Dermatofibrosarcoma protuberans: Our experience of 59 cases

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Abstract. Dermatofibrosarcoma protuberans (DFSP) is a rare soft tissue tumor with intermediate malignancy. It is initially located on the skin from where it is able to infiltrate the deep structures and has a tendency to recur locally following inadequate excision. A t(17;22)(q22;q13) chromosome translocation is the main cytogenetic alteration responsible for the onset of DFSP. Treatment options include complete surgical excision by performing conventional surgery with wide margins (>3 cm) or Mohs micrographic surgery. A retrospective study was conducted in our Department of Plastic and Reconstructive Surgery and all data were collected from medical records of 59 DFSP patients within this department from 1999 to 2011. A total of 13 of 59 (22%) cases were treated with conventional excision; 3 (5%) cases resulted in tumor-free margins, 8 (14%) cases required surgical revision and 2 (3%) cases lead to recurrence. A total of 46 of 59 (78%) cases were treated with wide excision; 43 (73%) cases resulted in tumor-free margins, 3 (5%) cases required surgical revision and 0 (0%) cases lead to recurrence. In conclusion, the data collected reveal the controversy surrounding the adoption of general guidelines regarding safe margins. Further studies are required to investigate the possibility of obtaining genotypically altered margins from margins that may appear phenotypically healthy.

Introduction

In 1924, Darier and Ferrand (1) first reported a case of progressive and recurrent dermatofibroma. One year later, Hoffman (2) described the tendency of the dermatofibroma tumor to develop into protruding nodules and termed the condition dermatofibrosarcoma protuberans (DFSP). In 1962, Taylor and Helwig (3) analyzed the histological characteristics of DFSP and in 1992 it was discovered that immunopositivity for CD34 correlated with negative immunostaining for factor XIIIa (4,5). Then, in 1997, Simon *et al* (6) identified that a translocation between chromosome 17 and 22 was the distinguishing cytogenetic alteration in neoplastic tissues responsible for the development of DFSP.

DFSP is classified as a rare tumor, however, it may be considered as the most common stromal tumor of cutaneous origin (7). Numerous epidemiological studies in the USA have reported a mean annual incidence rate between 0.8 and 4.5 cases per million individuals (8-10). Rutgers *et al* (11) reviewed 902 DFSP cases and identified a 3:2 incidence ratio of males to females. However, Criscione and Weinstock (12) studied 9 population-based cancer registries with a total of 2,885 DFSP cases and reported a higher incidence in females. It has also been found that DFSP has a higher incidence rate among individuals aged between 20 and 50 years (13); however, several studies have reported more than 160 pediatric cases of acquired DFSP and more than 35 congenital cases (7,14-19). In addition, it has been demonstrated that giant cell fibroblastoma is the juvenile form of dermatofibroblastoma arising in childhood (20).

Materials and methods

Patient data. A retrospective study was conducted in our Department of Plastic and Reconstructive Surgery and all data were collected from medical records of 59 DFSP patients within this department from 1999 to 2011 (Table I). The histopathological diagnosis and immunohistochemical studies were conducted by the Department of Anatomical Pathology within the same hospital. Each medical record included the age, gender, tumor location and presentation, clinical features, treatment modality, histopathological report, closure type and prognosis of each patient. Informed consent was obtained from each patient.

Methods. Surgical treatment was achieved by performing conventional and wide excision. Conventional surgery was adopted in areas where wide excision would have been difficult to perform, including the root of the nose, vulva, cheek and palpebral commissure. The mean margin used in this type of treatment was 1.07 cm. The majority of cases treated

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were subjected to wide excision with a mean margin of 3.4 cm. Both surgical options were performed by removing the skin, subcutaneous tissue and superficial fascia.

