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ORIGINAL ARTICLE – SARCOMA

Conservative Re-excision is a Safe and Simple Alternative to Radical Resection in Revision Surgery for Dermatofibrosarcoma Protuberans

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ABSTRACT

Background. Dermatofibrosarcoma protuberans (DFSP) is a dermal sarcoma often diagnosed by excision biopsy, and is often incompletely excised, with high recurrence rates. Traditional wide excision involves resection margins of 2–4 cm, often resulting in morbid procedures requiring surgical reconstruction. An alternative is conservative re-excision (CRE), which results in narrower margins and less-frequent reconstruction. The aim of this study is to assess the effectiveness of CRE in providing local control.

Patients and Methods. A retrospective review of patients treated for DFSP at a tertiary sarcoma centre over a 10-year period.

Results. Ninety-eight patients were analysed. Median follow-up was 53 months. Fifty-four patients had microscopically incompletely excised DFSP, and of these, 41 underwent CRE of DFSP scar. Seven (17.1%) patients required more than one CRE to achieve negative margins. The mean width of CRE was 15.4 mm. Fifty-four patients had resection of intact tumours, with 19 (35.2%) requiring surgical reconstruction. One patient (1%) developed local recurrence, and one patient (1%) distant recurrence—both of these patients had high-grade fibrosarcomatous DFSP. No patient with classical DFSP who had clear margins sustained recurrence, regardless of whether their surgery was CRE of scar or wide excision of tumour.

Conclusions. CRE is a safe and acceptable alternative to traditional wide excision, with no patients developing local recurrence (LR). CRE results in low rates of surgical reconstruction, and hence lower morbidity; this is partially offset by the higher rates of inadequate excision requiring further surgery. However, the lesser rate of inadequate excision compared with rates of reconstruction makes CRE an attractive option.

Dermatofibrosarcoma protuberans (DFSP) is a soft tissue sarcoma originating in the dermis that invades into the subcutaneous tissues. Classical DFSP, accounting for 90% of all DFSP, is considered a low-grade malignant neoplasm that has a propensity towards LR following resection but almost no metastatic potential.[1,2] The remaining 10% undergoes transformation into a high-grade fibrosarcomatous variant (FS-DFSP), which carries a higher metastatic risk (5–15%) and behaves more similarly to other high-grade sarcomas.[1,3,4]

Histologically, DFSP is characterised by circumferential spread along fibrous septae into the underlying fat,[5] and it is suggested that this microscopic appearance underpins the high rate of LR observed with narrow excisions, failing to remove all of these projections, with rates up to 40%.[1] However, whilst many guidelines and authors therefore recommend "wide" surgical excision margins, there is no accepted optimal width. The British Sarcoma Group guidelines recommend wide excision without specifying a margin, while the National Comprehensive Cancer Network (NCCN) guidelines state 2–4 cm.[6,7]

DFSP is often diagnosed unexpectedly after excision of a presumed benign abnormality. Patients are referred with a post-excision scar, with DFSP incompletely excised microscopically. These patients represent a management conundrum, with an absence of compelling evidence to guide further resection margins to gain local control. Wide

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excision of these scars with a margin of 2–4 cm frequently requires reconstructive surgery, with higher morbidity and longer hospitalisation. An alternative option is to perform a conservative re-excision (CRE), which involves an elliptical excision of the scar and tumour bed, including resection of the deep fascia. The excision is taken with at least 1 cm margin, but as wide as possible while still allowing primary closure.

The aim of this study is to review a large series of DFSP treated at a tertiary sarcoma centre, assessing for risk factors for recurrence. Primarily, we aim to assess the effectiveness of CRE in providing local control, as an alternative to traditional wide excision.

PATIENTS AND METHODS

The present study is a retrospective review of all patients treated for DFSP at a tertiary-referral sarcoma centre (Royal Marsden Hospital, London, UK) between 2006 and 2016. This study was approved by the institutional research committee. Medical records, operative reports and histological reports were reviewed for clinicopathological data. Patients with both classical DFSP and FS-DFSP were included. Follow-up generally consisted of 6-monthly clinical examination and chest x-ray for 10 years. Due to referral patterns, some patients were discharged to local hospitals for surveillance. As a result, for a small number of patients (nine), there was limited follow-up in medical records. These patients were contacted by telephone to ascertain any further events related to DFSP.

