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Recurrent Dermatofibrosarcoma Protruberance over Shoulder: An Unresolved Problem

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Authors' contributions

This work was carried out in collaboration between both authors. Author SSK designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author TK managed the analyses of the study and managed the literature searches. Both authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Introduction: We are reporting a case of recurrent Dermatofibrosarcoma protuberans (DFSP) over right shoulder in a 36 year young lady who underwent re-excision with secondary healing. DFSP is common in both, men and women with a slight male predominance. They are characterized by a unique translocation of chromosome i.e. t(17;22) (q22;q13). Majority of DFSPs are low grade (85-90 %) while the rest contain a high-grade sarcomatous component (DFSP-FS) and are considered to be intermediate-grade sarcomas. Trunk and proximal extremities are the most common location, usually on the chest and shoulders. Persistently recurring tumors have an increased risk for transformation into a more malignant form (DFSP-FS). Metastases to regional lymph nodes are extremely rare and distant hematogenous metastases are even rarer. Adequate lateral and deeper margin resection is necessary for excision of resectable primary DFSP and team approach is must for tackling recurrent and metastatic DFSP.

Keywords: Recurrent DFSP; metastatic; secondary healing; tumors; hematogenous metastases; surgical excision.

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1. INTRODUCTION

The overall incidence of Dermatofibrosarcoma protuberans (DFSP) in the United States is 0.8 to 4.5 cases per million persons per year and it is considered as a relatively rare tumor [1]. In the United States, DFSP accounts for 1 to 6% of all soft tissue sarcomas [2] and 18% of all cutaneous soft tissue sarcomas [3]. In a case series of Surveillance, Epidemiology and End Results (SEER) tumor registry from 1992 through 2004 elucidated DFSP was second only to Kaposi sarcoma with accountability of 71 % of cases [3]. The less common variant of DFSP is the Bednar or pigmented variant which accounts for less than 5 % of all DFSP cases with more common presentation in black persons [4,5]. This variant is differentiated by the dispersal of melanin-containing cells in an otherwise typical DFSP. The fibrosarcomatous variant of DFSP (DFSP-FS) accounts for approximately 5 to 15 % of DFSP cases [6]. It is found in all age groups but most often arises in adults in their thirties [7] with rare congenital presentation [8,9]. DFSP is found in similar frequencies in men and women however, some large series suggest a slight male predominance [10,11] with more common occurrence in blacks than in whites [1]. DFSPs are characterized by a unique translocation of chromosome i.e. t(17;22) (q22;q13) [12-16]. Majority of DFSPs are low grade which accounts for 85-90 % while the rest contain a high-grade sarcomatous component (DFSP-FS) and are considered to be intermediate-grade sarcomas [11]. They are located most commonly on the trunk and proximal extremities, usual on the chest and shoulders [10,17]. A large case series from the Surveillance, Epidemiology, and End Results (SEER) database between 2000 and 2010 reported their site distribution as follows [1]:

- Head and neck – 13%
- Upper extremity – 21%
- Lower extremity – 21%
- Trunk – 42 %
- Genitals – 1 %

Metastases to regional lymph nodes are extremely rare [18] and distant hematogenous metastases are even rarer. Persistently recurring tumors have an increased risk for transformation into a more malignant form (DFSP-FS). Metastases to brain, bone, and other soft tissues are reported however, the lungs are the most frequent site [19]. We are reporting a case of recurrent DFSP over shoulder in a 36 year young lady who underwent re-excision with secondary healing.