All specimens excised were subjected to formalin fixation and sectioning to confirm the tumor-free margins and histopathological positivity. The immunohistochemical stainings adopted in this study included: CD34 antigen (clone, QBEnd/10, NCL; Novacastra), Vimentin (clone, V9; Thermo Scientific), ACTML, Van Gieson, hematoxylin and eosin, Protein S100 (clone, 4C4.9; Thermo), CD68 (clone, KP1; NCL) and Perl's iron staining.

Follow up. Patient follow-up for recurrences ranged from 3 to 120 months with a mean follow-up time of 62 months. A variety of surgical techniques were adopted for the most suitable wound closure, including primary intention, local flaps or grafting.

No patient within this study had been treated with chemotherapy or radiation prior to treatment at our institution, and no additional adjuvant treatments were performed.

Results

Clinical and surgical data are presented in Tables I-III. As demonstrated in Table II, the mean patient age at time of diagnosis was 37 years (71% of cases were <50-years-old and 29% of cases were >50-years-old), and the majority of cases presented were female (61%). The tumor was located on the trunk, upper extremities, lower extremities and head and neck region in 49, 20, 15 and 16% of cases, respectively. The protruding form of DFSP was the most frequent clinical variety presented, occurring in 66% of all cases. Notably, 17% of patients reported a prior alteration of the cutis, including previous wounds, surgical scars, actinic keratosis, blue nevus and lentigo simplex. Additionally, no cases presented were recurrent at the time of their initial diagnosis.

A total of 13 of 59 (22%) cases were treated with conventional excision due to the difficult location of the tumor (Table III). Following surgery, 3 (5%) cases had tumor-free margins, 8 (14%) cases required surgical revision and 2 (3%)cases lead to recurrence. Although conventional excision may lead to a higher recurrence rate (as demonstrated by this study), in certain cases prognosis may be positively affected by this treatment option. The remaining 46 (78%) cases were treated with wide excision. No patient developed recurrences and only 3 (5%) cases required surgical revision. Additionally, no patient referred to in Tables I-III presented metastatic disease.

Discussion

The main etiological factor in the development of DFSP is the presentation of several prior traumas, including surgical scars (21), trauma scars (22), burns (23), radiodermatitis (24), vaccination sites (25), sites of central venous lines (26) and insect bites (27).

The most common anatomical site affected by DFSP is the trunk (42-72%), with the majority of cases found on the chest and trunk. A total of 16 to 30% of DFSP cases are located on the proximal extremities (particularly on the legs) and up to 16% of cases affect the head and neck areas (7,13).

Clinically, DFSP behaves as a slow-growing asymptomatic plaque and consequently, the majority of patients consult their doctors at a late stage (13). Initially, the neoplasm presents as a violaceous reddish-brown or pink indolent plaque with a hard consistency; at this stage the lesion may be misinterpreted as a hypertrophic scar. Over time, the tumor diffusely infiltrates the deep layers of the skin and the dermis, which leads to the development of several multiple nodules, which are indurated to palpation and adherent to the surrounding tissues, including the subcutaneous fat, fascia, muscle, periosteum and bone.

Martin *et al* (28) distinguished three clinical forms of non-protruding DFSP: morphea-like, atrophoderma-like and angioma-like (Table IV). However, the most frequent presentation described in adults is a large plaque presenting multiple nodules on its surface.

DFSP is characterized by a low rate of metastasis and an eccentric growth rate, which may determine a high level of local invasion. It was found that conventional surgery leads to local recurrence in up to 30% of cases (13).

Kim (29) described seven histological DFSP subtypes of which 90% of cases are represented by 'classic' DFSP (Table V). Histologically, the 'classic' subtype of DFSP appears as a well-differentiated fibrosarcoma initially located on the dermis. The neoplasm is composed of a poor stroma with a dense growth of monomorphous fusiform cells and a large elongated nucleus characterized by little pleomorphism and a low mitotic index. In addition, spindle cells are irregularly organized in linked fascicles with a storiform arrangement. Taylor and Helwig (3) reported a typical diagnostic pattern of DFSP, which is represented by a cartwheel arrangement where cells are arranged radially around a central acellular collagenous area.

