Research Article

Variability in Presentation of Dermatofibrosarcoma Protuberance: A Reterospective Review From Single Center

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Abstract

Background: Dermatofibrosarcoma protuberance(DFSP) is slow growing, locally aggressive tumor of skin and subcutaneous tissue. It has multiple variants which show different clinical features and malignant potential. The aim of this retrospective review is to compare variation in presentation and management of DFSP.

Objective: To better understand the variability in clinical presentation of dermatofibrosarcoma protuberance (DFSP) in patients treated at Shaukat Khanum Memorial Hospital & Research Center.

Methodology: We retrieved data, of patients with DFSP who underwent surgery from December 2014 to December 2020, from hospital data base system. Information about patient's demographics, clinical features, surgical treatment, complications and outcome was and collected on proforma.

Results: A total of 63 patients presented with DFSP with mean(SD) age 38.56(12.1) years, of which 69.8%(44) were males in their 3rd and 4th decade. Most common site was trunk in 41.3%(26). Most common tumor appearance was nodular in O-DFSP i.e. 26(49.1%) and 3(30%) in FS-DFSP group (p=0.03). Most of O-DFSP patients (84.9%) had size <10cm while more FS-DFSP patients (70%) had tumor size >10cm (p= 0.0001). FS-DFSP patients were more prone to develop post-operative complications. Most of the patients of both groups are alive without disease i.e, 60% of FS-DFSP group and 54.7% of O-DFSP group(p=0.05).

Conclusion: Clinical characteristics of O- DFSP are non-specific and variable mimicking benign lesions. Short duration, ulcerated lesion with discharge, enlarged regional lymph nodes, and local recurrence should raise suspicion ofFS-DFSP. Long-term follow-up is strongly recommended.

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Keywords | Dermatofibrosarcoma protuberance, O-DFSP, FS-DFSP, Wide excision, Recurrence, Radiotherapy.

Introduction

Dermatofibrosarcoma protuberans (DFSP) represents relatively rare skin sarcomas constituting 4 % of all skin malignancies.[1] Its variant with fibrosarcomatous transformation, being called fibrosarcomatous dermatofibrosarcoma protuberans (FS-DFSP), is said to have a 10–15 %rate of distant metastasis and poorer prognosis compared with ordinary DFSP (O-DFSP) that does not havefibrosarcomatous transformation.[2] (Figure 1)

DFSP is slow growing tumor affecting both genders of all ages, mostly in adult age (25-50 years) and occur most commonly on the trunk, proximal extremities, and head and neck regions.[3] Clinically, DFSP has variable presentation ranging from painless, skin-colored plaque with probable reddish brown or blue discoloration (similar to benign lesion)which later on becomes protuberant or ulcerated and tend to infiltrate adjacent structures but rarely metastasize. It has high local recurrence rate about 26-60%.[4] Surgical excision with wider margins

is recommended treatment.[5] Adjuvant radiation therapy has traditionally been used to reduce the risk of local recurrence when residual disease remains after surgery, but it has limited role.[6,7]

There is scarcity of studies showing variations in clinical features and treatment outcome of patients with both variants of DFSP in our country. Therefore, the aim of this study was to review the variability in clinical presentation of DFSP, its surgical treatment, complications and outcome, in patients who were treated at Shaukat Khanum Memorial Hospital & Research Center.

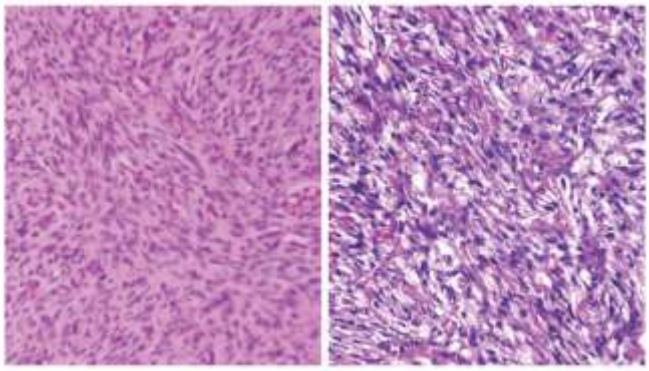

Figure 1: *Histopathology Image of Dermatofibrosarcoma protuberance (DFSP).*

a) *H & E stain showing spindle shaped tumor cells*

b) *Fibrosarcomatous DFSP showing plump spindle cells arranged in fascicles, high nuclear grade and increased number of mitosis/ HPF.*

Methods

After taking exemption from hospital institution review board (EX-14-08-19-01), retrospective review of cases who underwent surgery for DFSP from December 2014 to December 2020. Patients of both genders with age >14 years, having biopsy proven DFSP as primary disease, patients who underwent inadequate surgery for DFSP or recurrent disease were included in study. Patients having inoperable disease or distant metastasis were excluded.