2. CASE REPORT

A 36 year old young lady with Eastern Cooperative Oncology Group Performance Status –I (ECOG PS I) with no comorbidity and staying at remote village presented to our clinic with proliferative growth over right shoulder for the last 4 months. She had no significant past, medical and family history. She had noticed nodular growth over right shoulder of size approximately 2x1cm one year back. She consulted a surgeon and underwent nodule excision. Details of this surgery, post excision histopathology were missing. Again there was a recurrent proliferative lesion over the same site after 4 months of previous excision. She consulted a general surgeon who advised her to undergo re-excision. It was excised 6 months back and histopathology report was suggestive of complete excision of Dermatofibrosarcoma Protruberance however, excised margins were less than 0.5cm away from the tumor. It was closed with primary suturing. After three months , an ulcero-proliferative growth re-appeared at scar site with gradual increase in the size within a period of 5 months. She underwent biopsy from the growth at nearby local hospital which was in favour of recurrent DFSP lesion. With the biopsy report, she consulted at our clinic. On examination, an ulcero-proliferative growth was present over right shoulder (Fig. 1) measuring 5x 4cm in size which was movable with circumferential skin oedema. Right axillary lymph nodes were not palpable. We advised her to do MRI of right shoulder and CT thorax. CT thorax was normal and MRI was suggestive of 5 x 4.1x 1.5 cm lobulated, plaque – like hyperintense lesion over antero-superior aspect of right shoulder involving skin and subcutaneous plane with surrounding mild soft tissue edema (Figs. 2, 3). Bone was uninvolved with no intra-articular extension and underlying muscles appeared normal. Case was discussed in our institutional multidisciplinary tumor board and decision was planned to re-wide excision of the lesion with adequate margins as it was resectable lesion. She underwent re-wide excision of the lesion with macroscopic margins of 3cm away from the tumor as the lesion had recurred twice (Fig. 4). Final histopathology report was suggestive of an uncircumscribed spindle cell lesion with infiltrative margins in the dermis and subcutaneous tissue with pattern less arrangements where whirling and honeycomb

pattern identified at some places with absence of mitosis, nuclear anaplasia and necrosis with no evidence of definitive fibrosarcomatous transformation (Figs. 5, 6, 7, 8). All margins with base were free from tumor with clear margins measuring 2.8 cm away from the tumor. As the lesion was sitting over acromian process of clavicle we shaved off the tissue close to bone. Bone was exposed, hence we closed the wound with primary suturing. She was discharged on 1st postoperative day. On 8TH postoperative day, wound dehiscence occurred. It was managed conservatively with dressing and after a month, wound healed completely with secondary intension. Case was rediscussed in our institutional multidisciplinary tumor board for adjuvant treatment planning in view of recurrent tendency of the lesion. As there were no supporting literature for adjuvant treatment of recurrent DFSP lesion with adequately excised margins, she had been advised close follow up with no adjuvant treatment. She is on periodic follow up with us according to our institutional follow up protocol and after one year of completion of surgery, there is no recurrence.