DFSP has the tendency to expand from the central focus and invade the surrounding tissues. The tentacle-like projections invade the septa and fat lobules and adopt a honeycomb (30%) or multilayered (70%) subcutaneous pattern (30,31). In both patterns, tentacle-like projections can be inadvertently omitted during wide excision, determining a possible cause of tumor recurrence followed by fascia, muscle and bone invasion.

The first immunohistochemical marker identified for DFSP was the CD34 antigen. It is expressed in up to 90% of cases, differentiating DFSP from other fibrohistiocytic tumors (32,33) (Table VI). Previous studies have revealed that CD34 is also expressed by other sarcomas and benign fibrohistiocytic lesions, including solitary fibrous tumor (34), sclerotic fibroma (35), superficial acral fibromyxoma (36), cellular digital fibromas (37), dermatofibromas (38) and nuchal-type fibroma (39). Consequently, CD34 may be considered as a non-specific marker for DFSP. Other immunohistochemical markers, including factor XIIIa, stromelysin III, apolipoprotein D and CD163, have been found to be positive in dermatofibromas and negative in DFSP (13,39-41). Bandarchi *et al* (42) also reported that D2-40 may be used as a marker for the differential diagnosis between DFSP and dermatofibroma (Table VI).

Molecular biology techniques, including reverse-transcriptase polymerase chain reaction and fluorescent *in situ* hybridization, have revealed that DFSP is characterized by

Table I. Summary of 59 cases of dermatofibrosarcoma protuberans between 1999 and 2011.

Patient no.	Date of diagnosis	Age (years)	Gender	Location	Presentation	Clinical features	Surgical modality	Immunohistochemistry and cytogenetic results	Closure type	Recurrence or surgical revision
1	21/04/1999	20	M	Back	On prior scars	Morphea-like	WE	$CD34^+$ $Vimentin^+$	1 closure	No
2	19/05/2000	30	F	Left arm	On apparently normal cutis	Morphea-like	WE	$CD34^+$ $Actin\ 1A4^-$ $Vimentin^+$	Local flap	Surgical revision
3	23/09/2000	30	M	Abdomen	On apparently normal cutis	Protruding	WE	$CD34^+$ $Vimentin^+$	1 closure	No
4	03/10/2000	9	F	Left ankle	On prior surgical scar	Protruding DFSP	WE	$CD34^+$	1 closure	No
5	03/10/2000	68	F	Left shoulder	On apparently normal cutis	Protruding DFSP	WE	$CD34^+$	Local flap	No
6	03/11/2000	54	F	Forehead and root of the nose	On prior fronto-temporal	Morphea-like, protruding DFSP fibrosarcoma	CE	$CD34^+$ $Vimentin^+$ $S100^-$	Local flap	Recurrence
7	06/11/2000	60	F	Right inguinal region	On prior surgical scar	Protruding DFSP	WE	$CD34^+$ $Vimentin^+$ $CD68^+$	1 closure	No
8	27/01/2001	57	F	Right supraclavicular region	On apparently normal cutis	Protruding DFSP	CE	$CD34^+$	1 closure	Surgical revision
9	26/06/2001	36	F	Right flank	On apparently normal cutis	Morphea-like	CE	$CD34^+$ $CD68^-$	1 closure	Recurrence
10	04/07/2001	34	M	Left thigh	On apparently normal cutis	Protruding DFSP	WE	$CD34^-$	Graft	No
11	29/10/2001	14	F	Left leg	On apparently normal cutis	Morphea-like	WE	$CD34^+$	1 closure	No
12	09/05/2002	27	F	Left shoulder	On apparently normal cutis	Atrophoderma-like	CE	$CD34^+$	1 closure	Surgical revision
13	30/09/2002	32	F	Back	On prior surgical scar	Protruding DFSP	WE	$CD34^+$ $S\text{-}100^+$	1 closure	No
14	10/12/2002	66	M	Scalp	On prior actinic keratosis	Atrophoderma-like	WE	$CD34^+$ $Actin\ 1A4^+$	1 closure	No
15	28/12/2002	34	F	Right supraclavicular region	On apparently normal cutis	Protruding DFSP	WE	$CD34^+$ $CD68^-$	Local flap	No
16	10/01/2003	24	M	Right cheek	On apparently normal cutis	Protruding DFSP	CE	$CD34^+$ $Vimentin^+$	Local flap	No
17	03/02/2003	57	M	Nape	On apparently normal cutis	Protruding DFSP	WE	$CD34^+$ $Vimentin^+$ $Actin\ 1A4^-$ EMA^- $CD31^+$ $Factor\ VIII^+$ $CD99^+$ $Bcl\text{-}2^+$	1 closure	No

