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DermatoFibrosarcoma Protuberans - A rare dermatologic malignancy: 120 case reports

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ABSTRACT: *Background:* The dermatofibrosarcoma protuberans is a rare skin tumor with a low grade malignancy. It is characterized by a random and asymmetric local extension and a spontaneous tendency to local recurrence. This characteristic is the main difficulty in the management of dermatofibrosarcoma protuberans. The aim of our study was to evaluate our experience in the management of this disease and to clarify the epidemiological, clinical, therapeutic and prognostic characteristics of this rare tumor.
Methods: This was a retrospective, single-center, covering 120 cases of dermatofibrosarcoma protuberans treated at the Institute Salah Azaiez, over a period of 21 years from 1 January 1992 to 31 December 2012.
Results: The average age at diagnosis was 41.5 years, ranging from 7 to 82 years. . Our population was consisted of 51 women and 69 men. The chief complaint most frequently found was the rapid growth of a nodule (39.2% of cases). The average consultation time was 51 months. The predilection was the trunk in 71 patients (59%) and members in 42 patients (35%). The average lesion size was 6 cm, with a range of 1 to 20 cm. The most common appearance was an isolated nodule in 60% of cases. Ultrasound soft tissue was done in 15 cases (12.5%). Therapeutically, our patients underwent a wide excision in 118 cases and adjuvant radiotherapy in two cases. We observed nine cases of recurrence after a median follow up of 29 months. We observed ten cases of sarcomatous transformation six of which have developed lethal metastases.
Conclusion: The prognosis of this disease depends on the surgery performed in first intention which must be complete from the start. Any inappropriate surgery increases the risk of recurrence, sarcomatous degeneration and metastasis.

KEYWORDS: Dermatofibrosarcoma protuberans, local malignancy, surgery, recurrence, prognosis

1 INTRODUCTION

The DermatoFibroSarcoma Protuberans (DFSP) is a rare coetaneous tumor; with an estimated incidence of 4,2 to 4,5 new case per million person per year (1,2).

The DFSP is a low grade coetaneous sarcoma known for its slow evolutivity and a high tendency to relapse.

The degenerated DFSP accounts for less than 10 % of the cases with a high risk of distant metastasis.

The cornerstone of treatment is surgery. The quality of the surgical margin represents the essential prognostic factor for local relapse. The wide excision with a margin of 2 to 3 cm initially recommended has been replaced by the micrographic surgery allowing the study of the full circumference of the tumor with a reduced surgical margin and a complete removal of the tumor.

The place of the adjuvant treatment is yet not well defined. Radiation can be used to reduce local recurrence in case of insufficient surgical margin. There is no proven efficient chemotherapy. Lately the discovery of the protein COL1A-PDGFB is giving the rational for the use of tyrosine kinase inhibitor such as Imatinib.

The aim of our work is to report the characteristic features of the DFSP through a 120 case study.

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2 METHODS

A retrospective study about 120 case of DFSP followed up in Salah Aziez institute of Oncology in Tunis Tunisia from January 1992 to December 2012.

We included patient with DFSP confirmed in the final histological examination. We excluded the patient with a Survival of less than one month. The therapeutic decisions were made in a multidisciplinary meeting with a surgical oncologist radiation oncologist and medical oncologist.

The statistical analysis was conducted using SPSS ver. 21 (SPSS, Inc., Chicago, Illinois). Pb0.05 was defined as statistically significant; all tests were 2-tailed. The recurrence curves were calculated using the Kaplan–Meier method and the log-rank test was used to compare the recurrence curves. Univariate and multivariate analyses were performed using Cox's regression model. Pearson's chi-squared or Fisher's exact test was used to compare the differences of proportions.

The review of the literature was made with google scholar using the following key words: DFSP, skin sarcoma, Mohs surgical resection

3 RESULTS

The median age was 39 years (7-82 years). There were 69 men for 51 women with a sex ratio men/women of 1,35. Figure one shows the distribution of patient according to sex and age.