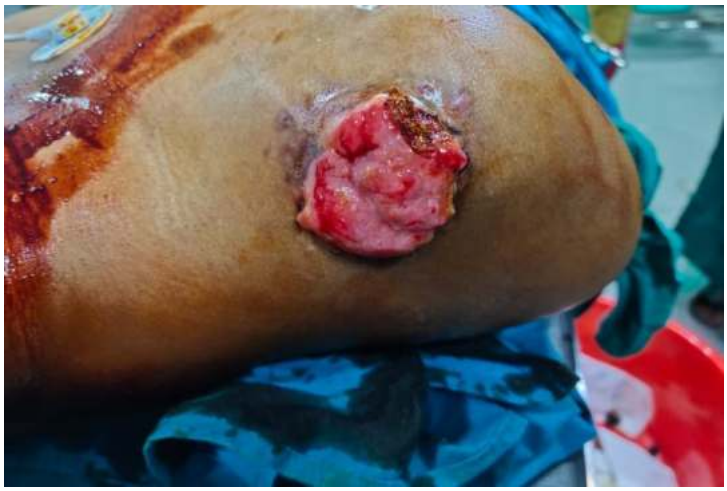

Fig. 1. Proliferative DFSP over right shoulder

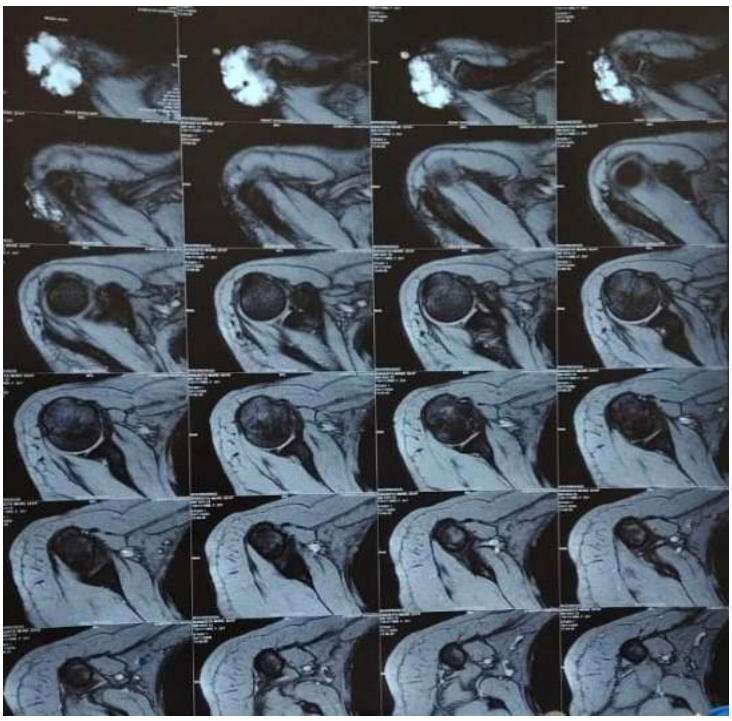

Fig. 2. MRI - Axial view of right shoulder

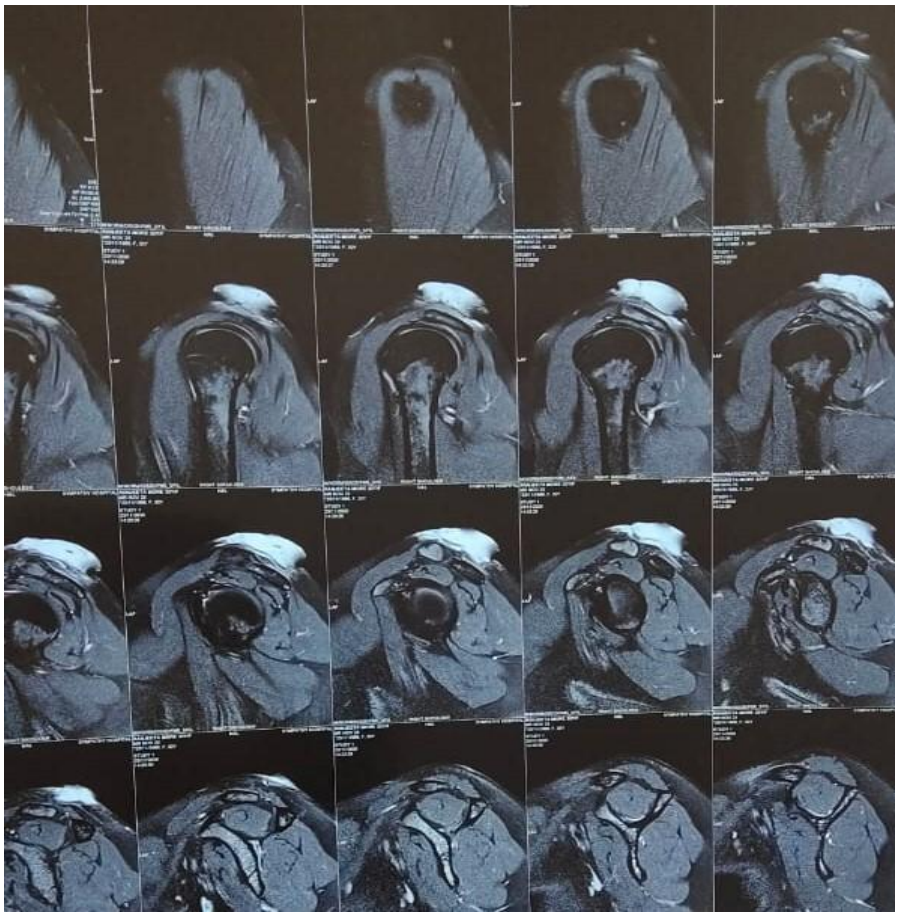