Table I. Continued.

Patient no.	Date of diagnosis	Age (years)	Gender	Location	Presentation	Clinical features	Surgical modality	Immunohistochemistry and cytogenetic results	Closure type	Recurrence or surgical revision
18	21/03/2003	64	F	Right leg	On prior blue nevus and lentigo simplex	Pigmented DFSP	WE	Hemosiderin$^+$ CD34$^+$ S-100$^-$	1 closure	No
19	07/04/2003	67	M	Right foot	On apparently normal cutis	Morphea-like	WE	CD34$^+$	1 closure	No
20	28/04/2003	28	F	Left breast	On apparently normal cutis	Pigmented DFSP	WE	CD34$^+$ Actin 1A4$^+$ S-100$^-$	Local flap	No
21	06/05/2003	54	F	Left breast	On apparently normal cutis	Protruding DFSP	WE	CD34$^+$ S-100$^-$	Local flap	No
22	16/06/2003	14	F	Left shoulder	On apparently normal cutis	Protruding DFSP	WE	CD34$^+$	1 closure	No
23	23/06/2003	26	F	Left arm	On apparently normal cutis	Protruding DFSP	WE	CD34$^+$	1 closure	No
24	03/07/2003	21	F	Right thigh	On apparently normal cutis	Pigmented DFSP	WE	CD34$^+$	Graft	No
25	21/07/2003	26	F	Left shoulder	On apparently normal cutis	Protruding DFSP	WE	CD34$^+$ Vimentin$^+$	Local flap	No
26	11/08/2003	18	M	Right forearm	On apparently normal cutis	Protruding DFSP	WE	CD34$^+$	1 closure	No
27	17/09/2003	24	M	Right arm	On apparently normal cutis	Protruding DFSP	WE	CD34$^+$ Actin 1A4$^+$ Desmin, CK$^-$	1 closure	No
28	27/10/2003	39	F	Abdomen	On apparently normal cutis	Protruding DFSP	WE	CD34$^+$	1 closure	No
29	24/03/2004	19	F	Right arm	On apparently normal cutis	Protruding DFSP	WE	CD34$^+$	1 closure	No
30	05/08/2004	28	M	Chest	On apparently normal cutis	Morphea-like	WE	CD34$^+$	1 closure	Surgical revision
31	18/09/2004	25	M	Left leg	On apparently normal cutis	Ulcerated protruding DFSP	WE	CD34$^+$ Actin 1A4$^+$ Bcl-2$^+$	1 closure	No
32	21/10/2004	19	F	Scalp	On prior surgical scar	Ulcerated protruding DFSP	WE	CD34$^+$ Actin 1A4$^-$ S-100$^-$	1 closure	No
33	12/05/2004	19	F	Left shoulder	On apparently normal cutis	Protruding DFSP	WE	CD34$^+$	1 closure	No
34	05/01/2005	23	F	Chest	On apparently normal cutis	Protruding DFSP	WE	CD34$^+$	1 closure	Surgical revision
35	08/04/2005	52	F	Left laterocervical region	On apparently normal cutis	Protruding DFSP	CE	CD34$^+$	1 closure	Surgical revision

Table I. Continued.