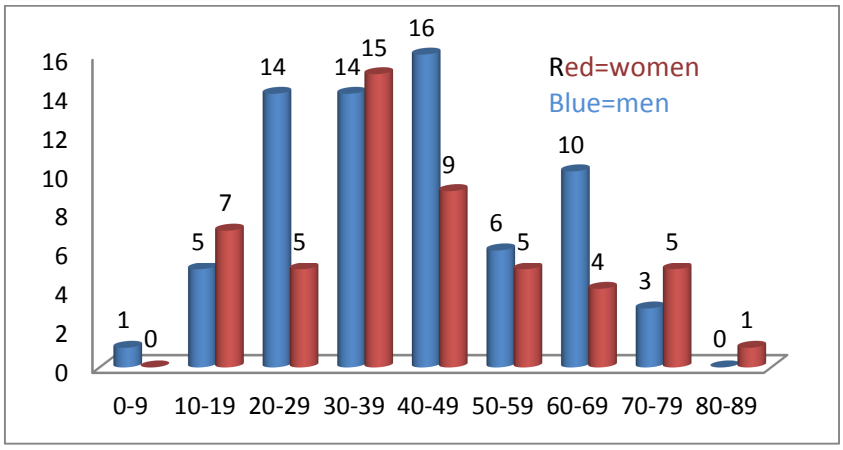


Fig. 1. Distribution of patients according to sex and age

Nine cases (15,3%) had a prior history of skin trauma in the site of the DFSP.

Table 1. distribution of patient according to the Origin of the trauma

Type of trauma	Frequency	Percentage
Post-traumatique scar	5	8,5%
Post-surgery scar	1	1,7%
Burn Scar	1	1,7%
Post-vaccination Scar	1	1,7%
Scarification	1	1,7%
Total	**9**	**15,3%**

The chief complaint was a fast growing coetaneous lump.

Table 2. Distribution of patient according to the chief complaint

Functional sign	Frequency	Percentage
Fast growing Lump	47	39,2%
Painful Lump	21	17,5%
Pruritis	10	8,3%
Total	**78**	**65%**

The most common location was the trunk 71 patients (59%) followed by the limbs 42 patients (35%).

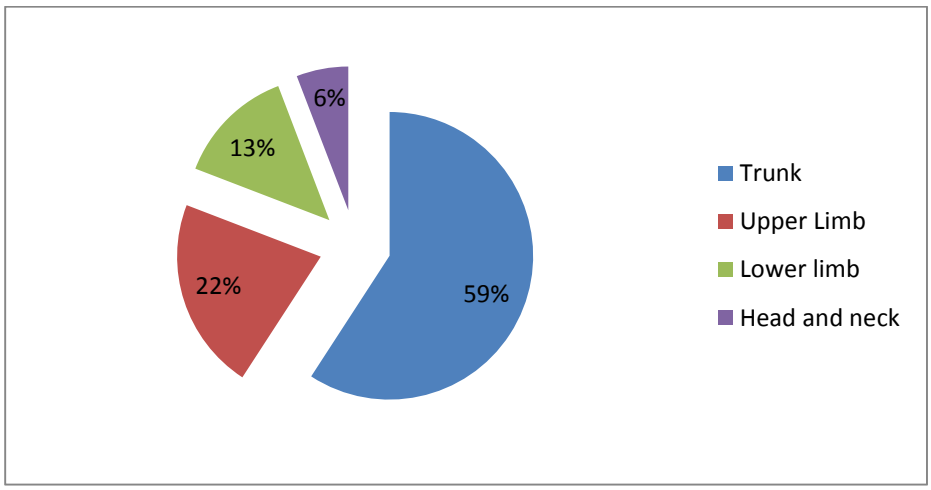
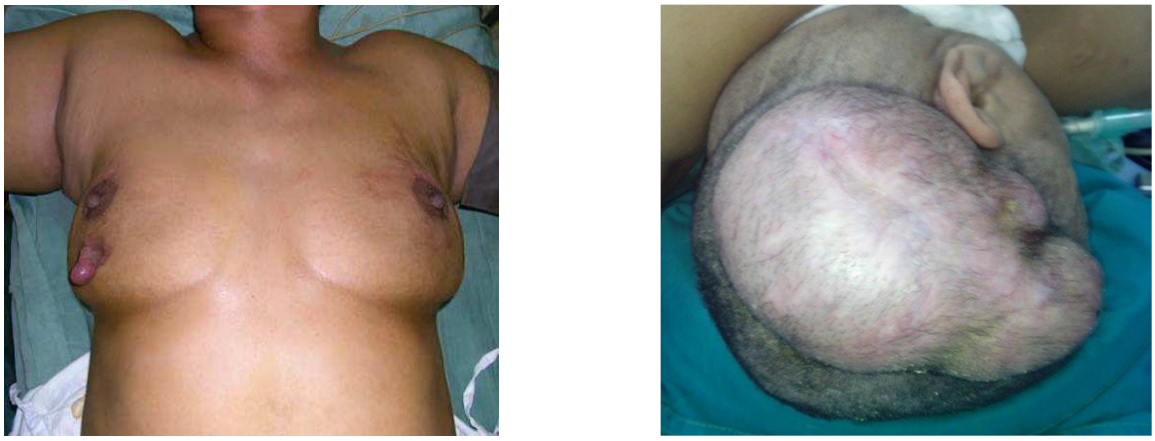