All the patients were initially seen in OPD where history and examination completed and surgery planned. Wider excision with tumor free margins on frozen section done in all patients after taking consent followed by wound closure directly, by grafting or flap.

Data was retrieved from hospital database of Shaukat Khanum Memorial Cancer Hospital and Research Center (SKMCH & RC), Lahore, where study was conducted. Data was collected on standard proforma containing demographics, variability in clinical presentation of DFSP, its surgical treatment, complications and outcome.

Descriptive variables were presented by proportions, mean or median values, and percentage as appropriate by data distribution. Age (14-50 or ⩾ 50 years) and dura-tion of recurrence were dichotomized. In Ordinary and Fibrosarcomatous DFSP patients, categorical variables like age, gender, size of tumor, duration of tumor, Lymph node status, and outcome measures were compared using chi square test. Data of variables like anatomical site, histological subtype, complications and current status were compared by T-test. Statistical analysis was performed using SPSS 21.0 statistical software. Statistical significance was defined as p value <0.05.

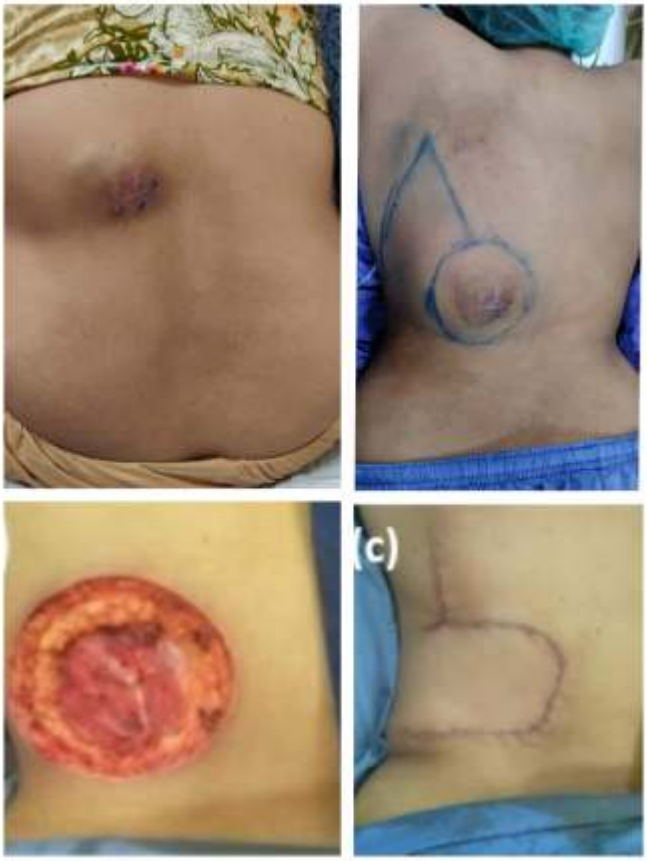

Figure 2: *O-DFSP in 36 years old Female*

a) *DFSP of nodular variety on left side of back*

b) *Marking of 3cm excision margins and rhomboid flap*

c) *Muscle deep defect of 8x7cm*

d) *Rhomboid flap insetting on defect*

Results

A total of 63 patients presented with biopsy proven DFSP and underwent surgery for DFSP from December 2014 to December 2020.Among them, 53 (84.1%) had biopsy proven O-DFSP while 10 (15.9%) had FS-DFSP. Mean follow up period after surgery was 42.3 months (3.5 years) with range of 9.6-78 months (0.8-6.5 years).

The Mean (S.D) age 38.56(12.1) years, of which 69.8% (44) were males.Patients with age 14-50 years were more likely develop DFSP of both varieties i.e, 43 (81.1%) of O-DFSP group and 9 (90%) of FS-DFSP group. The Mean(S.D) size of tumor was 6.56 cm (2.7). Among them, more patients of O-DFSP group had size <10 cm (45 out of 53 i.e, 84.9%) while FS-DFSP group had more tumor size >10 cm (7 out of 10 i.e, 70%) and it was found to be statistically significant (p=0.0001).

