CASE REPORT

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# A male case of dermatofibrosarcoma protuberans in the breast presenting as gynecomastia

## Dermatofibrosarkom protuberans muške dojke prezentovan kao ginekomastija

**Viktorija Vučaj Ćirilović*†, Miloš Vuković*†, Jasmina Boban*†, Nenad Šolajić‡§, Milan Ranisavljević‖¶, Nataša Prvulović Bunović*†**

**University of Novi Sad, Faculty of Medicine, *Department of Radiology, ‡Department of Pathology, ‖Department of Surgery, Novi Sad, Serbia; Oncology Institute of Vojvodina, †Center for Imiging Diagnostics; §Department of Pathoanatomical and Laboratory Diagnostics, ¶Clinic for Oncological Surgery, Novi Sad, Serbia**

**Abstract**

**Introduction.** Dermatofibrosarcoma protuberans (DFSP) is a very rare mesenchymal tumor that accounts for approximately 0.1% of all malignancies. It is a locally aggressive fibrous tumor, with a high recurrence rate, which sometimes gives rise to distant metastases, usually to the bones and lungs. DFSP usually occurs on the trunk and extremities with only a small number of cases in the breast, especially in men. **Case report.** We presented a rare case of DFSP in the male breast. A 66-year-old man presented with gynecomastia of the left breast. The diagnostic work-up comprised of clinical examination, ultrasonography, core biopsy, and mammography. Immunohistochemistry revealed diffuse and strong positivity for vimentin, CD99, and CD34, while the tumor cells were completely negative for keratin, S100 protein, STAT6, CD31, and factor VIII, highly suggestive for DFSP. Subsequently, a radical mastectomy was performed and preoperative diagnosis of DESP was confirmed by pathological examination and immunohistochemistry. The patient was still disease-free six months after the surgical treatment. **Conclusion.** DFSP is a soft tissue sarcoma that rarely occurs in the breast, especially in men. The most common clinical presentation in the breast is a mass with extensive nodules on the surface, but it can also be presented as gynecomastia, as in our case. The diagnosis of DFPS is based on anatomopathology with immunohistochemistry analysis since there are no specific imaging features for this rare entity. Surgical excision with wide and negative margins is optimal for reducing the risk of recurrence.

**Key words:**
**breast neoplasms, male; dermatofibrosarcoma; diagnosis, differential; immunohistochemistry; rare diseases.**

**Apstrakt**

**Uvod.** Dermatofibrosarkom protuberans (DFSP) je veoma redak mezenhimalni tumor koji čini otprilike 0,1% svih maligniteta. To je lokalno agresivni fibrozni tumor, sa velikom stopom recidiva, koji ponekad može dati udaljene metastaze, obično u kostima i plućima. DFSP se obično javlja na trupu i ekstremitetima, a samo kod malog broja obolelih u dojci, posebno kod muškaraca. **Prikaz bolesnika.** Prikazan je redak slučaj DFSP u levoj dojci 66-godišnjeg muškarca koji se manifestovao kao ginekomastija. Dijagnostička obrada obuhvatila je klinički pregled, ultrazvučni pregled, "core" biopsiju i mamografiju. Imunohistohemija je pokazala difuznu i jaku pozitivnost za vimentin, CD99 i CD34, dok su tumorske ćelije bile potpuno negativne na keratin, S100 protein, STAT6, CD31 i faktor VIII, što je sugerisalo da se radi o DFSP. Nakon toga, izvršena je radikalna mastektomija i pregledom patologa i imunohistohemijskim metodama potvrđena je preoperativna dijagnoza DFSP. Bolesnik je šest meseci posle hirurškog lečenja i dalje bio bez bolesti. **Zaključak.** DFSP je sarkom mekog tkiva koji se izuzetno retko razvija u dojkama muškaraca. Uobičajena klinička prezentacija na dojci jeste masa sa širokim krvžicama na površini, mada se može prezentovati i samo kao ginekomastija, kao u opisanom slučaju. Dijagnoza DFPS se zasniva na patoanatomskoj i imunohistohemijskoj analizi jer ne postoje specifični znaci za ovaj retki entitet, vidljivi primenom različitih tehnika snimanja. Hirurška ekscizija sa širokim i negativnim marginama je optimalna za smanjenje rizika od recidiva.

