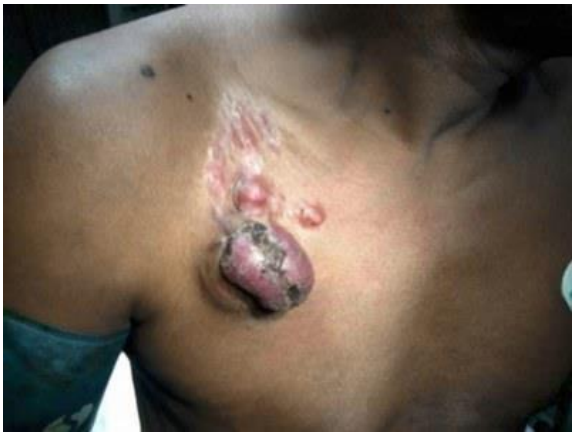
Cancer Association of South Africa (CANSA)

Fact Sheet
on
Dermatofibrosarcoma Protuberans

Introduction

A sarcoma is a cancer that arises from transformed cells of mesenchymal origin. Malignant tumours made of cancellous bone, cartilage, fat, muscle, vascular, or haematopoietic tissues are, by definition, considered sarcomas. This is in contrast to a malignant tumour originating from epithelial cells, which are termed carcinoma. Human sarcomas are quite rare. Common malignancies, such as breast, colon and lung cancer, are almost always carcinoma.



[Picture Credit: Dermatofibrosarcoma Protuberance]

Dermatofibrosarcoma Protuberance

Dermatofibrosarcoma Protuberans (DFSP) is a rare type of cancer, a soft tissue sarcoma that develops in the deep layers of skin. It is sometimes described as having tentacles that can grow into surrounding fat, muscle and even bone. DFSP is most commonly found on the torso, but can also be seen on the arms, legs, head and neck. It has a tendency to recur in the same location after it is removed. However, it only spreads to other parts of the body in about 5% of cases.

Hussain, N., Naveed, M.Z. & Haider, G. 2015.
"Dermatofibrosarcomaprotuberans is a rare, soft tissue tumour with high rate of recurrence. It is locally aggressive, with a low rate of metastasis. Dermatofibrosarcoma Protuberance is often treated with chemotherapy and radiotherapy."

DFSP most often starts as a small, firm patch of skin, approximately one to five centimetres in diameter. The skin is occasionally flat or depressed. It can be purplish, reddish or flesh-coloured. The tumour typically grows very slowly (over months to years) and can become a raised nodule.

DFSP tends to affect people between the age of 20 and 50, but it has been diagnosed in people of all ages. The tumours affect black patients about twice as much as white patients.

Rare Variants of Dermatofibrosarcoma (DFSP)
There are several variations of DFSP that can be identified under a microscope:

Bednar tumours (pigmented DFSP) - contain dark-coloured cells called melanin-containing dendritic cells. Melanin is the substance that gives skin its colour. As a result, this type of tumour may contain various colours, including red and brown. Bednar tumours account for approximately 1%-5% of all DFSP cases.

Myxoid DFSP - tumours contain an abnormal type of connective tissue that is called myxiod stroma. This type of tumour is uncommon, presents a diagnostic challenge and is important to recognise in order to prevent both under- and over-treatment.

Giant cell fibroblastoma - referred to as juvenile DFSP because it typically affects children and adolescents, is characterised by giant cells in the tumour. It appears to be histologically similar to DFSP and in rare instances can be found within the same tumour in conjunction with DFSP, resulting in a hybrid lesion.

Rarely, the tumours involved in the different types of DFSP can have regions that look familiar to fibrosarcoma, a more aggressive type of soft tissue sarcoma. In these cases, the condition is called Fibrosarcomatous (FS) DFSP. These tumours are more likely to metastasise than tumours in the other types of DFSP.

Incidence of Dermatofibrosarcoma Protuberance in South Africa
The National Cancer Registry (2017) does not provide any information regarding the incidence of Dermatofibrosarcoma Protuberance in South Africa.