Fig. 2. Distribution of patients according to localization of DFSP



Picture 1 and 2: DFSP of the right breast and of the Scalp

The Median size of the tumor was 5 cm (1-20cm). One quarter of the patient had radiologic examination prior to surgery; 15 had Locoregional sonography and 9 had a Computed Tomography (CT) scan. Showing that the radiologic median size was superior to the one measured clinically (7cm Vs 5cm).

Thirty nine patients were initially treated outside of our institution and referred for either incomplete resection or local relapse.

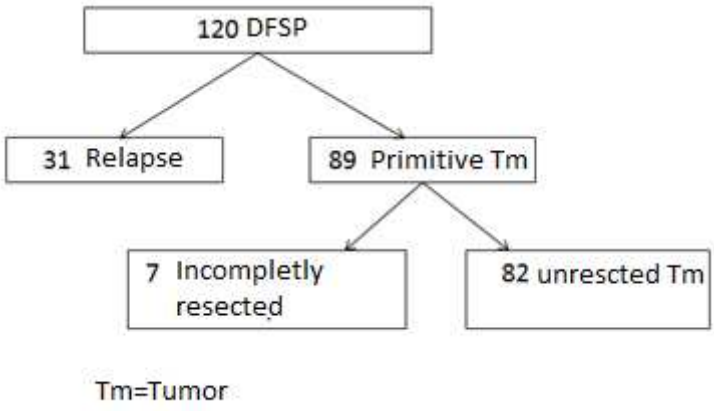


Fig. 3. Distribution of patients depending of the Tumor Status

One hundred eighteen have undergone surgery in our institution and two received only radiation therapy.

The histological margins were free of disease in 83% of the cases.

For the insufficient margins rescission was indicated in all the cases but done for 16 patients.

Table 3. Distribution according to histological Margin

Histologique examination	Frequency	Percentage
Clean Margin	98	83%
Invaded Deep Margin	12	10%
Invaded Lateral Margin	6	5%
Narrow deep margin	1	1%
Narrow lateral margin	1	1%
Total	**118**	**100%**

During the follow up nine patients relapsed. The median time to relapse was 29 months (10-85 months).

Over the 120 patient 86 (72%) never relapsed after the initial surgery. Ten patients (8%) showed sarcomatous degeneration.