Fig. 3. MRI – Coronal view of right shoulder

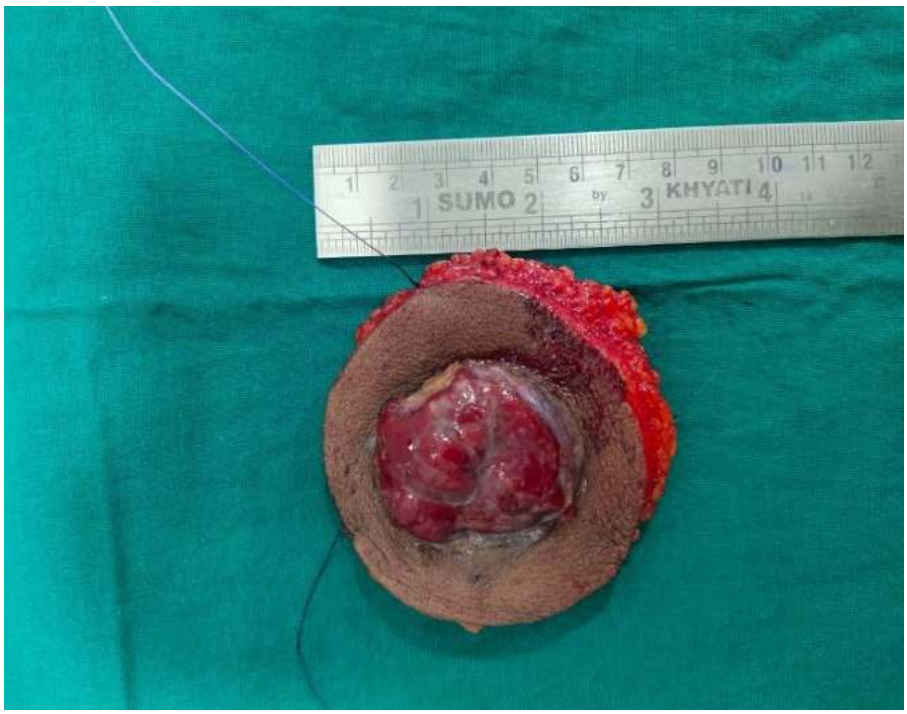

Fig. 4. Excised specimen of right shoulder DFSP

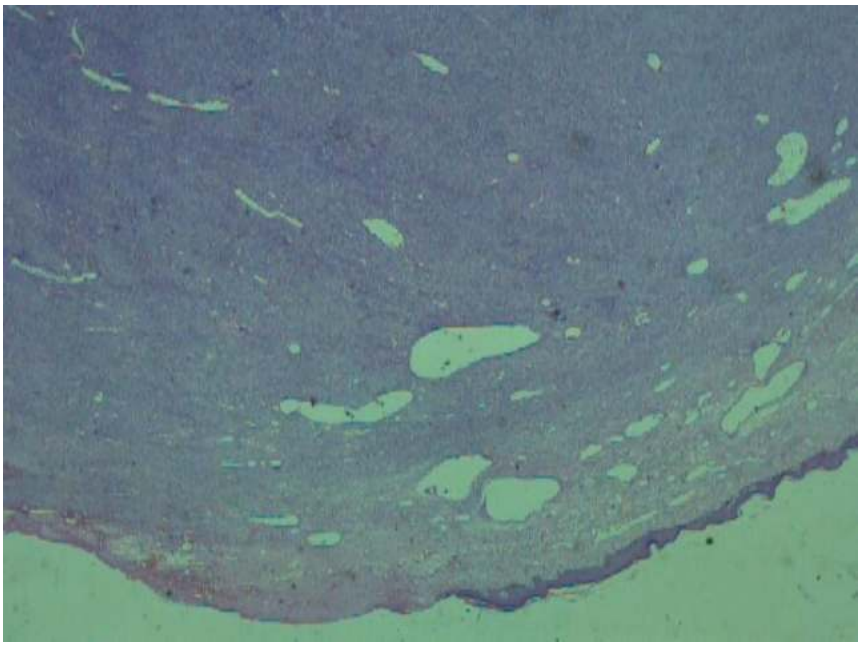

Fig. 5. DFSP (Low magnification)