Ogun, G.O., Ezenkwa, U.S. & Ayandipo, O.O. 2020.
Background: Dermatofibrosarcoma protuberance (DFSP) is the commonest, yet rare, dermal sarcoma globally. There are few reports in the literature of this neoplasm in Nigerians and indeed in sub-Saharan Africa. This study documents our institutional practice observation and compares it with those from other regions of the world.
Methods and materials: This study was a retrospective review of all cases of histologically diagnosed DFSP at the University College Hospital, Ibadan, Nigeria, spanning a period of 27 years (January 1989-December 2016). Data on patient age, gender, tumour location, size, tumour recurrence and metastasis status were obtained from clinical and surgical pathology archival files and records.
Results: Sixty-nine cases of DFSP were recorded over the period reviewed with a male-female ratio of 1.6:1. The mean age of the study population was 39.6 years. The youngest patient was 5-year old, while the oldest was 86 years and the modal age group was the 4th decade. The trunk was the commonest anatomic tumour location. Recurrences were seen in seven cases with recurrence interval ranging from 6 to 240 months. The correlation between tumour size and age was non-significant (r = -0.183; p = 0.182). There was fibrosarcoma-like transformation in three cases (4.3%) studied.
Conclusion: Dermatofibrosarcoma protuberance is rare in our population and occurs more commonly in males and on the trunk. Recurrence can occur beyond the recommended follow-up period of 10 years.

Causes and Risks for Dermatofibrosarcoma Protuberance (DFSP)
The cause is unknown, but an injury to the affected skin may be a predisposing factor. Recent advances show tumour cells carry abnormal chromosomes within the tumour cells - t(17;22)(q22;q13) - resulting in the fusion gene COL1A1-PDGFB. This encodes a protein that causes the tumour to grow.

DFSP is rare, and affects less than 1 person in every 100 000 inhabitants per year. The tumour is rare in children. Males are affected slightly more frequently than females. There would appear to be a racial predilection towards individuals who are classified as black.

Dermatofibrosarcoma protuberans (DFSP) is associated with a rearrangement (translocation) of genetic material between chromosomes 17 and 22. This translocation, written as t(17;22), fuses part of the COL1A1 gene from chromosome 17 with part of the PDGFB gene from chromosome 22. The translocation is found on one or more extra chromosomes that can be either the normal linear shape or circular. When circular, the extra chromosomes are known as supernumerary ring chromosomes. Ring chromosomes occur when a chromosome breaks in two places and the ends of the chromosome arms fuse together to form a circular structure. Other genes from chromosomes 17 and 22 can be found on the extra chromosomes, but the role these genes play in development of the condition is unclear. The translocation is acquired during a person's lifetime and the chromosomes containing the translocation are present only in the tumour cells. This type of genetic change is called a somatic mutation.

Diagnosis of Dermatofibrosarcoma Protuberance (DFSP)
Although routine imaging is not necessary, magnetic resonance imaging (MRI) may be helpful to evaluate the gross local extent of the tumour and may be important in preoperative planning for larger tumours.

In patients with prolonged or recurrent DFSP or when sarcomatous changes are evident (DFSP-FS (see below)) a CT of the chest should be obtained to evaluate for pulmonary metastases. A CT scan of the local area may be useful if bony involvement is suspected.

Diagnosis is made using either a core needle or an open incisional biopsy. While the role of fine needle aspiration is established in cases of recurrent disease, initial biopsies should be larger samples that demonstrate the histologic architecture of the tumour.

A core needle biopsy (or core biopsy) involves removal of a very small amount of tumour and is performed by inserting a hollow needle through the skin and into the organ or abnormality to be investigated. The needle is then advanced within the cell layers to remove a sample or core. This procedure takes a few minutes to perform and may be undertaken in an outpatient setting.

An incisional biopsy removes only a portion of the tumour for the pathologist to examine. An incisional biopsy is generally reserved for tumours that are larger and offers the pathologist a larger specimen with which to work. This type of biopsy has a slightly higher diagnostic success rate and is usually carried out in the operating room.

An excisional biopsy involves removal of the entire tumour and is typically reserved for very small

lesions in which an incisional biopsy or a core needle biopsy is not practical. It is usually performed in cases where removing the entire lesion along with a narrow margin of normal tissue is easily accomplished and tolerated by the patient. This is also often performed in the operating room.

Prognosis of Dermatofibrosarcoma Protuberance (DFSP)
Because DFSP rarely spreads, this cancer has a high survival rate. Treatment is important, though. Without treatment, DFSP can grow deep into the fat, muscle, and even bone. If this happens, treatment can be difficult.

Treatment of Dermatofibrosarcoma Protuberance (DSFP)
Most cases of DFSP can be adequately treated by a dermatologist, as he or she is a specialist who routinely diagnoses and treats lesions of the skin. However, in cases of very large or advanced DFSPs, or when major reconstructive surgery is indicated, a multi-disciplinary approach may be necessary. This team may involve a dermatologist, pathologist, radiologist, oncologist, radiation oncologist, orthopaedic surgeon (specialising in tumour surgery) and plastic surgeon (for reconstruction, if the tumour has invaded deep tissues and bone).