Table 4. Summary of the patients with sarcomatous degenresence

	Age	Sex	Localization	size (cm)	Place of first surgery	Type of surgery ISA	Time to degeneration	Number of relapse	Metastasis
Cas 1	25	M	Abdomen	5	ISA	Conservatrive	D'emblée	0	non
Cas 2	29	F	Back	2	Hors ISA	Conservatrive	D'emblée	0	oui
Cas 3	39	F	Inferior limb	11	Hors ISA	Hip Amputation	109 mois	8	non
Cas 4	41	M	Superior limb	10	Hors ISA	Conservatrive	12 mois	1	non
Cas 5	44	M	Superior limb	15	Hors ISA	Conservatrive	8 mois	0	oui
Cas 6	53	M	Superior limb	20	Hors ISA	IST Desarticulation	31 mois	4	oui
Cas 7	55	M	Inferior limb	9	ISA	Conservatrive	D'emblée	1	oui
Cas 8	78	F	Inferior limb	14	Hors ISA	Conservatrive	71 mois	0	oui
Cas 9	67	M	Abdomen	13	Hors ISA	Conservatrive	D'emblée	1	oui
Cas 10	79	F	Superior limb	14	Hors ISA	IST Desarticulation	36 mois	4	non

IST= inter-scapulo-thoracic ISA=Institut Salah Azeiez

Metastases as shown in table 4 were seen in 6 cases of degenerated DFSP with a median time of 49 months (3-73 months).

The mean period of follow up was 42,5 months (1-250 months). One hundred and twelve (93,3%) were in complete remission. Six patients died within this period due to their metastases.

The Local Recurrence Free Survival (LRFS) was 90% at 5 years and 81%at 10 years.

The Distant Recurrence Free Survival (DRFS), was at 5 and ten years respectively of 92,4% and 86,2%.

The univariate analysis found that quality of fist excision and histological Grade have a significant influence in both LRFS and DRFS.

Table 5. Summary of the univariate analysis

Prognostic Factors	LRFS	DRFS
Age	NS	NS
Time to first consultation	NS	NS
Head localization	0,003	NS
Histological size	0,005	NS
Lateral MArgin	$<10^{-4}$	NS
Quality of fiirst excision	$<10^{-4}$	$<10^{-4}$
Histologic deep invasion	$<10^{-4}$	NS
Histological Grade	$<10^{-4}$	$<10^{-4}$
Local recusrrence	-	$<10^{-4}$

NS= non-significant

In the multivariate analysis, no independent factors influencing the survival have been found.

4 DISCUSSION

The DFSP is according to the OMS 2013 classification is classified as an intermediate malignant fibroblastic tumor. The DFSP is characterized by its slow progression, high risk for local recurrence and low risk for metastatic disease. The sarcomatous degenresence is rare(3).

DFSP is a rare skin tumor accounting for 0,1 % of adult malignancies (4) and 1 to 6% of the soft tissue sarcoma (5). The degenerated DFSP incidence is estimated between 5 to 15% of the cases (6). In our study it was 8%.

In ten to twenty percent of the cases a prior medical history of skin trauma was found (7,8).

It's usually a local trauma, happening two months to 20 years prior to the DFSP lesion (9).

In our study 9 patients had a prior medical history of skin trauma. It was usually a non-significant local skin trauma. However no clear relation has been established.

Clinically, the majority of DFSP appears as an indolent skin lump with a long period of evolution(10) delaying the diagnoses. The clinical features of the degenerated DFSP are similar to the classic DFSP, and neither medical history nor physical examinations are useful to clearly distinguish between the two aspects of the disease.(11)

The principal localization of the disease are the trunk and the proximal part of the Limbs (12,13). The same results were found in our study with 59% localized to the trunk and 35% to the limb.

DFSP appears as a poorly circumscribed tumor that infiltrates the whole dermis destroying the preexisting structures and spreading into the cellular subcutaneous tissue.The main histologic characteristic of DFSP is its capacity to invade surrounding tissues to a considerable distance from the central focus of the tumor. The cellularity is greater in the central zone than in the peripheral part of the tumor,where the edges invade the surrounding dermis and subcutis.(5)

This may lead to in insufficient initial resection with narrow or invaded margin, leading to an elevated risk for local recurrence (14). Even though, local recurrence can be treated by surgery they tend to have a superior capability for deep invasion leading to more tissue removal and substantial parietal loss. Local recurrences are also known to be associated with higher risk of distant metastasis.(14,15)

For all those reasons a complete surgical excision is mandatory. Two techniques can be used Wide Local Excision (WLE) or Mohs micrographic surgery (MMS).