**Ključne reči:**
**dojka, neoplazme, muškarci; dermatofibrosarkom; dijagnoza, diferencijalna; imunohistohemija; bolesti, retke.**

**Correspondence to:** Viktroija Vučaj Ćirilović, University of Novi Sad, Faculty of Medicine, Department of Radiology, Hajduk Veljkova 3, 21 000 Novi Sad, Serbia. E-mail: viktorija.vucaj-cirilovic@mf.uns.ac.rs

## Introduction

Dermatofibrosarcoma protuberans (DFSP) is an uncommon mesenchymal tumor that accounts for approximately 0.1% of all malignancies [1] and represents less than 5% of all soft tissue sarcomas occurring in adults aged 30 to 40 years [2]. The overall incidence is five cases in every 1 million persons annually [3].

This sarcoma usually arises in the dermis and can also extend to the deeper subcutaneous tissues [3]. Rare cases of deep-seated DFSP have been reported [4]. It is a locally aggressive fibrous tumor, with a high recurrence rate [3]. Therefore, it is important to achieve negative margins to minimize disease recurrence [5]. DFSP can give rise to distant metastases, usually to the bones and lungs (incidence is less than 5%) [6].

The most common presentation in a male's breast is a mass with extensive nodules on the surface [7]. The tumor tends to spare adnexal structures and is commonly superficially located, but in recurrent cases and untreated tumors, it can spread to more deeply situated structures [8, 9].

The early symptoms are often non-specific. Consequently, diagnosis is challenging, with a high incidence of misdiagnoses [10]. Due to the lack of pathognomonic clinical and imaging findings, DFSP can be mistaken for a keloid, hypertrophic scar, sebaceous cyst or lipoma. In cases with prior trauma, suspicion of DFSP must be raised in the differential diagnosis [11].

DFSP usually occurs on the trunk and extremities with only a small number of cases in the breast, especially in men [1, 2, 5, 7, 12–14]. We reported a rare case of DFSP in the male breast that clinically presented as gynecomastia.

## Case report

A 66-year-old man presented with gynecomastia of the left breast that was slowly growing over the past year. In his personal history, there were no risk factors for breast cancer. There was no information about recent trauma, or scars in the breast area. Family history was unremarkable for breast cancer. Physical examination was delayed due to the patient's psychological discomfort. It showed an enlarged breast with a palpable nodule beneath the skin without any skin changes on the surface. One year after the breast enlargement was observed, the patient finally underwent ultrasound (US) investigation that showed a well-defined hypoechoic lesion with sharp and smooth edges, located in the superior medial quadrant, between 10 and 12 o'clock, measuring 45 x 22 mm in diameter (Figure 1). The distance from the skin was 9 mm. Ipsilateral axillary lymph nodes were inconspicuous.

Additional digital mammography was performed, showing a hyperdense mass without calcifications or fat (Figure 2).

Based on US and mammography findings, the lesion was graded according to the Breast Imaging Reporting and Data System (BI-RADS) as IV lesion, and malignancy could not be excluded. The US-guided core biopsy under local anesthesia was performed. Histological examination revealed

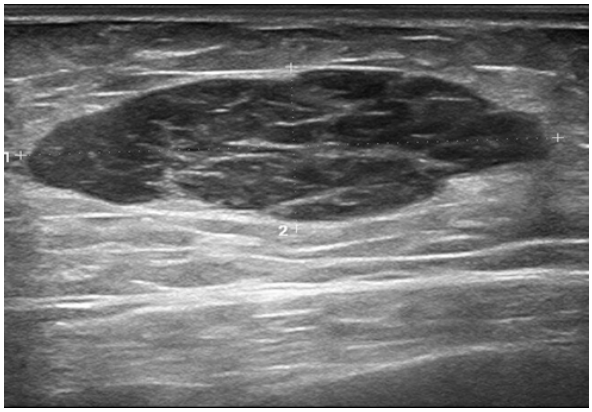

**Fig. 1 – Dermatofibrosarcoma protuberans on the ultrasound examination shows hypoechoic well defined oval lesion in subcutaneous fat.**