In determining what type of treatment is appropriate, a dermatologist will consider how deeply in to the skin the tumour has grown, where it is located on the person's body and the person's overall health.
Treatment options may include:

Mohs micrographic surgery involves removing one layer of skin at a time. Each layer that is removed is then placed under a microscope in order to look for cancer cells. The process continues until cancer cells are no longer found. The procedure is most often performed in a dermatologist's office with local anaesthesia. Because the treatment continues until cancer cells are no longer found, Mohs surgery reduces the risk that the DFSP will return.

Excision is a surgical procedure that may be utilized if a tumour is large in size. It involves surgically removing the DFSP and a portion of normal-looking skin. The procedure may be performed in a dermatologist's office or in some cases, an operating room.

Nakamura, T., Kawai, A., Asanuma, K., Hagi, T. & Sudo, A. 2021.
Background: Owing to its rarity, dermatofibrosarcoma protuberance (DFSP) is often inappropriately excised. After unplanned excision (UE), additional excision is commonly performed. We aimed to elucidate the effect of additional excision after UE.
Patients and methods: We examined 306 patients with primary DFSP. We analyzed surgical outcomes in 291 patients who received planned excision (PE) or additional excision after UE.
Results: Of 306 patients, 194 received PE and the remaining 112 received UE. Of 112 patients, 97 received additional excision after UE. Additional surgery due to complications was more frequent in patients with UE than in those with PE. The 5-year local recurrence-free rate in patients without additional excision after UE was significantly worse than that in those with additional excision after UE.
Conclusion: If UE is performed, we recommend additional excision for preventing local recurrence; however, the surgical wound should be carefully observed.

Keywords: Dermatofibrosarcoma protuberance; local recurrence; soft tissue sarcoma; survival; unplanned excision.

van Lee CB, Kan WC, Gran S, Mooyaart A, Mureau MAM, Williams HC, Matin R, van den Bos R, Hollestein LM. 2019.
"Dermatofibrosarcoma protuberans is a rare soft tissue tumour with a very low (p < 0.5%) rate of metastasis. Rates of re-excision and recurrence were determined using data from the Netherlands Cancer Registry between 1989 and 2016. Of the 1,890 instances of dermatofibrosarcoma protuberans included, 87% were treated with excision, 4% with Mohs micrographic surgery, and 9% otherwise or unknown. Linked pathology data were retrieved for 1,677 patients. Half of all excisions (847/1,644) were incomplete and 29% (192/622) of all re-excisions were incomplete. The cumulative incidence of a recurrence was 7% (95% confidence interval (95% CI) 6-8) during a median follow-up of 11 years (interquartile range (IQR) 6-17). After Mohs micrographic surgery (n = 34), there were no recurrences during a median follow-up of 4 years (IQR 3-6). Due to the high rate of incomplete excisions and recurrences after excision, this study supports the European guideline, which recommends treating dermatofibrosarcoma protuberans with Mohs micrographic surgery in order to decrease the rate of recurrence."

Allen, A., Ahn, C. & Sangüeza, O.P. 2019.
"Dermatofibrosarcoma protuberans (DFSP) is an uncommon dermal neoplasm that exhibits a high rate of local recurrence and infiltrative behavior, but has a low risk of metastasis. It arises as a slowly progressive, painless pink or violet plaque. Histologically, DFSP is characterized by a monomorphous spindle cell proliferation in a storiform pattern. The gold standard of treatment is surgical resection with negative margins. In cases where obtaining clear margins is not possible, radiation and systemic therapy with tyrosine kinase inhibitors, such as imatinib mesylate, has been shown to be effective."

In cases of advanced DFSP, the cancer has grown deeply and may have reached muscle or bone, even spreading to other parts of the body in rare instances. More than one treatment may be used to increase the likelihood that all of the cancer is killed or removed.

Treatment options for advanced DFSP include:

Currently, conventional chemotherapy is rarely used in the treatment of dermato-fibrosarcoma protuberans (DFSP). Limited case reports have not shown any significant value of conventional chemotherapy in the treatment of DFSP.

Systemic Therapy - while chemotherapy does not appear to be beneficial, the targeted therapy ***Imatinib*** has been approved by the U.S. Food and Drug Administration (FDA) for the treatment of DFSP. It targets and turns off proteins that allow cancer cells to grow.

