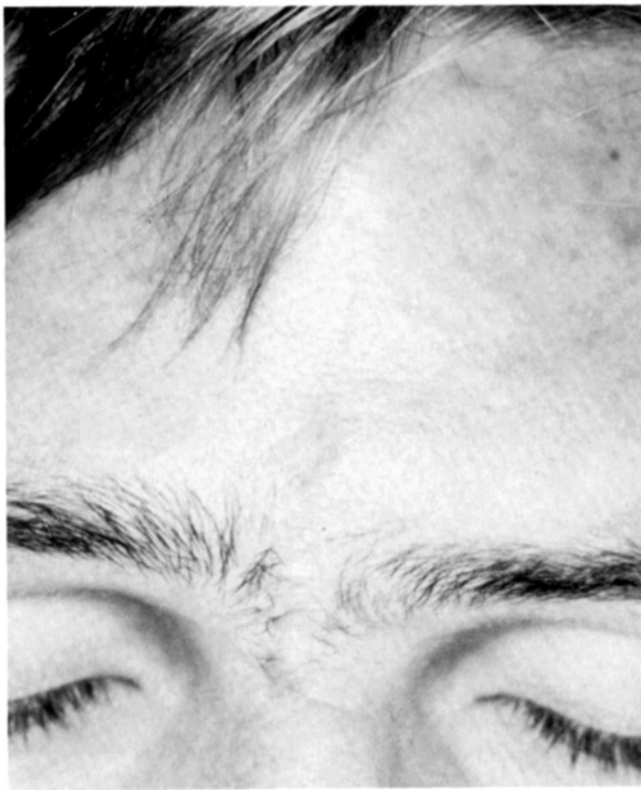

FIGURE 4. One-month follow-up.

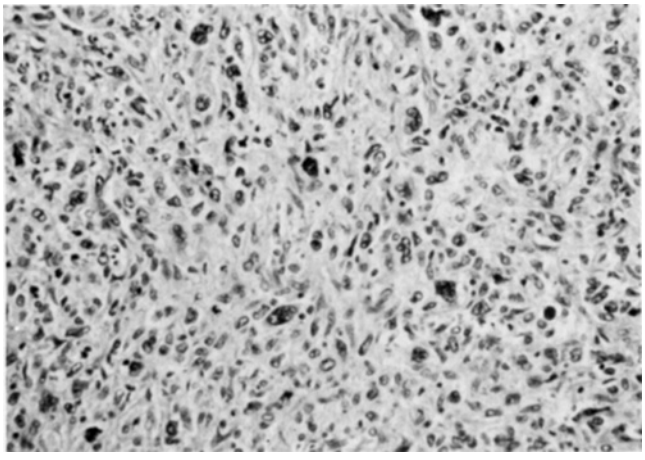

FIGURE 5. 40× magnification of MFH tumor cells.

ing mass of several months duration. The tumors are usually solitary, may be multinodular, are painless, and can be as large as 5.0–10.0 cm in size. The average size in our patient population was about 3.0 cm. Occasionally, fever and leukocytosis may occur with tumor presentation. The extremities are the most common site of involvement, especially the thigh, buttock, and limb skeletal muscles, although any area of the body can be involved. In our series, the tumor appeared to have an unusual propensity for the head and facial areas. The retroperitoneum is also a common site of involvement of deep MFH tumors, especially of the inflammatory type. MFX tumors have been classified as superficial and deep. Superficial MFX tumors are confined to the subcutaneous tissue, but may be attached to fascia. Deep MFX tumors can extend from subcutaneous tissue through fascia into muscle, or may be situated entirely within muscle. Most MFH tumors are deep lesions, with twice as many deeply situated tumors as superficial ones.[7] MFH tumors may arise in the subcutaneous tissue and/or skin, although less than 10% are confined to the subcutis without evidence of deeper fascial involvement. Most of the tumors we treated were of this more superficial location, with origin in the skin or subcutis. The etiology of this aggressive tumor is unclear. There is some circumstantial evidence that previous radiation exposure may be a predisposing factor,[15,16] although only two of our patients had a previous history of such.

The MFH manifests a broad range of histologic appearances and is divided into five subtypes, which are not mutually exclusive.[1,2] The vast majority of our patients showed the storiform, pleomorphic pattern, which is the most common type. This tumor is classically composed of plump, pleomorphic spindle cells, histiocytes, and numerous multinucleated giant cells. The morphologic pattern is highly variable, with frequent transitions from storiform areas to pleomorphic areas. Focal myxoid change is common. Although such tumors may resemble DFSP,there are distinctive histologic differences. The numerous atypical mitotic figures, less prominent storiform pattern, marked pleomorphism, and typical foam and giant cells are all key differential elements. Histologically, the differential diagnosis of MFH also includes leiomyosarcoma, pleomorphic variants of lipo and rhabdomyosarcoma, epitheloid sarcoma, and histiocytic lymphoma. Headington et al.[17] define the key diagnostic criteria for MFH as threefold: (1) a nodular neoplasm similar to the histologic pattern of DFSP; (2) angioinvasion; and (3) frequent penetration of the subcutis and deeper tissue.