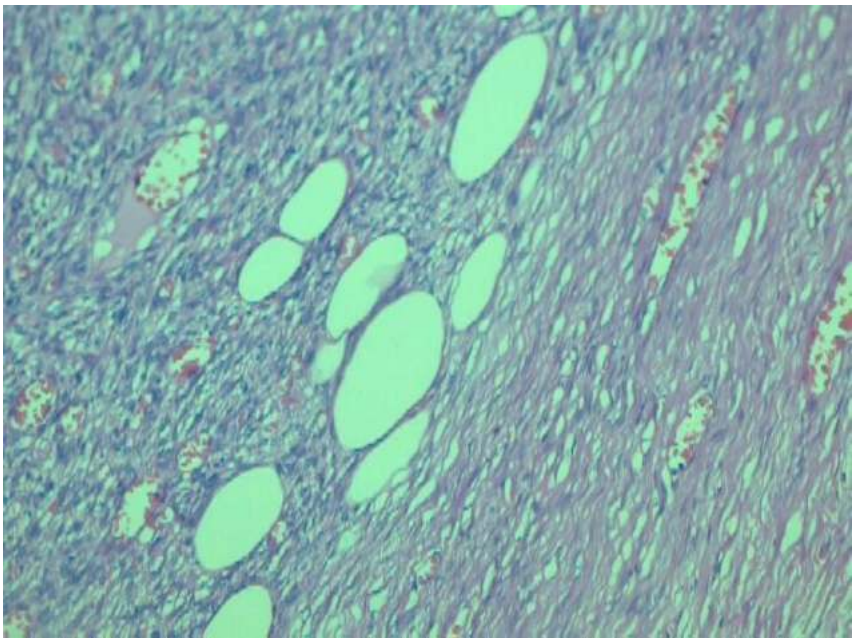

Fig. 6. DFSP (Circumscribed dermal tumor)

3. DISCUSSION

The unique translocation, t(17;22) (q22;q13) in DFSP results in the formation of supernumerary ring chromosomes. These ring chromosomes contain a unique fusion gene in which the gene for platelet-derived growth factor beta polypeptide (*PDGFB* gene) is fused with the highly expressed collagen type1A1 (*COL1A1*) gene [20]. Usually PDGFB gene is inhibited under the activity of *COL1A1* promoter. However, PDGFB/COL1A1 fusion protein produces continuous autocrine activation of the platelet-derived growth factor receptor b (PDGFR b), a tyrosine kinase [21]. It is considered to be the fundamental process in the development of DFSP [22]. The definitive diagnosis of DFSP is possible with core needle biopsy or incision biopsy. Fine Needle Aspiration Cytology (FNAC) does not provide enough tissue to contribute an

accurate diagnosis [23], however, it may be useful to establish the diagnosis of recurrent disease [24]. DFSP usually stains positively for CD34, hyaluronate, vimentin, and negatively for factor XIIIa (Table 1) [25,26]. CD34 is one of the most useful stains to differentiate DFSP from dermatofibroma and other soft tissue tumors. Imaging studies are not routinely required in each case of DFSP, but can be helpful in large, recurrent tumors or suspicion of bone invasion to define the extent of disease. Magnetic resonance imaging (MRI) is useful to define the deep extent of the tumor, particularly with large or recurrent lesions.

