

Short Review

Dermatofibrosarcoma Protuberans: Clinicopathological Aspects of an Unusual Cutaneous Tumor

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Abstract. *Dermatofibrosarcoma protuberans is a rare cutaneous tumor with particular characteristics and a high frequency of recurrence after inadequate primary treatment. Its histopathological diagnosis might be difficult. Dermatofibrosarcoma protuberans can be safely distinguished from other similar neoplasms of mesenchymal origin based on the immunohistochemical expression of CD34 antigen and the genetic presence of specific chromosomal translocations. Although rarely metastatic, it is followed by a significantly high rate of locoregional failure due to an indolent subcuticular tissue spread. Aggressive surgical management is the therapeutic approach of choice. A wide resection with microscopically disease-free margins is always recommended. Mohs' micrographic surgery together with advanced reconstructive techniques provides satisfactory results even for tumors involving the face or distal extremities.*

Following Taylor's original report (1) in 1890 of a cutaneous tumor that looked like a keloid and had the potential to recur, Darier and Ferrand (2) described a clinical entity that Hoffmann named dermatofibrosarcoma protuberans (3). Since then, numerous publications (4-11) have described dermatofibrosarcoma protuberans as the following: a rare tumor that is difficult to confirm histologically, one that has a high recurrence rate in the absence of adequate local resection, and one that has the potential to transform into fibrosarcoma with subsequent metastatic spread (10, 11).

Dermatofibrosarcoma protuberans (DFSP) is a rare tumor. Its estimated incidence is one case per million per year. Although it can occur at any age, DFSP is rare in

children, where its clinical findings are similar to the adult DFSP. It occurs predominantly in middle-aged males with a clear peak in the fourth and fifth decades of life. It usually presents as a firm pink nodule (0.5 to 1 cm in diameter) fixed to the deep planes (10, 11). Its benign appearance leads to the patient referring late, often up to 3 years after initial symptoms of mild discomfort. If neglected, the tumor enlarges, protrudes through the skin, and eventually ulcerates. DFSP primarily affects the trunk and proximal extremities and, despite its slow infiltrative growth and tendency for local recurrence, metastasis is very unusual.

The pathogenesis of DFSP has not yet been fully clarified. The exact origin of DFSP remains a matter of controversy, although fibroblastic, myofibroblastic, histiocytic and neuroectodermal histogenic lines have been proposed based on immunohistochemical, ultrastructural and tissue culture studies (12).

Histopathology

In 1962, the histological features of DFSP were characterized as a storiform or cartwheel pattern of fusiform cells with no nuclear atypia or increased mitotic activity (5). Infiltration of the dermis and surrounding fat (12) in combination with the clinical picture are highly suggestive of the diagnosis. Nevertheless, other pathological aspects in microscopy can lead to erroneous reports (5, 13-15) and have contributed to various histogenetical theories of DFSP origin (16, 17). General immunochemistry is useful but not conclusive in establishing the diagnosis and is likely to invalidate the neuroectodermal feature of DFSP (12, 18).

Several histological variants have been described: pigmented (Bednar tumour), myxoid, myoid, sclerosing, with granular cells, with multinucleated giant cells (resembling giant cell fibroblastoma), atrophic and with fibrosarcomatous areas. This latter form is believed to have a more aggressive behaviour. DFSP may be difficult to distinguish from other 'fibrohistiocytic' neoplasms, particularly dermatofibroma

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with extension to the subcutis (19). Some authors refer to the presence of epidermal hyperplasia and the existence of a Grenz zone between the epidermis and the underlying tumour as a feature to distinguish it from DFSP (20). The pattern of extension in the subcutis is also used by many authors to differentiate these two tumours: dermatofibroma is usually well demarcated and bulging or penetrating along the hypodermis septa while DFSP spreads in a honeycomb-like or multilayered fashion, parallel to the skin surface (21). Malignant fibrous histiocytoma (MFH), atypical fibroxanthoma (AT) and fibrosarcoma are other 'fibrohistiocytic tumours' said to be possibly confused with DFSP, but the morphological features of MFH and AT – marked cellular atypia and pleomorphism, high mitotic activity and characteristic bizarre giant cells – allows one to make the correct diagnosis. The problem may be more difficult with spindle cell atypical fibroxanthoma. In such cases immunohistochemistry can play a very important role. Fibrosarcoma is a deeper tumor of spindle cells arranged in a characteristic herringbone pattern. In DFSP, areas of fibrosarcomatous differentiation may be found, and this change has been associated with unfavourable course, higher tendency to recur and increased risk of metastasis, but its true prognostic significance is still controversial.

Immunohistochemical markers, particularly the highly sensitive CD34, have proved to be very important for the differential diagnosis. CD34, a human haematopoietic progenitor cell antigen, is a marker of endothelial cells and tumors of vascular origin; it is also present in 20-30% of dermal dendritic cells (around eccrine glands and the mid-portion of the hair follicle and interstitially in the reticular dermis). It has been considered for the past few years to be the most important immunohistochemical marker for the accurate diagnosis of DFSP. Its use may become more common in the future in patients submitted to several surgical treatments, as in Mohs' surgery, by improving the recognition of disease-free surgical margins and differentiating between images of fibrosis and persistence of tumor (12).