Brooks, J. & Ramsey, M.L. 2020.
"Dermatofibrosarcoma protuberans (DFSP) is a rare soft tissue tumor that involves the dermis, subcutaneous fat, and in rare cases, muscle and fascia. The tumor typically presents as a slowly growing, firm plaque on the trunk of young adults. The cause of dermatofibrosarcoma protuberans is not clearly understood. Studies have implicated a chromosomal translocation, resulting in the fusion protein COL1A1-PDGFB, which promotes tumor growth through overproduction of platelet-derived growth factor (PDGF). Diagnosis is made via skin biopsy. Dermatofibrosarcoma protuberans is

considered an intermediate-grade malignancy with a low likelihood of metastasis but a high rate of local recurrence. Given its propensity for a subclinical extension, the optimal treatment modality for dermatofibrosarcoma protuberans is Mohs micrographic surgery (MMS), a surgical technique which allows complete margin assessment and tissue preservation. Alternatively, dermatofibrosarcoma protuberans can be treated with wide local excision. The chemotherapeutic agent imatinib mesylate is currently FDA-approved for adults with unresectable, recurrent, or metastatic dermatofibrosarcoma protuberans."

Zhou, X., Sun, D., Liu, Y., Sun, O., Yuan, Z., Luio, X., Yang, J. & Chen, J. 2020.
Background: Dermatofibrosarcoma protuberans (DFSP) is a rare soft tissue sarcoma. Its high recurrence rate is a clinical challenge.
Objective: To analyze DFSP clinicopathologic factors and review our experience of treatments.
Materials and methods: A total of 80 patients who were treated between 2007 and 2017 in Shanghai Ninth People's Hospital were evaluated. Outcomes were compared focusing on recurrence following different treatment methods. Classical DFSP and transformed DFSP were classified as the two subtypes.
Results: The recurrence rate after local excision was significantly higher than that after wide margin excision. Patients undergoing wide margin excision (margins over 3 cm) were found to have lower recurrence rate compared with those margins less than 3 cm, while 10 underwent Mohs surgery were not found recurrence. Transformed DFSP had a greater tendency to recur.
Conclusions: Clean margin of excision should be achieved to prevent recurrence of DFSP. Slow Mohs surgery is recommended to treat DFSP.

McGee, M.W., Boukhar, S.A., Monga, V., Weigel, R. & Phadke, S.D. 2019.
Background: Dermatofibrosarcoma protuberans is a rare soft tissue malignancy that, if left untreated, can be locally destructive and life-threatening. Dermatofibrosarcoma protuberans is uncommon in the breast, and the similarity of its morphologic features with other spindle cell malignancies can make correct identification difficult. Immunohistochemistry and molecular testing can aid in the correct diagnosis when there is diagnostic uncertainty. Imatinib, a selective tyrosine kinase inhibitor, has been used for adjuvant treatment of dermatofibrosarcoma protuberans following surgical resection. When used as a neoadjuvant treatment, imatinib offers the opportunity to decrease tumor size prior to surgery to lessen the chance for disfigurement.
Case presentation: We present the case of a Caucasian woman who was 46-year-old when she first noted a mass in her right breast in 2015; she was initially diagnosed as having metaplastic breast carcinoma. Mastectomy and systemic chemotherapy were planned; however, after review of pathology at a referral center, the diagnosis was changed to dermatofibrosarcoma protuberans. She was treated with 4 months of neoadjuvant imatinib with adequate tumor shrinkage to perform breast conservation.
Conclusion: This patient's case stresses the importance of correctly diagnosing this rare breast tumor through the histopathologic appearance of dermatofibrosarcoma protuberans, molecular pathogenesis, and immunohistochemistry. These techniques can help differentiate dermatofibrosarcoma protuberans from metaplastic breast carcinoma and other spindle cell lesions of the breast. This is critical, as the treatment options for metaplastic breast carcinoma significantly differ from treatment options for dermatofibrosarcoma protuberans. This case describes the use of imatinib as a neoadjuvant option to reduce preoperative tumor size and improve surgical outcomes.

Radiation therapy (RT) has had a limited role in the past, but, recently, it has been used as an adjunct to surgery. Radiation therapy may be recommended for patients if the margins of resection are

positive or for situations in which adequate wide excision alone may result in major cosmetic or functional deficits. Postoperative adjuvant RT may reduce the risk of recurrence when clear surgical margins are not confident. The complete radiation therapy dose ranges from 50-70 Gy. Overall, the risk of severe complications from RT is low. Close follow-up care after radiation therapy is warranted because some DFSP tumours may become more aggressive.

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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