With WLE the median recurrence rate Go from 6 to 8 % but in some studies it can reach 47 %(13–15). This variation can be explained by the fact that no minimal excision margin has been defined. The NCCN(national comprehensive center network) recommends a 2 to 4 cm margin, the removal of muscle fascia or the periosteum and with non-invaded hitologic margin.(16). However those margins are rarely feasible without an esthetic or functional burden.

If positive margins were found after WLE, most of the guidelines including the NCCN recommend Reexcision followed by adjuvant Radiation therapy or targeted therapy(16).

MMS is an approach to skin cancer removal that aims to achieve the highest possible rates of cure and to minimize the size of the wound and consequent distortions at critical sites such as the eyes, ears, nose, and lips. MMS is a two-step, same-day procedure performed with local anesthetic. It involves removing the tumor in stages by histologically confirming clear margins on frozen sections and by addressing the resultant defect. Options for healing include second intent, primary closure, local flaps, interpolation flaps, and grafts. Larger tumors may require referral for reconstructive surgery. MMS is the treatment of choice for skin tumors in critical sites, large or recurrent tumors, tumors in sites of radiation therapy, and tumors with aggressive histologic features.

ThE MMS showed a clear advantage compared to the WLE reducing the recurrence rate by 4,5 times. This difference is far greater for head and neck tumors where the recurrence rate for MMS is 1,9 % compared to 51,8% for WLE(17).

However, there is controversy over the use of one or the other procedure. One reason is the lack of randomized controlled trials and the paucity even of comparative studies.

Although the litterature shows that MMS is more effective than WLE, it does have drawbacks. Considerable training and a specialized team are required. The learning curve is long and the procedure labor-intensive, requiring the performance and interpretation of numerous histopathological sections. For many patients, this means a staged surgical procedure of several hours over multiple days. The average number of stages in Paradisi serie (17) was 1.8, with a range of 1–5. Finally, as Mohs surgery is performed under local anesthesia, limitations regard size of resectable tumors, total amount of local anesthesia that can be used safely, and patient comfort.

WLE may thus be preferable in most trunk and limb lesions, which afford easier excision. It also is a typically short procedure. The majority of post-operative defects on trunk and extremities can be closed primarily, avoiding subsequent reconstructive procedure.

The lymph node dissection is not mandatory due to the rarity of the lymphnodes invasion.(8)

In the adjuvant setting radiation therapy, chemotherapy or targeted therapy can be used.

Radiation therapy is recommended for tumor with multiple recurrences, insufficient of invaded margin with no possibility for rexcision, big size tumor and localization enabling large excision(18).

The finding of degenerated DFSP is not an indication to Radiation therapy and the NCCN recommend Radiation for Degenerated DFSP for high volume tumor or insufficient margin resection(16).

About chemotherapy few data is available but it suggests a lack of efficiency for the drugs (such as isofosfamid and doxorubicin) used to treat soft tissue sarcoma(19,20)

Recently with the discovery of the gene COL1A1-PDGFB which induces an activation of the tyrosine kinase pathway served as a rational to start imatinib clinical trial.(21)

DFSPis characterized by high rates of local recurrence and low risk of metastasis. Most of the recurrence happens during the three years following the surgery, but cases of distant recurrence have been reported(22). Thus, the patients need to be seen every six months the 3 first years and then annually (22). A physical examination is mandatory and no further examination is needed unless oriented by the physical examination.

5 CONCLUSION

Dermatofibrosarcoma protuberans (DFSP) is a rare superficial tumor characterized by high rates of local recurrence and low risk of metastasis. DFSP occurs most commonly on the trunk and proximal extremities, affects all races, and often develops between the second and fifth decade of life. The cornerstone of treatment is WLE with a 3 to 5 cm margin. The MMS can be used to reduce the volume of excised tissue but has an elevated cost and need a trained team. Adjuvant Radiation therapy can be used for high volume tumor, insufficient or positive margin with no possible rexcision, tumor located in critical areas and radiation can be used by its own for unresectable tumors.

Imatinib is now indicated for metastatic or unresectable DFSP.

The prognosis of the disease is strongly related to the recurrence of the disease thus a regular long term follow up is needed.

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