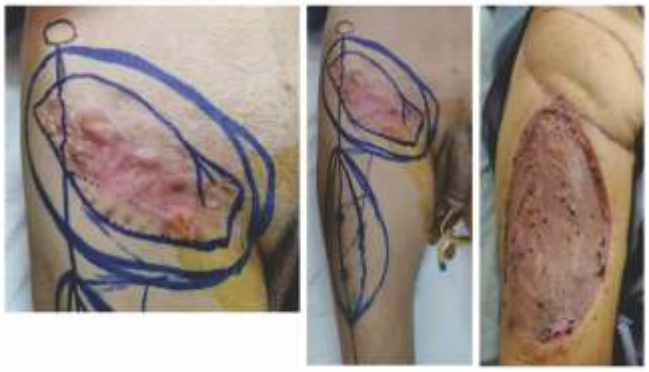

Figure 3: *O-DFSP in 45 years old Male*

a) *DFSP of Indurated nodular variety on Right groin*

b) *Marking of 3cm excision margins and pedicled Anterolateral thigh flap for a defect of 18×10cm defect*

c) *Day 20 post op showing well healed pedicle ALT flap and skin graft*

Table 1: *Main tumor clinical features.*

Patient characteristics	Ordinary DFSP patients (%)	Fibrosarcomatous DFSP patients (%)	*Total (%)*	*P value*
Patient Number	53 (84.1)	10 (15.9)	63 (100)	
Age				
14-50 years (n=52)	43 (81.1)	9 (90)	52 (82.5)	0.5
⩾50 years (n=11)	10 (18.9)	1 (10)	11 (17.4)	
Gender				
Male (n=44)	36 (67.9)	8 (80)	44 (69.8)	0.44
Female (n=19)	17 (32.1)	2 (20)	17 (30.2)	
Anatomical location				
Head and neck (n=2)	1 (1.9)	1 (10)	2 (3.2)	0.46
Trunk (n=26)	21 (39.6)	5 (50)	26 (41.3)	
Upper limb (n=15)	13 (24.5)	2 (20)	15 (23.8)	
Lower limb (n=20)	18 (34)	2 (20)	20 (31.7)	
Clinical data				
Duration of tumor (Months)				
⩽48	40 (75.5)	9 (90)	49 (77.8)	0.31
>48	13 (24.5)	1 (10)	14 (22.2)	
Tumor size				
⩽10 cm	45 (84.9)	3 (30)	48 (76.2)	0.0001
>10 cm	8 (15.1)	7 (70)	15 (23.8)	
Tumor Appearance				
Nodular	26 (49.1)	3 (30)	29 (46.03)	0.03
Cystic Nodule	7 (13.2)	1 (10)	8 (12.7)	
Indurated nodule	3 (5.7)	2 (20)	5 (7.9)	
Diffuse swelling	5 (9.4)	2 (20)	7 (11.1)	
Swelling with atrophoderma	8 (15.1)	1 (10)	9 (14.3)	
Fungating growth	4 (7.5)	1 (10)	5 (7.9)	
Tumor with mobility	33 (62.3)	5 (50)	38 (60.3)	---
Tumor with Ulceratin	18 (34)	7 (70)	25 (39.7)	---
Recurrent tumor	28 (52.8)	4 (40)	32 (50.8)	---
Enlarged regional lymph nodes				
Yes	13 (24.5)	3 (30)	16 (25.4)	
No	40 (75.5)	7 (70)	47 (74.6)	0.71
Adjuvant Radiotherapy	25 (47.2)	10 (100)	35 (55.6)	

Mean (S.D) duration of tumors was 32.95 (24.85). Nodular variety was most common in both groups with 26 (49.1%) of O-DFSP group and 3 (30%) of FS-DFSP group. Their comparison was found to be statistically significant (p=0.03).

Total number of tumors with ulceration and discharge was 39.7% (25). This included 18 out of 53 (34%) patients of O-DFSP group and 7 out of 10 (70%) for FS-DFSP group showing that there are more chances of developing fibrosarcomatous changes in patients having DFSP with ulceration and discharge. Most of the O-DFSP group tumors were mobile i.e, 33 (62.3%) compared to 5 (50%) of FS-DFSP group. Also more of the O-DFSP group tumors were recurrent 28 (52.8%) compared to 4 (40%) of FS-DFSP group tumors.