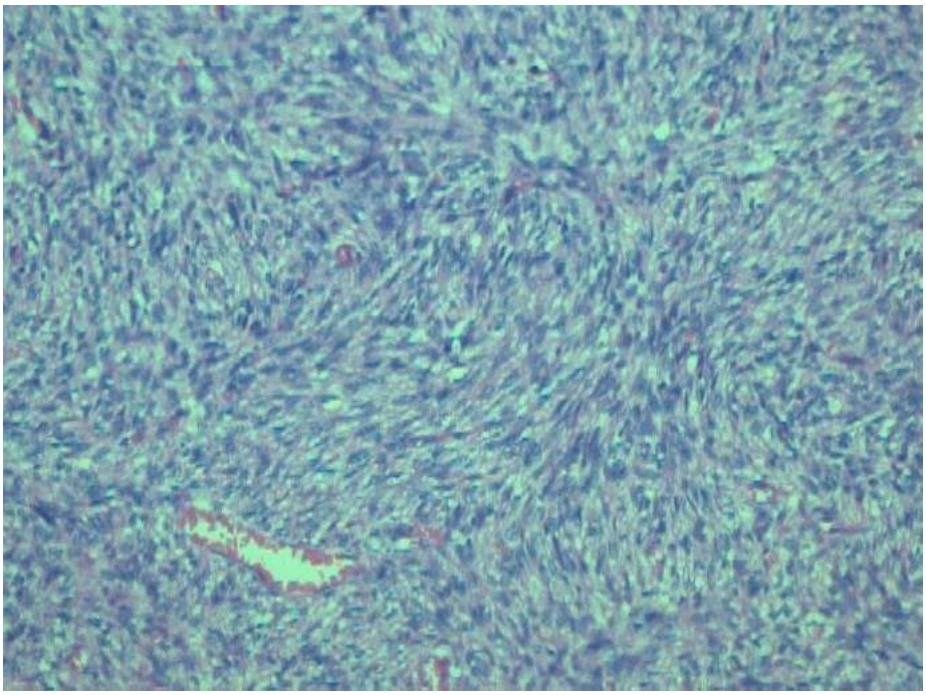

Fig. 7. DFSP (Whorling pattern)

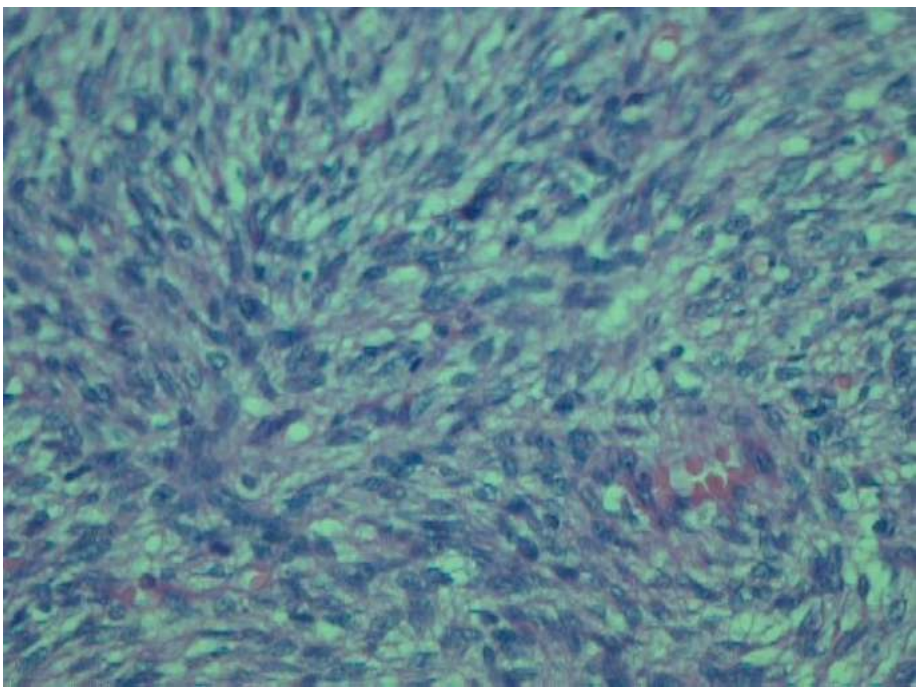

Fig. 8. DFSP (Spindle cells)

Table 1.