Patient no.	Date of diagnosis	Age (years)	Gender	Location	Presentation	Clinical features	Surgical modality	Immunohistochemistry and cytogenetic results	Closure type	Recurrence or surgical revision
36	12/04/2005	43	F	Left inguinal region	On prior surgical scar	Protruding DFSP	WE	$CD34^+$	Local flap	No
37	10/05/2005	37	M	Left shoulder	On apparently normal cutis	Morphea-like	CE	$CD34^+$	1 closure	Surgical revision
38	14/10/2005	31	M	Right inguinal region	On apparently normal cutis	Morphea-like	CE	$CD34^+$	1 closure	Surgical revision
39	11/02/2006	56	F	Abdomen	On apparently normal cutis	Morphea-like	WE	$CD34^+$	1 closure	No
40	01/04/2006	32	M	Right arm	On apparently normal cutis	Protruding DFSP	WE	$CD34^+$ Vimentin$^+$ $CD163^-$ Actin $1A4^-$	1 closure	No
41	20/12/2006	29	M	Abdomen	On apparently normal cutis	Protruding DFSP	WE	$CD34^+$	1 closure	No
42	06/02/2007	28	F	Left arm	On apparently normal cutis	Pigmented DFSP	WE	$CD34^+$	1 closure	No
43	12/03/2007	52	F	Left scapular region	On apparently normal cutis	Morphea-like	CE	$CD34^+$ $S\text{-}100^-$	1 closure	Surgical revision
44	26/06/2007	63	M	Left arm	On apparently normal cutis	Protruding DFSP	WE	$CD34^+$	1 closure	No
45	16/11/2007	37	M	Abdomen	On apparently normal cutis	Morphea-like	WE	$CD34^+$	1 closure	No
46	09/01/2008	37	F	Left arm	On apparently normal cutis	Atrophoderma-like	WE	$CD34^+$	1 closure	No
47	29/02/2008	37	F	Right arm	On pigmented cutis	Pigmented DFSP	WE	$CD34^+$	Graft	No
48	19/03/2008	69	F	Right shoulder	On apparently normal cutis	Protruding DFSP	WE	$CD34^+$ $S\text{-}100^-$ Actin $1A4^-$	1 closure	No
49	30/03/2009	53	M	Right thigh	On apparently normal cutis	Protruding DFSP	WE	$CD34^+$	Graft	No
50	28/07/2009	57	M	Scalp	On apparently normal cutis	Protruding DFSP	WE	$CD34^+$ $CD31^-$ $Desmin^-$	1 closure	No
51	04/12/2009	29	M	Left cheek	On apparently normal cutis	Protruding DFSP	CE	$CD34^+$ $CD117^+$ $CD31^-$ $CD68^-$ $CD163^-$	Local flap	Surgical revision
52	23/12/2009	35	F	Vulva	On apparently normal cutis	Protruding DFSP	CE	$CD34^+$	1 closure	No
53	29/04/2010	33	F	Palpebral commissure	On apparently normal cutis	Protruding DFSP	CE	$CD34^+$	Local flap	No

Table I. Continued.

Patient no.	Date of diagnosis	Age (years)	Gender	Location	Presentation	Clinical features	Surgical modality	Immunohistochemistry and cytogenetic results	Closure type	Recurrence or surgical revision
54	20/07/2010	43	F	Left thigh	On apparently normal cutis	Protruding DFSP	WE	$CD34^+$ $CD68^+$	Graft	No
55	24/12/2010	42	M	Left arm	On apparently normal cutis	Pigmented DFSP	WE	$CD34^+$	1 closure	No
56	15/03/2011	32	F	Gluteus	On apparently normal cutis	Protruding DFSP	WE	$CD34^+$	Local flap	No
57	20/05/2011	1	F	Left flank	On apparently normal cutis	Protruding DFSP	WE	$CD34^+$	1 closure	Surgical revision
58	04/08/2011	47	M	Temporal region	On apparently normal cutis	Protruding DFSP	WE	$CD34^+$	Local flap	No
59	04/10/2011	64	M	Left shoulder	On apparently normal cutis	Protruding DFSP	WE	$CD34^+$	1 closure	No

DFSP, dermatofibrosarcoma protuberans; CE, conventional excision; WE, wide excision.