In patients presenting with a tumour in situ, surgery consisted of wide excision of the tumour including the deep fascia as the deep margin. In patients undergoing re-excision of a scar with microscopically involved margins (for previously incompletely excised DFSP), CRE was performed as described above. Reconstructive surgery was performed at the discretion of the treating surgeon where it was felt that CRE could not be performed in a safe or cosmetically acceptable manner. In the case of involved margins on permanent pathological analysis, further CRE was performed until negative margins were achieved, where possible. Radiotherapy or systemic therapy was not routinely administered but given on a case-by-case basis.

Pathological examination involved routine formalin-fixed paraffin-embedded sections coupled with immunohistochemistry for CD34. Intra-operative frozen sections were not performed. Surgical margins were collected from operative notes or, where this was not recorded, by macroscopic margins to tumour or scar as reported on the pathology report.

RESULTS

A total of 107 patients were identified, 3 of whom presented with metastatic disease after treatment elsewhere for fibrosarcomas arising in DFSP and were excluded from the subsequent analysis. A further 6 patients who were referred for management advice after radical surgery and reconstruction at other institutions were also excluded, leaving 98 patients for analysis. The clinicopathologic characteristics of the patients are summarised in Table 1. Five (5.1%) patients had FS-DFSP, four of whom were primary presentations while the other one presented with a recurrent tumour. Median follow-up was 53 months (range 0–144 months).

Patients Treated with Tumour Bed Excision

Of the 98 patients, 44 had undergone an initial excision biopsy at the referring institution, usually for a presumed benign abnormality. All of these patients had primary DFSP; none were recurrent tumours. They presented to the sarcoma clinic with a post-excision scar only and had no clinical or radiological evidence of residual disease. Of these patients, 41 underwent CRE with primary closure, and only 3 underwent wide excision with reconstructive surgery. One of these patients had been closed with a local flap at the time of their excision biopsy and required resection of the entire flap, with a latissimus dorsi flap reconstruction; the other two had tumours on the scalp and lower limb, both sites well known for their limited skin laxity and frequent need for reconstructive surgery. The median size of the tumours excised prior to referral in this group was 30 mm (range 3–70 mm).

On average, the width of excision around the scar was 15.4 mm (therefore, total excision width of specimen was 30.8 mm), with no patients undergoing excision of less than 10 mm margin.

Seven patients who had conservative re-excision (17.1%) had inadequate pathological margins and required further surgery to attain negative margins (Table 2). The mean width of these re-excisions was 13.8 mm (range 10–20 mm). Five of these patients had negative margins achieved with a second conservative re-excision, while one patient required three conservative re-excisions. One patient had repeated positive margins with three conservative re-excisions, and finally a wide resection with latissimus dorsi reconstruction was performed with negative histological margins.

TABLE 1 Clinicopathologic characteristics

	Tumour bed excision (n = 44)	Macroscopic tumour excision (n = 54)
Tumour type, n (%)		
Primary	44 (100)	33 (61.1)
Recurrent	0 (0)	21 (38.9)
Fibrosarcomatous change, n (%)	1 (2.3)	4 (7.4)
Tumour size (mm), median (range)	30[a] (3–70)	50 (5–150)
Excision width (mm), mean (range)	15.4 (10–35)	24 (20–50)
Tumour site, n (%)		
Head and neck	5 (11.4)	10 (18.5)
Trunk	28 (63.6)	25 (46.3)
Lower limb above knee	5 (11.4)	10 (18.5)
Lower limb below knee	2 (4.5)	4 (7.4)
Upper limb above elbow	3 (6.8)	4 (7.4)
Upper limb below elbow	1 (2.3)	1 (2.3)
Reconstructive surgery, n (%)	3 (6.8)	19 (35.2)
Inadequate margins requiring re-excision, n (%)	7 (17.1)	4 (7.4)
Local recurrence, n (%)	0 (0)	1 (1.9)