Trunk was most common site 41.3% (26) and enlarged regional lymph nodes were found in 25.4% (16) of patients. Adjuvant radiotherapy was done in 10 (100%) patients of FS-DFSP group and 47.2% (25) of O-DFSP group patients.(Table 1)

FS-DFSP group patients were more prone to develop complications post-operatively like hypertrophic scar 70% (7), wound healing issues 60% (6), distant metastasis 40% (4) and local tumor recurrence 20% (2) and their comparison with that of O-DFSP group was not statistically significant (p=0.1).

Most of the patients of both groups are alive without disease i.e, 60% (6) of FS-DFSP group and 54.7% (29) of O-DFSP group followed by 19.04% (12) who are alive with disease, 15.9% (10) who lost follow up and 9.52% (6) who died during course of treatment. Outcome comparison was also found to be statistically significant (p=0.05). (Table 2)

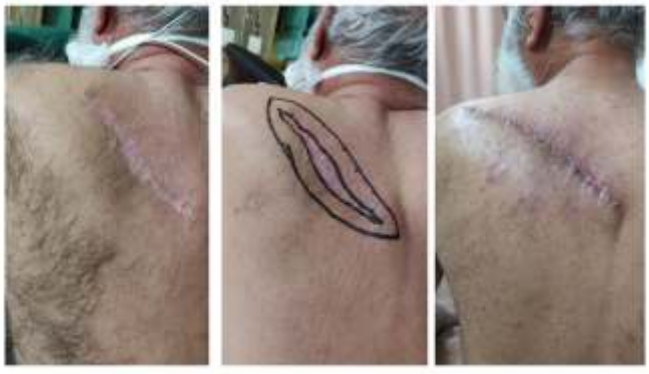

Figure 4: *FS-DFSP in 68 years old Male*

a) *Residual FS-DFSPon Left Scapular region*

b) *Marking of 2cm excision margins followed by direct closure*

c) *Day 22 post op showing well healed scar*

Table 3: *Complications and outcome after surgical treatment.*

Complications				
Wound healing issues	10 (18.9)	6 (60)	16 (25.4)	0.1
Wide & Hypertrophic scar	32 (60.4)	7 (70)	39 (61.9)	
Local recurrence	7 (13.2)	2 (20)	9 (14.3)	
Distant metastasis	6 (11.3)	4 (40)	10 (15.9)	
Outcome				
Alive without disease	29 (54.7)	6 (60)	35 (55.6)	
Alive with disease	11 (20.8)	1 (10)	12 (19.04)	0.05
Death	4 (7.5)	2 (20)	6 (9.52)	
Lost follow up	9 (17)	1 (10)	10 (15.9)	

Discussion

The term of dermatofibrosarcoma protuberance (DFSP) was coined by Hoffmann in 1925.[8] It behaves like benign tumor to start with but in 2-5 % of cases, it can metastasize. A typical feature is its invasion in surrounding tissue by irregular subcutaneous projections which makes it impossible to determine its real boundary on clinical examination. Histologically composed of monomorphic spindle cells with low mitotic index, it tends to infiltrate subcutaneous tissue in honey comb pattern. The diagnosis of DFSP is confirmed by incisional biopsy and it is excised with wide margins (at least 3 cm) to get tumor clearance.

DFSP is a rare entity and even rare is its variety with fibrosarcomatous changes. Many studies show incidence of FS-DFSP to be 5-20%.9 In our study, we found incidence of FS-DFSP to be 15.9%. Du K et al.[10] found that DFSP has a male predominance in their 3rd and 4th decade. Same was observed in our study with both varieties of DFSP being common in males (69.8%),in their 3rd and 4th decade (50.8%).

Patients with DFSP tend to seek treatment late as these tumors are usually painless in start and mimic benign skin lesions.[11] Same was the observation in this study where most of the patients presented after > 2 years of first appearance of tumor. As DFSP is a slow growing tumor, mostly patients of this study had size <10 cm in both groups and about 70% of FS-DFSP had associated ulceration with discharge. Li Y and colleagues 12 found nodular variety as most common type of DFSP. We also observed nodular variety to be most common in both groups with (46.03 %) followed by swelling with atrophoderma (14.3%), Cystic nodule (12.7%), Diffuse swelling (11.1%), Indurated nodule (7.9%) and Fungating growth (7.9%).