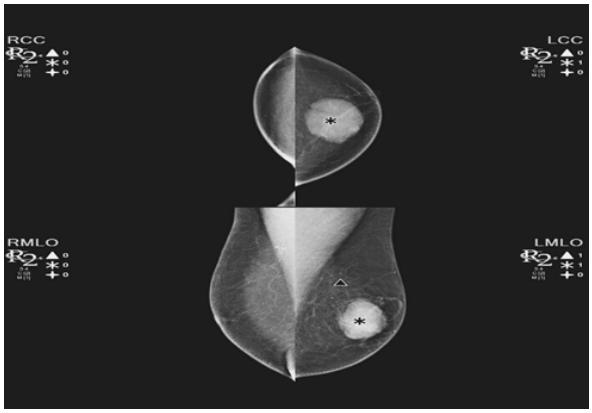


**Fig. 2 – Mammogram of the left breast shows a circumscribed, hyperdense mass without calcifications or identifiable fat, while the right breast is normal.**

a tumor composed of relatively uniform spindle cells with moderately hyperchromatic nuclei and low mitotic activity. The cells were arranged haphazardly and in short fascicles (Figure 3). No tumor necrosis was found. Immunohistochemistry revealed diffuse and strong positivity for vimentin, CD99 and CD34 molecules (Figure 4) and

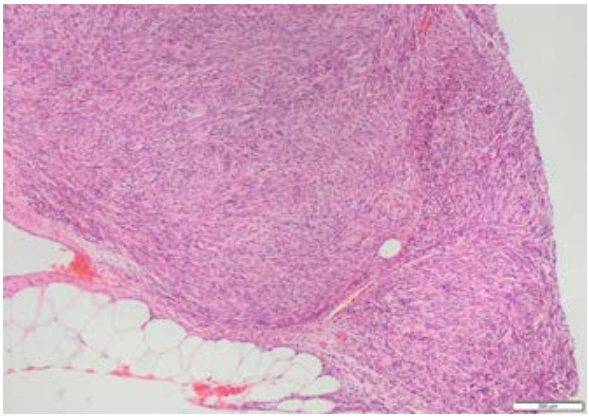

**Fig. 3 – Dermatofibrosarcoma protuberans at low magnification. The tumor border is sharp, but there is an entrapped adipocyte in the lower right quadrant (hematoxylin-eosin staining, 40x).**

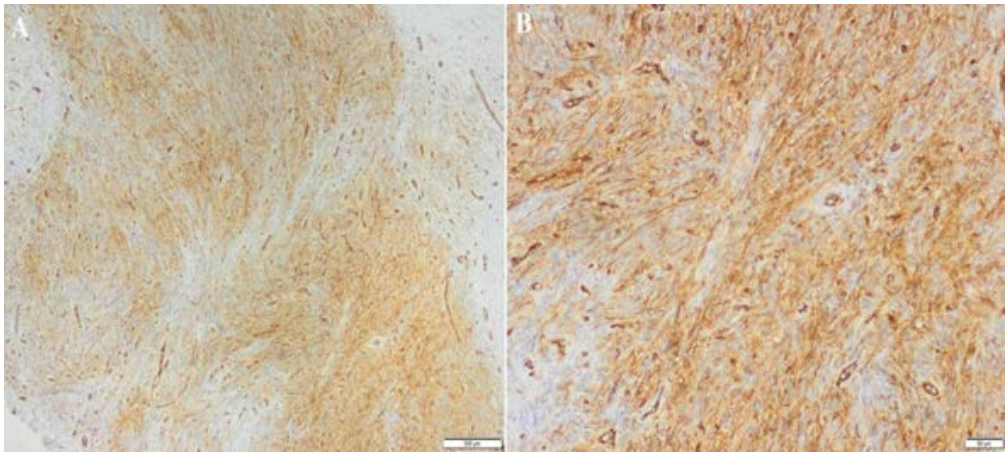

**Fig. 4 – Diffuse tumor cells immunoreactivity for CD34.**
**Immunoperoxidase with hematoxylin counterstain: A) 40x; B) 100x.**

focal and weak reaction for smooth muscle actin. The tumor cells were completely negative for keratin, S100 protein (Figure 5), STAT6 (Figure 6), CD31 and factor VIII. Such a combination of morphology and immunophenotype was highly suggestive for DFSP regardless of its subcutaneous localization. Subsequently, a radical mastectomy was performed without any adjuvant treatment. Pathologic examination revealed a firm, tan, well-circumscribed oval tumor just beneath the skin, measuring 40 x 30 mm (Figure 7). Histological and immunohistochemical analyses confirmed the biopsy findings and the diagnosis remained the same. The postoperative care was uneventful without any additional treatment. The patient was disease-free six months after the surgical treatment.