[a]Size of tumour prior to excision biopsy

TABLE 2 Number of conservative re-excisions required

Number of re-excisions	Number of patients, n (%)
1	34 (82.9)
2	5 (12.2)
3	1 (2.4)
4	1 (2.4)

Patients Treated with Excision of Macroscopic Tumour

Fifty-four patients were treated for clinically apparent disease, either with a palpable tumour or a soft tissue mass visible on magnetic resonance imaging (MRI). Thirty-three were primary tumours diagnosed by core, punch or incisional biopsy, while 21 presented with locally recurrent tumours after a previously treated primary DFSP at another institution.

The median size of tumours in this group was 50 mm (range 5–150 mm). The mean excision margin around the tumour was 24 mm. Reconstructive procedures were required in 19 (35.2%) of these patients. Eight of these reconstructive procedures were performed for tumours located in the head and neck. No patient who underwent a wide excision with reconstruction had inadequate histological margins.

Four (7.4%) patients—two with primary DFSP and another two with locally recurrent DFSP—underwent resection with primary closure and gained inadequate margins, with a mean excision margin of 18.8 mm (range 15–20 mm). All of these patients were then treated with conservative re-excision with negative margins found on the subsequent excision.

Use of Radiotherapy

Two patients (2.0%) received local radiotherapy to the tumour site because further surgery was not possible. Both of these patients had tumours located in the head and neck; one was a recurrent tumour, and the other was FS-DFSP. Neither of these patients developed LR.

Outcomes

There were two patients who developed recurrent disease, both of whom had FS-DFSP. Only one of these patients recurred locally (1%), 4 years after his initial resection, with the other one developing distant recurrence.

No patient with classical DFSP developed local recurrence, regardless of whether the surgery performed was a conservative re-excision or a more radical resection. This included those patients requiring multiple re-excisions to achieve negative margins.

DISCUSSION

CRE is a safe and acceptable alternative to traditional wide excision of scars following excision of DFSP. This study has demonstrated a local recurrence rate of zero

using the CRE technique. This is an instructive finding for a relatively common scenario in sarcoma referral centres—patients referred after an excision biopsy that unexpectedly diagnoses DFSP, with only a residual scar evident clinically. Almost half the patients in this series presented in that way, and there is scant evidence to guide practice in these cases.

Previous series have described experiences with revision surgery after initial inadequate surgery. Lindner et al.[8] reported a series of 35 patients (including 17 recurrent tumours) with an LR rate of 8% at 58 months follow-up. They concluded with a recommendation for a 2.5–3-cm excision margin. Khatri et al. reported 24 cases (11 primary, 13 recurrent) of inadequately treated DFSP with LR-free survival of 100% at 54 months, with excision margins of 2.5–3.5 cm.[9] However, in both of these series, the large width of excision resulted in extremely high rates of reconstructive procedures, 48% and 50%, respectively. With the use of CRE, excision margins in this series were around half the width of the series described above (mean 1.5 cm).

CRE is not possible in all cases, however. Tumours in sites renowned for limited skin redundancy, for example the scalp and lower leg, still required soft tissue reconstruction, but overall, this approach resulted in a far lower frequency of reconstruction, only 6.8%. This leads to shorter operating time, shorter hospitalisation, and reduced donor-site and surgical-site morbidity.

The obvious compromise of narrower excision margins is a higher rate of microscopically incomplete excision. It is well established that tumour bed excisions of previously incompletely excised DFSP have a high rate of residual tumour, in one series shown to be 62%.[10] In this current series, residual disease led to microscopically involved margins in the CRE specimen in 17% of patients. Most of these patients were then adequately treated with a further CRE, but two patients required three or more re-excisions. Despite this, there was no detrimental oncologic effect, with none of these patients experiencing local recurrence regardless of the number of re-excisions required to gain negative margins. In addition, in all but one of these patients, the subsequent excisions were still performed with a CRE technique and so remained low-morbidity procedures.