Most common anatomical site in our patients of both groups, was found to be Trunk (41.3%) followed by lower limb (31.7%), upper limb (23.8%) and head and neck (3.2%) and it was similar to various studies.[13,14]

As the tumor shows radial growth pattern in subcutaneous plane and due to its asymptomatic features, mostly physician treat them as benign lesion taking close margins and that's why many patients with DFSP show high rate of local recurrence.[15] In this study, 52.8% of the O-DFSP and 40% of FS-DFSP were recurrent tumor with most of them having first recurrence (46.03%) combined.

The overall risk of metastasis to regional lymph nodes or distant organs is reported to be <5%.[16] In this study, one fourth of the cases i.e, 25.4% were observed to have enlarged regional lymph nodes with more cases (30%) in FS-DFSP group as compared to O-DFSP (24.5%). It was in contrast to other studies and was most likely due to delayed presentation.[17,18,19]

None of our patients received treatment with Imatinib Mesylate, a tyrosine kinase inhibitor which works against activated PDGFB and is indicated for recurrent, unresectable or metastatic disease, due to its unavailability at our center. All our patients underwent wide local excision with recommended 2-3cm margins with frozen section.[20] Adjuvant radiotherapy was given to all of FS-DFSP patients and 47.2% of O-DFSP patients.

Almost all the patients with FS-DFSP developed postoperative complications. Wide and hypertrophic scar being most common in both FS-DFSP (70%) and O-DFSP (60.4%). Wound healing issues (wound dehiscence, infection, graft or flap loss) were also common in FS-DFSP (60%) and 18.9% in O-DFSP patients and were managed conservatively. It was comparable to results of various studies.[16] Saiga P et al.[21] found that FS-DFSP has more propensity for developing distant metastasis which is similar to as observed in this study (40% of FS-DFSP and 11.3% of O-DFSP cases). Local recurrence occurred in 20% of FS-DFSP and 13.2% of O-DFSP of our cases with mean time to local recurrence 24 months.

There are certain studies showing guidelines regarding the follow up of DFSP patient suggesting 6 monthly follow up for first 5 years and then annual examination till ten years.[22] In our study, follow up was done for duration of 9.6-78 months (0.8-6.5 years). A total of 55.6% of patients are alive without disease with 60% patients of FS-DFSP group followed by 19.04% still having disease (20.8% of O-DFSP group). The total patients who lost follow up were 15.9% combined and 9.52 % patients died during course of treatment.

Our study has certain strengths and limitations. Main strength of this study is detailed analysis of demographical, clinical characteristics, surgical and follow up data of DFSP with respect to ordinary and fibrosarcomatous changes in patients presenting to our center. The main limitation of our study is that it is a retrospective cohort from a single center leading to more chances of selection bias. Patient number was also small and results were based on relatively short follow up period (6.5 years instead of 10 years) and therefore our study results cannot be generalized.

Conclusion

This is a single center study assessing the clinical features, surgical treatment along with its complications and outcome at 5 year follow up in both varieties of DFSP. The data presented here demonstrate that the clinical characteristics of O- DFSP are non-specific and variable mimicking benign lesions. While FS-DFSP variety is associated with short duration, ulcerated lesion with discharge, enlarged regional lymph nodes, and local recurrence commonly. Any lesion with these clinical features should raise suspicion of aggressive disease. Due to its high local recurrence rate, follow-up for a longer period i.e, at least 10 years, is recommended.

Conflict of Interest *None*

Funding Source *None*

References

1. Hayakawa K , Matsumoto S, Ae K, et al. Risk factors for distant metastasis of dermatofibrosarcoma protuberans. J Orthop Traumatol. 2016 Sep; 17(3): 261–266.
2. Li Y, Liang J, Xu X, Jiang X, Wang C, Chen S, et al. Clinicopathological features of fibrosarcomatous Dermatofibrosarcoma Protuberans and the construction of a back-propagation neural network recognition model. Orphanet J Rare Dis 2021; 16(48): 1-9.
3. Chiang K.T, Lee S.Y, Chu H. Dermatofibrosarcoma protuberans, a rare but locally aggressive tumor on finger: clinical and aeromedical considerations. Case Reports Plast Surg Hand Surg. 2015; 2(1): 15–18.
4. Rasheed AA, Barwad A, Dhamija E, Garg R, Pandey R, Shamim SA, et al, Advanced dermatofibrosarcoma protuberans: an updated analysis of cases from an Indian sarcoma clinic. Future Science OA 2021; 7(9):1-11.
5. Li Y , Wang C, Xiang B, et al. Clinical Features, Pathological Findings and Treatment of Recurrent Dermatofibrosarcoma Protuberans. J Cancer. 2017; 8(7): 1319–1323.
6. Huis In 't Veld EA, van Coevorden F, Grunhagen DJ, Smith MJ, van Akkooi ACJ, Wouters M, et al. Outcome

after surgical treatment of dermatofibrosarcoma protuberans: is clinical follow-up always indicated? Cancer. 2019;125(5):735–41.