Table II. Clinical features of 59 DFSP patients.

Clinical features	No. of cases	Total cases (%)
Gender		
Male	23	39
Female	36	61
Age at diagnosis		
Mean age (years)	37	-
<50-years-old	42	71
>50-years-old	17	29
Clinical presentation		
Morphea-like	11	19
Atrophoderma-like	3	5
Angioma-like	0	0
Protruding DFSP	39	66
Pigmented DFSP	6	10
Location		
Trunk	29	49
Upper extremities	11	20
Lower extremities	9	15
Head and neck region	10	16
Presentation		
On apparently normal cutis	49	83
On pigmented/prior altered cutis	10	17

DFSP, dermatofibrosarcoma protuberans.

Table III. Correlation between excision modality and prognosis.

Prognosis	No. of cases treated		Total (%)
	Conventional excision (%)	Wide excision (%)	
Tumor free	3 (5)	43 (73)	46 (78)
Surgical revision	8 (14)	3 (5)	11 (19)
Tumor recurrence	2 (3)	0 (0)	2 (3)
Total	13 (22)	46 (78)	59 (100)

supernumerary ring chromosomes or a reciprocal translocation between chromosome 17 and chromosome 22 t(17;22)(q22;q13) (6,43). This translocation involves the collagen type 1 α 1 (COL1α1) gene located on chromosome 17 and the PDGFβ gene located on chromosome 22. In DFSP, COL1α1 is highly expressed and acts as an inducer of gene transcription (44). COL1α1-PDGFβ fusion leads to the transcription of a fully active PDGFβ protein, which triggers mitosis through the activation of the PDGFβ receptor (PDGFβR) via autocrine and paracrine stimulation of its functional ligand (45). The PDGFβR is composed of three structural domains: an extracellular binding, a transmembrane and a cytoplasmic domain with tyrosine kinase activity. The tyrosine kinase

Table IV. Clinical variants of the preprotuberant stage of DFSP as described by Martin *et al* (25).

Variant	Clinical features	Onset
Morphea-like	White or brown indurated plaque appearing as a scar, morphea, morpheaform basal cell carcinoma or dermatofibroma plaque	Childhood
Atrophoderma-like	Soft depressed white or brown plaque similar to atrophoderma or anetoderma	Congenital
Angioma-like	Indurated red or violaceous plaques with clinical appearance similar to vascular malformations or angiomas	Uncommon

DFSP, dermatofibrosarcoma protuberans.

Table V. Histological subtypes of DFSP as described by Kim (29).

Subtype	Histological characteristics	Clinical features
'Classic' DFSP	Monomorphous fusiform cells (spindle cells) with large elongated nucleus and poor cytoplasm, low mitotic index	Most common subtype (90%) Rare metastasis (≤0.5%)
Giant cell fibroblastoma	Giant multinucleated cells, sinusoidal vessels, myxoid stroma	Frequently observed in childhood
Bednar tumor	Melanocytes and deposits of melanin	Observed in African and American patients
Sclerotic DFSP	Abundant stroma with several layers of collagen and areas of denser cellularity	Rare subtype
Myxoid DFSP	Spindle cells grouped in nodules with eosinophilic cytoplasm	Rare subtype
Atrophic DFSP	Atrophic mid-dermis with subcutaneous tissue close to the epidermis	Frequently observed in childhood
Fibrosarcomatous DFSP	High mitotic index with high cellularity and marked nuclear pleomorphism	Subtype with the highest recurrence rate and metastatic potential, most aggressive variant

DFSP, dermatofibrosarcoma protuberans.