Although the MFH has a clinical appearance of being a circumscribed tumor, it often spreads for considerable distances along fascial planes or between muscle fibers.[1] This invasive behavior accounts for its high rate of local recurrence, estimated to be 40–50%, even after wide local excision. Unfortunately, the metastatic rate is also in the range of 40–50% with a high associated mortality. The 2-year survival rate is only 60%.[6] Metastatic disease usually occurs within 2 years of diagnosis, most frequently to the lung (82%), lymph node (32%), liver (15%), and bone (15%).[6] The depth and size of the tumor appears to correlate best with the risk of metastatic spread.[7] Fewer than 10% of tumors confined entirely to the subcutis without deeper fascial or muscle involvement metastasize. Certainly, one of the reasons for our excellent results to date may be related to the fact that most of the MFH tumors we treated were smaller (average 3.0 cm) and more superficial (skin and subcutis), although extension to fascia and muscle was encountered.

Headington et al.[17] have previously noted that there is every indication that the superficially located MFH tumors have a prognosis that is superior to those tumors arising in deeper soft tissue. MFH tumors of the retroperitoneum have the worst prognosis. Patients with distally located tumors have a better 5-year survival than proximally located tumors.[7] Histologic features, including degree of anaplasia and the number of mitoses, appear to have little prognostic value.

Because this tumor spreads a considerable distance beyond the gross tumor mass, an aggressive, wide, and deep local excision or even possible amputation have been recommended. We felt that Mohs surgery was well suited for the treatment of this invasive tumor, particularly when confined to

a more superficial location. Mohs micrographic surgery is capable of tracing out the deepest and widest extensions of the tumor as it spreads underneath the normal-appearing skin. Mohs surgery allowed for complete removal of the tumor while preserving as much normal tissue as feasible, which is of great cosmetic importance in the head and facial regions. Weiman and Ceilley[18] have previously described the successful use of Mohs surgery using permanent paraffin embedded sections in treating one patient with a myxoid variant of MFH. Our results to date would concur that Mohs surgery is an extremely effective surgical modality for treatment of these difficult tumors.

In addition, we treated five patients with atypical fibrous xanthomas, which is considered to be a superficial form of an MFH. Initially, AFX was interpreted as a benign reactive lesion, but because of its histologic similarity to MFH and because of the occasional occurrence of metastatic disease in regional lymph nodes, it is now regarded as a neoplasm of low-grade malignancy.[19] This tumor is seen most often in actinically damaged skin on the head and neck of elderly patients. Clinically, it appears as an asymptomatic, solitary nodule or ulcer, most commonly on the nose, cheek, and ear. However, it has been rarely described on the trunk and extremities, usually in younger persons.[19] The tumor is usually less than 2.0 cm in size; the appearance is not distinctive and often must be differentiated from a squamous cell carcinoma, basal cell carcinoma, or pyogenic granuloma. Occasionally, the tumor is eroded or ulcerated. It is histologically indistinguishable from pleomorphic forms of MFH, but does not invade subcutis or deeper structures such as fascia or muscle. Pleomorphism, particularly in the form of bizarre xanthomatous cells, is the cytologic hallmark of the AFX.[18,19] A well-developed storiform pattern is rarely noted in AFX. Necrosis, which is a prominent feature of MFH, is rarely seen and if present to a significant degree, should raise the question of a proper diagnosis of AFX. Because the AFX is considered an early form of MFH, the distinction of the two is to some extent arbitrary, but it is important to separate them because of their differing natural histories. AFX, due to its in situ dermal location and less invasive nature, has a much better prognosis than MFH. In the largest series in the literature, only 9 out of 140 patients developed a recurrence, and no metastatic lesions were found.[8] However, in rare instances, this tumor can metastasize, and an apparent AFX can progress to an MFH.[19] If only a portion of the entire tumor is submitted for pathologic interpretation, such as in a shave biopsy, it is sometimes difficult to assess the true depth and nature of invasion.

All of the AFX tumors that we treated were primary neoplasms, relatively small, and easily cleared with one stage of Mohs surgery. Although a conservative fusiform excision may have been sufficient treatment, Mohs surgery assured us of totally free margins with no invasion of deeper subcutaneous layers. It also conserved tissue in important facial areas.

In conclusion, we have now treated a total of 25 neoplastic fibrohistiocytic tumors (excluding DFSP). The results to date have been extremely encouraging with an average tumor-free interval of 3 years. Certainly, follow-up over the ensuing years will be necessary to better define the long-term survival rate. Surgery was well tolerated with negligible morbidity and high patient acceptance. Mohs surgery offered a precise surgical approach for the removal of these invasive, recurrent, and potentially metastatic fibrohistiocytic tumors. Considerable cosmetic benefit was obtained, especially in the facial areas, by avoiding unnecessary wide local excisions. In comparison to cure rates quoted in the literature with other surgical procedures, Mohs surgery appears to have an excellent chance of local control and no metastatic disease. The more superficial location and relatively smaller size of the tumors we treated may also have contributed to our successful cure rate. For these reasons, we strongly recommend the use of Mohs surgery for the surgical treatment of neoplastic fibrohistiocytic tumors, specifically malignant fibrous histiocytoma and atypical fibrous xanthomas.

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