Recent advances in basic genetic research have shown specific chromosomal translocations, generally termed "ring chromosomes", in DFSP. These arise from a fusion of chromosome regions 17q22 and 22q13, the gene loci which code the alpha chain of type I collagen and Factor XIIIa. Their wide acceptance and use will eventually simplify the prompt and accurate diagnosis of this unusual oncologic entity (15, 18).

Clinical Management

Surgery remains the therapeutic modality of choice for DFSP. The locally infiltrative growth pattern features clinically unapparent fine tumor fascicles extending into the adjacent connective tissue and fat for long distances in a

horizontal plane. These tumor extensions cannot be safely detected by conventional imaging techniques (22). They are best delineated by an uninterrupted histological examination of all margins, including the base (3-D-histology), with paraffin sections. Re-excision of tumor-positive areas until tumor-free margins are obtained ("histographic surgery") ensures a high cure rate (97%) while preserving normal tissue (22).

The accuracy of the initial operative procedure is the main prognostic factor for locoregional recurrence and overall survival. Previous studies reported a significantly high risk of tumor relapse in up to 50% of patients (5, 12, 23, 25, 26). Roses *et al.* (23) demonstrated that the recurrence rate was highly dependent on the resection margin, and in 1951 Pack and Tabah (4) recommended removal of a disease-free anatomic zone. Arnaud and colleagues (24) have seen a 1.75% rate of recurrence in primary resections and a 10% recurrence rate in the patients referred for secondary treatment (incomplete excision or recurrent disease) (24). The frequency of recurrence was shown to be correlated with the number of previous surgical attempts and not the size of the original tumor (25). Secondarily treated tumors were shown to recur more often (26).

In large series, patients with DFSP who were treated with wide surgical excisions in both the peripheral and deep planes had a low rate of recurrence even after a 5-year follow-up (24). The aggressiveness of the resection seemed to play a fundamental role, especially in primary treatment. In small series, dermatofibrosarcoma protuberans treated initially with a 0.5-cm margin recurred in 66% among 12 patients (25), in 54.5% among 11 patients (26) and in 30% among 41 patients (12). Taylor and Helwig (5) reported a 41% rate of recurrence, but the status of the patients was not specified as to whether tumors were primary or secondary. In McPeak's series (6), the rate of recurrence was 11% after extirpation with a 3 cm margin of resection.

To improve cure rates by conventional surgery, a wide local excision with 3 cm margins beyond the tumor border down to the fascia has been recommended. Such a margin is not possible when DFSP involves the face or distal extremities. Mohs' micrographic surgery is considered by many investigators to be the best treatment for DFSP (26). The recurrence rate with this method ranges between 0% to 6% in various studies (27, 28). Mohs' microsurgery enables the surgeon to map the location of all tissue removed and microscopically examine the entire deep and lateral margins of a horizontally sectioned specimen. This is important in a tumor with a macroscopically indistinguishable border. Such a tissue-sparing technique is particularly important when the tumor involves the face or distal extremities.

In the extremities (29, 30) or the face (31-33), tumors should be initially treated with a less than 5 cm resection margin, but the physiological importance of the functional

and aesthetic units in these anatomic regions should be taken into consideration. These units are important in the strategy of reconstruction and may represent beds for spread or diffusion of cells. In the case of the face, the extension of surgical resection to one or two aesthetic units is a good compromise for extirpative and reconstructive reasons. The principle of a wider resection up to a 5 cm margin should be applied to all other cases. Aesthetics should be of no concern in treating secondary tumors of the face or in all other locations, whether they are primary or secondary.

Reconstruction by flaps is the most challenging, but the simplest solution should be always preferred if satisfactory in both functional and aesthetic perspectives. Flaps are always indicated after histological confirmation in cases of resection of the periosteum, full-thickness resection, or localization in the shoulder region. In the latter, a muscular latissimus dorsi flap covered with a skin graft is preferred for aesthetic reasons (33). In all cases, radical resections necessary for effective treatment of the tumor are nevertheless acceptable, since modern reconstructive surgery can deal with defects of any size.

Prophylactic lymphadenectomy is unnecessary as lymphatic metastases from DFSP are uncommon. In the rare case of metastatic DFSP, distal spread is through the bloodstream and usually affects the lung parenchyma. Adjuvant radiotherapy seems to reduce the risk of local failure after surgery with close or positive margins, particularly in recurrent disease (20). Chemotherapy is not useful in the treatment of localized DFSP. It may have a role in metastatic disease, but significant benefits remain to be demonstrated.

Conclusion

Dermatofibrosarcoma protuberans is an unusual cutaneous tumor with a tendency to recur locally after inadequate management. Histopathological confirmation can be difficult and differential diagnosis should include specific immunohistochemical studies. Wide surgical resection with microscopically healthy margins and appropriate reconstruction remains the cornerstone of treatment.

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