7. Hao X, Billings S.D, Wu F, et al. Dermatofibrosarcoma Protuberance: Update on the Diagnosis and Treatment. J Clin Med. 2020 Jun; 9(6): 1752.
8. Ahmad I, Mir MA, Bariar LM, Afroz N. Recurrent Dermatofibrosarcoma Protuberance and its Management with Radical Excision and Interval Skin Grafting: A case Report. World J Plast Surg 2016;5(1):67-71.
9. Stacchiotti S, Astolfi A, Gronchi A, et al. Evolution of Dermatofibrosarcoma Protuberans to DFSP-Derived Fibrosarcoma: An Event Marked by Epithelial-Mesenchymal Transition–like Process and 22q Loss. Mol Cancer Res 2016;14:820-829.
10. Du K, Li J, Tang L, Lin X, Kong X, Liao X, et al. Role of postoperative radiotherapy in dermatofibrosarcoma protuberans: a propensity score-matched analysis. Radiat Oncol. 2019;14(20):1-8.
11. Effiom OA, Olojede ACO, Akinde OR, Olawuyi AB, Amoo AT, Arotiba GT. Dermatofibrosarcoma Protuberans: clinicopathologic presentation in Nigerians. Pan Afr Med J. 2018; 31(25): 1-7.
12. Li Y, Wang C, Xiang B, Chen S, Li L, Ji Y. Clinical Features, Pathological Findings and Treatment of Recurrent Dermatofibrosarcoma Protuberans. J Cancer. 2017 May 12;8(7):1319-1323.
13. Larbcharoensub N, Kayankarnnavee J, Sanpaphant S, et al. Clinicopathological features of dermatofibrosarcoma protuberans. Oncol Lett. 2016 Jan;11(1):661-667.
14. Kashyap L, Noronha V, Patil V, et al. Dermatofibrosarcoma protuberans of head and neck: Clinical outcome of nine cases treated with imatinib. Cancer Res Stat Treat 2019;2(1):112-8.
15. Yadav S, Verma N, Khurana N, Neogi S. Recurrent DermatofibrosarcomaProtuberanswith Pigmentation and Myoid Differentiation. Sultan Qaboos Univ Med J. 2018 May;18(2):e228-e230.
16. Kim BJ, Kim H, Jin US, et al. Wide Local Excision for Dermatofibrosarcoma Protuberans: A Single-Center Series of 90 Patients. Biomed Res Int. 2015; 2015: 642549.
17. Ramirez-Fort MK, Meier-Schiesser B, Niaz MJ, et al. Dermatofibrosarcoma Protuberans: The Current State of Multidisciplinary Management. Skinmed. 2020; 18(5):288-293.
18. Rutkowski P, Debiec-RychterM. Current treatment options for dermatofibrosarcoma protuberans. Expert Rev Anticancer Ther 2015;15(1):901–9.
19. Liang CA, Jambusaria-Pahlajani A, Karia PS, et al. A systematic review of outcome data for dermatofibrosarcoma protuberans with and without fibrosarcomatous change. J Am Acad Dermatol 2014;71(1):781-6.
20. Nardelli AR, Marcarini R, De Franco MFB, et al. Dermatofibrosarcoma protuberans rapid growth after incisional biopsy. Med Cutan Iber Lat Am. 2017;45(1): 41-44.
21. Saiga P, Grob JJ, Lebbe C, et al. Diagnosis and treatment of dermatofibrosarcoma protuberans. European consensus-based interdisciplinary guideline. Eur J Cancer 2015 Nov; 51 (17): 2604-8.
22. Brooks J. Dermatofibrosarcoma protuberans. [Updated 2022January, Cited 2022 March] Available from: [https://www.ncbi.nlm.nih.gov/books/NBK513305]