	CD34	XIIa	S-100	SMA	Desmin	Vimentin	CD44	Hyaluronate
DFSP	+	-	-	-	-	+	+/-	+
Dermatofibroma	-	+	-	+	-	+	+	+/-
Nodular fasciitis	-	-	-	+	-	-		
Nerve sheath tumors	+/-	-	+	-	-	-		
Fibrosarcoma	-	-	-	+	-	+		
Malignant fibrous histiocytoma	+/-	-	-	-	+/-	+		

SMA- Smooth Muscle Actin

DFSPs are strongly positive for hyaluronate while CD44 staining is diminished or absent

The ideal preferred initial treatment for a localized DFSP is surgical resection with pathologically negative margins. There is no role for prophylactic regional node dissection as metastases to lymph nodes are extremely rare [18]. Simple surgical excision carries a risk of around 50 % chances of local recurrence and it may be higher with pathologically positive margins [27]. The most important prognostic factor in patients with DFSP is the status of the surgical margin and it had been studied by some major case series [28]. Locally recurrent tumors have a tendency for deep invasion into fascia , muscle or bone and also predisposes to distant metastases [29]. There is no clear cut definition of minimum resection margin to achieve local control. In one series of 66 French patients with DFSP who underwent resection between 1982 to 2002, local recurrences were significantly higher among those with a resection margin of <3 cm, as compared with margins of 3 to 5cm (47 Vs 7%) [30]. These data form the basis of the recommendation that resection margins should be at least 3 cm and as wide as 5 cm, depending on the primary tumor size [31,32]. Consensus-based guidelines from the National Comprehensive Cancer Network (NCCN) [12] and a European interdisciplinary group [13] recommend margins of 2 to 4 cm, to the investing fascia of muscle or pericranium with clear pathologic margins. However, it is a difficult task to achieve such clear margin at anatomically challenging areas of head and neck region and at these sites, reconstruction with skin flap or graft is frequently required.

The preferred surgical techniques for surgical resection of DMSP are Wide Local Excision (WLE) and Moh's Micrographic Surgery (MMS). The available data from nonrandomized comparative and non-comparative single-center studies suggest that local recurrence rates are lower after MMS than after WLE [14,15,16,33]. MMS is the preferred choice of surgery at cosmetically sensitive areas, where achieving narrow margins is preferable. In other less cosmetically sensitive areas, WLE with 2 to 4 cm margins and histologic margin confirmation is still an acceptable procedure. In case of DFSP-FS, WLE is the preferred choice of surgery.

There are no randomized trials addressing the benefit of Radiation Therapy (RT) after resection. Several retrospective case series and cohort studies have been reported where adjuvant RT has been administered post local excision [34-36]. However, in these studies, there was no statistically significant difference in the pooled estimates of local recurrence between surgery alone arm and surgery combined with RT arm. Presence of sarcomatous component within the tumor (DFSP-FS) is not considered as an indication for adjuvant RT . Even NCCN guidelines [12] do not suggest RT for tumors with a sarcomatous component unless the tumor is large or the margins are close or positive. A tyrosine kinase inhibitor, imatinib (Gleevec), inhibits the PDGF receptor as well as other receptor tyrosine kinases such as c-kit and has revolutionized the treatment of chronic myeloid leukemia, gastrointestinal stromal tumors (GIST) and DFSP. Several reports suggest that patients with advanced DFSP may benefit from imatinib with sustained complete clinical remission [37-39]. Imatinib is approved in the United States and Europe for use in adult patients with unresectable, recurrent, and/or metastatic DFSP. Use of imatinib in the neoadjuvant setting for large unresectable, recurrent or metastatic tumors has been described by two prospective trials with their early results [37,40]. The optimal duration of neoadjuvant therapy and the appropriate imatinib dose remain unanswered questions. Further studies are also needed to determine the value of imatinib in cases of positive margins after surgical excision. Limited

data available about the use of other tyrosine kinase inhibitors (sunitinib, sorafenib) and conventional chemotherapy which is used in other soft tissue sarcoma.

4. CONCLUSION

The goal of surgical excision of DFSP is to achieve wide and adequate lateral and deeper margins to avoid local recurrence. In case of recurrent and metastatic DFSP a multidisciplinary team approach is essential. A standard follow up protocol should be planned and it is necessary to detect recurrent lesion earlier.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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