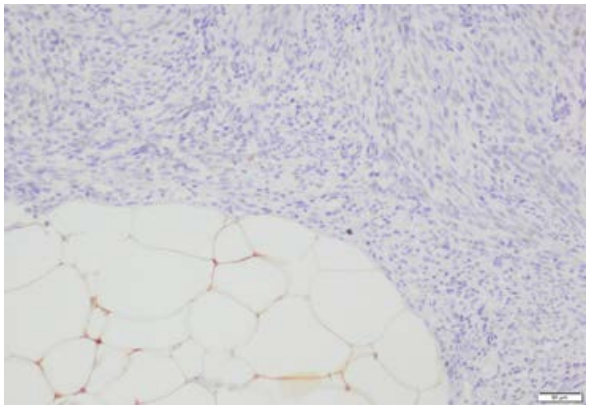

**Fig. 5 – No positivity for S100 protein with a few immunoreactive adipocytes as an internal positive control.**
**Immunoperoxidase with hematoxylin counterstain (100x).**

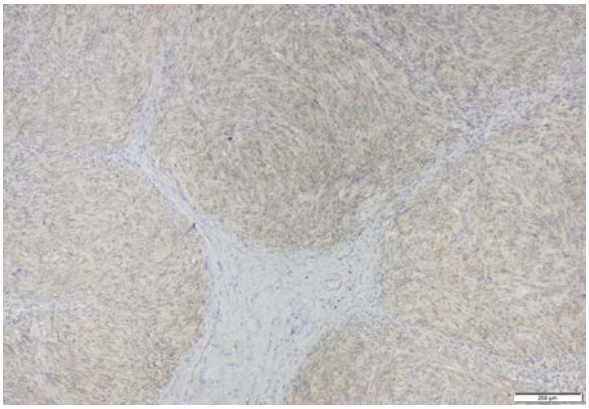

**Fig. 6 – Nonspecific cytoplasmic positivity for STAT-6. No visible nuclear staining.**
**Immunoperoxidase with hematoxylin counterstain (40x).**

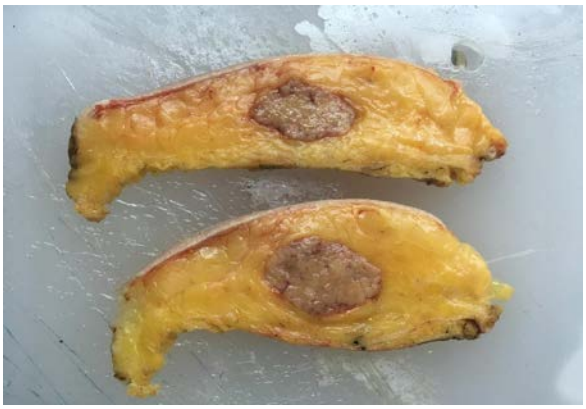

**Fig. 7 – Macroscopic examination shows a firm, tan, well-circumscribed oval tumor just beneath the skin.**

## Discussion

DFSP represents a low-grade malignant soft tissue tumor that arises from the dermis and extends to the deeper structures. There are several histopathological variants of DFSP that have been described, including pigmented DFSP or Bednar tumor, myxoid, juvenile DFSP or giant cell fibroblastoma, atrophic, sclerosing and myoid, occurring in pure form or admixed with one of the others creating hybrid lesions. A small subset of DFSP patients presents with fibrosarcomatous progression that is more aggressive and has higher rates of recurrence and metastasis [11].

The results of some studies concerning the distribution of DFSP between genders showed that women have higher incidence rates than men, except among the elderly [15], but other authors reported that men are slightly more commonly

affected than women [9]. In our case, the tumor on the male breast appeared much later, at the age of 66, compared to the recently published review of Bouhani et al. [7] who state that the mean age of DFSP in the male breast is 32.6 years. The tumor is usually less than 5 cm in size, similarly to our case. DFSPs are superficial in 77% of patients and, according to the report of Bowne et al. [16], invade deeper structures in only 22% of patients.