Table VI. Immunohistochemical markers used for differential diagnosis of DFSP.

Marker	Expressed	Not expressed
CD34	DFSP, inflammatory fibrosarcoma, myofibrosarcoma, angiosarcoma, epithelioid sarcoma	Dermatofibroma, malignant fibrous histiocytoma, pediatric myofibromatosis, fibrosarcoma, hypertrophic scars or keloids
Factor XIIIa	Dermatofibroma	DFSP
Stromelysin III	Dermatofibroma	DFSP
Apolipoprotein D	Dermatofibroma	DFSP
CD163	Dermatofibroma	DFSP
D2-40	Dermatofibroma	DFSP

DFSP, dermatofibrosarcoma protuberans.

activates an intracellular signaling cascade that affects physiological cell processes, including chemotaxis, proliferation and apoptosis (13).

Primary treatment of DFSP consisted of complete surgical excision of the lesion. It has been reported (46) that standard surgical resection leads to a local recurrence rate of up to 60%,

Table VII. Correlation between surgical margins and local recurrence rate in DFSP wide local excision.

Author (Refs.)	Surgical margin (cm)	Recurrence rate (%)
Chang *et al* (46)	5	<5
Fiore *et al* (47)	3	20
Gloster *et al* (48)	<2	40

DFSP, dermatofibrosarcoma protuberans.

which is due to the occult spreading of the tentacle-like projections beneath the clinically normal-appearing skin margins.

The main challenge in DFSP surgery is to achieve satisfactory local control. To obtain the lowest recurrence rate, two surgical treatments may be performed: wide local excision and Mohs micrographic surgery (MMS). In addition to surgical methods (recurrent and metastatic lesions), molecular targeted therapy with imatinib mesylate may be considered as a suitable alternative or additional treatment option for DFSP.

Several studies have demonstrated a significant correlation between wide excisions and low recurrence rates (46-48) (Table VII). According to previous studies, it is recommended that surgical excisions be performed at least 2-3 cm away from the gross margin. Furthermore, it is important to perform a three dimensional en bloc removal of the tumor, including skin, subcutaneous tissue and fascia. If the underlying bone structures are affected it is necessary to perform a wide resection of the periosteum and bone (7).

MMS can be used to produce a local control that is more effective. MMS is a surgical procedure characterized by precise histological resection margin control. According to Dim-Jamora and Perone (49), MMS should be the first choice for DFSP treatment. The most important technical aspect in MMS is continual sequential horizontal sectioning (5-7 μm) with immediate microscopic examination of the frozen sections of the resected tissue until a clear margin is obtained. Guillen and Cockerell (50) revealed through MMS that tentacle-like formations can extend beyond 3 cm in the horizontal direction. Loss and Zeitouni (51) consider MMS as the treatment of choice in anatomically challenging areas, including the head or neck. Although the efficacy of MMS is highly recognized, this technique is also considered to be elaborate, time-consuming and labor-intensive (7).

According to the cytogenetic role of PDGFβR in the pathogenesis of DFSP, several studies have focused on the most suitable strategy to inhibit the mitogen process. Imatinib competes with adenosine triphosphate and prevents tyrosine kinase receptor autophosphorylation. This leads to inhibition of the aberrant signal transduction pathway and a partial restoration of intracellular signaling.

Data in the present study demonstrate the controversy surrounding the adoption of general guidelines regarding safe margins. However, we are confident to use the guidelines proposed by Chang *et al* (46), Fiore *et al* (47) and Gloster *et al* (48). Future treatments for DFSP may adopt other parameters, including the cytogenetical study of surgical margins, since margins that are phenotypically recognized to be tumor-free, may hide the genetical translocation t(17;22) (q22;q13). Further studies should investigate the possibility of obtaining genotypically altered margins from margins that may appear phenotypically healthy. This may improve the accuracy of tumor excision and the predictability of further possible recurrences.

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