Therefore, the choice of approach remains a balance: the morbidity of wide excision with its frequent requirement for reconstructive procedures versus the morbidity of CRE with its increased risk of inadequate margins and further excision. It seems that either option is satisfactory oncologically, with both affording excellent local control. However, the lesser rate of inadequate excision with CRE (17%) compared with the high rate of reconstruction with wide excision (50%) suggests that CRE is the more attractive and resource-efficient method.

This current series reinforces a developing paradigm, where classical DFSP may be adequately treated with narrower excision margins than traditionally recommended. Previous studies have suggested a very high rate of LR with margins less than 3 cm, up to 47%.[11] More recently, however, a large multi-centre series by Farma et al.[12] reported LR of only 0.9% in 206 patients using 1–2 cm margins. The current series, with no local recurrences in patients with classical DFSP using similar margins, is consistent with that and challenges traditional recommendations for wider margins. The reasons for these differences in outcome are unclear. Perhaps this is due to greater centralisation of care for rare diseases, leading to improved outcomes. Alternatively, it may be that improved histological assessment of DFSP leads to improved detection of inadequate resection, prompting further treatment. This follows past debate regarding the utility of Mohs micrographic surgery for DFSP, with some authors finding lower rates of involved margins and LR in patients undergoing Mohs.[13,14] However, a review article on the topic noted that the higher LR rate in wide excision is probably due to pathological sampling error with less extensive assessment of the entire margin, concluding that the histopathological technique is probably more important than the surgical technique.[15]

On a similar theme, intra-operative frozen sections have been suggested as a method to decrease the rate of involved margins and the requirement for further surgery.[16] However, frozen section is notoriously unreliable in DFSP assessment, as fibroblastic proliferation associated with previous surgery (from the excision biopsy) has a very similar appearance to DFSP, leading to false positives.[17] CD34 immunohistochemistry, which is not performed in frozen sections, is required to accurately differentiate between fibroblastic tissue (CD34 negative) and DFSP (CD34 positive). Therefore, the authors do not recommend the use of frozen sections for margin assessment.

Our data are consistent with contemporary series which identify the major risk factors for both local and distant recurrence in DFSP as post-operative margin and fibrosarcoma transformation status. Bowne et al. and Huis In't Veld et al. have shown that margin status and fibrosarcomatous change are independent risk factors for LR.[2,18] The only patient who had local recurrence in this series had FS-DFSP. Similarly, whilst others have identified FS-DFSP as an independent prognostic factor for DFSP metastasis,[19] the only patient in the current series who suffered metastasis also had FS-DFSP.

The very low recurrence rate for classical DFSP resected with negative margins also raises the question about the ideal surveillance protocol for these patients. It has been previously shown that only 3.7% of local recurrences are detected by routine clinical surveillance, and in the same series, all distant recurrences (in FS-DFSP patients) presented with symptoms (prompting investigation)—none were found by routine surveillance imaging.[2] Coupled with the low-risk nature of patients with these clinicopathological features, it seems reasonable to omit imaging surveillance of both the primary site and the lungs, unless there is some complicating circumstance, for example flap reconstruction, where recurrence detection may be difficult with examination alone. At our institution, in general, clinical examination alone every 6–12 months for 10 years is performed, particularly for tumours at sites that are not easily self-examinable (back, perineum). Patients able to easily self-examine the area are often discharged to primary care after post-operative review, with clear advice to return in the event of concerns for recurrence.

This study is limited by its retrospective nature and the problems inherent to that design. Also, whilst the overall median follow-up was 53 months, there were some patients who had been discharged to local services and only short-term follow-up data were available.

CONCLUSIONS

CRE is a safe and acceptable alternative to traditional wide excision, with no patients developing LR. CRE results in low rates of surgical reconstruction, and hence lower morbidity; this is partially offset by the higher rates of inadequate excision requiring further surgery. However, the lesser rate of inadequate excision compared with rates of reconstruction makes CRE an attractive option.

DFSP without fibrosarcomatous change and clear histologic margins has an extremely low rate of local or distant recurrence.

DISCLOSURES The authors have no disclosures to declare.

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