The pathogenesis of DFSP is poorly explained. DFSP was observed to occur in pre-traumatic areas, including vaccination sites, burn scars, tattoos, surgical scars, and radiotherapy [11]. Almost all molecularly characterized cases have been found to have a COL1A1-PDGFB fusion gene. It was found that DFSP with the new COL6A3-PDGFD fusion variant has a predilection for breast and also has typical histologic and immunohistochemical features [8]. Several case reports and epidemiologic studies suggest that hormones may also be involved in the pathogenesis of DFSP. Kreicher et al. [17] proved no significant association between hormone receptor expression and demographics, but the loss of receptor expression was observed in all recurrent tumors. The presentation of the tumor in our case as gynecomastia suggests that there may be a connection between primary reasons of gynecomastia and occurrence of DFSP in the male breast. It remains unclear if higher estrogen levels or disbalance with testosterone levels can be a potential risk factor for developing this kind of malignancy. Regarding the recently published literature review [7], this case represents the 12th case of the breast DFSP in men, which shows the rarity of this entity.

Most DFSPs are typically small and superficial and diagnosis may be suspected based on the tumor's clinical appearance and pathologic examination. When found in the breast region, patients usually undergo only breast US and mammography without the need for magnetic resonance (MR) imaging (MRI) [11]. Nevertheless, there is a possibility of the *in vivo* usage of MR spectroscopy (MRS) that gives additional valuable information of a normal cholin resonance peak which, combined with other imaging and pathohistological characteristics, can be suggestive of the diagnosis of DFSP [18]. Pathological and immunohistochemical examinations are currently the gold standard for diagnosing DFSP [11].

Immunohistochemically, DFSP usually shows strong positivity for CD34 (in 97% of the patients) [1], vimentin and negative staining for cytokeratin, S-100, epithelial membrane antigen and variable staining for smooth muscle actin (SMA) [12]. The present case showed positivity for CD34 along with negativity for S-100 and only focal positivity for SMA, similar to the most recent reported DFSP case in the male breast [7].

The main differential diagnosis of DFSP of the breast includes primary breast tumors with spindle cell differentiation like benign fibrous histiocytoma, phyllodes tumor, cellular fibroadenoma, dermatofibrosarcoma, neurofibroma, nodular fasciitis, fibrosarcoma, and inflammatory myofibroblastic tumor [12].

It was found that older age and male sex were significant predictors of mortality of patients with DFSP[19]. Factors like histologic subtype, high mitotic index, cellularity, size, location of the tumor, and recurrent lesions were found to be associated with higher recurrence rates [14]. The treatment of DFSP is primarily surgical. In our case, the more radical approach was made, and the patient underwent a mastectomy, like in the similar recently published case [7]. In our case, following the patient's desire, a left mastectomy was performed.

In lesions with positive margins after surgery, or in cases where resection is limited due to anatomical location, adjuvant radiotherapy is suggested [2]. Prognostic factors that are shown to be significant are tumor location, surgical margins, and the presence of a high-grade component [20]. However, these factors are identified for DFSP in locations other than breast. No impact on survival was found in patients undergoing radiation therapy [21]. Imatinib mesylate, a protein tyrosine kinase inhibitor, is used for the treatment of unresectable, recurrent and/or metastatic DFSP in adult patients because it inhibits the overactivity of platelet-derived growth factor (PDGF) receptor in these tumor cells [11]. A response rate of approximately 65% has been achieved among DFSP patients treated with imatinib. A small subset of DFSP lacking the classic translocation t(17:22) seems to have no response to imatinib [14].

Long-term follow-up requires strict US monitoring every 6 to 12 months with biopsy in cases of suspected recurrence. The 5-year survival rate of patients with DFSP is higher than 99% [2].

## Conclusion

DFSP is a soft tissue sarcoma that rarely develops in the breast of male patients. The clinical presentation includes a firm, erythematous, subcutaneous lump that has an indolent growth pattern. The diagnosis of DFPS is based on anatomopathology with immunohistochemistry because there are no specific signs for this rare entity. Surgical excision with wide and negative margins is optimal for reducing the risk of recurrence.

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