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CASE REPORT

When an old pigmented lesion becomes serious: the problematic diagnosis of low-grade skin malignancies – Bednar tumor with fibrosarcomatous transformation

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Abstract

Bednar tumor is a rare cutaneous neoplasm, regarded as a variant of dermatofibrosarcoma protuberans with melanotic colonization and it usually affects young and middle-aged adults or children. This lesion is considered a low-grade malignant tumor, which can be associated with multiple local recurrences after surgical excision. Although a rare phenomenon, these lesions may undergo fibrosarcomatous transformation, which implies a poorer prognosis of the disease, as the tumor has a more locally aggressive behavior and patients might also develop distant metastases.

We present the case of a 53-year-old female patient, with no significant medical history, who presented with a subcutaneous nodule on her upper back, for which a wide surgical excision was performed. The gross examination of the specimen showed a solitary protuberant grey-white nodule with a bluish shade and flecked with pigment. The microscopic examination revealed a malignant proliferation with a predominantly fascicular growth pattern, composed of spindle cells with highly pleomorphic nuclei and high mitotic rate, as well as the presence of dendritic cells with abundant melanin. Upon immunohistochemical analysis, the proliferation showed negative staining for CD 34 and AE 1/ 3, whereas the scattered dendritic cells stained positive with S100 protein. Ki 67 was positive in 15% of the tumor cells and the absence of p53 expression was noted. Thus, the diagnosis of Bednar tumor with fibrosarcomatous transformation was established.

The aim of this paper was to gain further knowledge about the histopathological and immunohistochemical features, as well as about the treatment of Bednar tumor, especially considering its rarity.
Keywords: dermatofibrosarcoma, DFSP, Bednar, immunohistochemistry, sarcoma

Introduction

Even though the most frequent dermal soft tissue sarcoma, dermatofibrosarcoma protuberans (DFSP) is still a rare entity, accounting for less than 2% of all sarcomas [**1**]. It is widely considered a low-grade malignancy, as it grows slowly and has a low potential of metastasis. Nevertheless, it can be locally aggressive and tends to reoccur locally [**2,3**]. In the recent years, several types of DFSP have been described such as atrophic, fibrosarcomatous, giant cell fibroblastomatous, myxoid, myoid and pigmented variant [**2-4**]. This latter one is also known as Bednar tumor and is one of the rarest forms of DFSP, representing less than 5% of all cases, and being most often found on the back and shoulders [**5,6**]. Its clinical features are usually uncharacteristic. It usually presents as a dark-colored nodule or plaque than can easily be mistaken for other skin tumors such as melanoma, cellular blue nevus or neurofibroma [**7,8**]. It is defined by the presence of melanin-filled dendritic cells intermingled with blunt spindle cells in a storiform growth pattern [**6,7**]. This unusual tumor was first described in 1957 by Bednar, who, at that time, considered it to be a type of "storiform neurofibroma" [**9**]. However, its neuroectodermal origin has since been disputed and the lesion is now most likely considered to be a DFSP with melanocytic colonization [**10,11**].

Because of the rarity of this neoplasia, its unique features are still to be fully understood and its treatment is still under discussion [**11**].

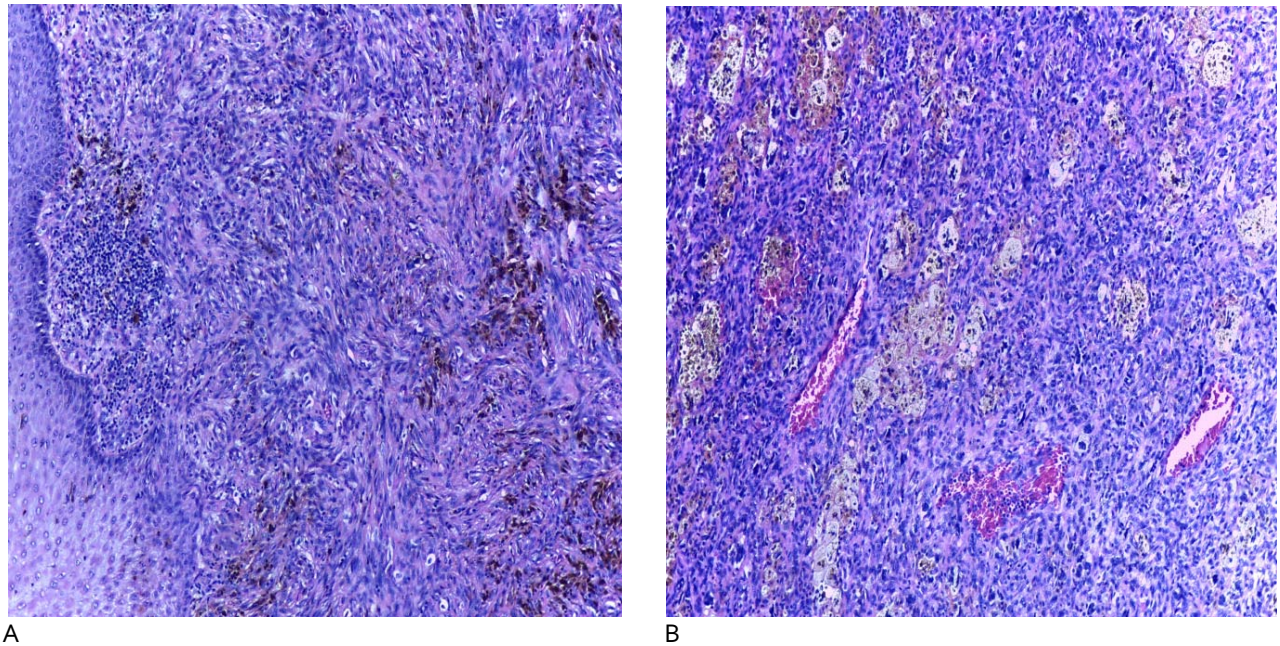
Materials and methods

Our patient presented to the University Emergency Hospital in Bucharest with a firm, brownish nodule on her upper back, measuring 3/ 2/ 1.5 cm. Dermoscopy showed that the nodule displayed bluish structureless background and whitish veils and no peripheral pigment network. As the tumor was suspicious for melanoma, a wide surgical excision was performed. Specimen samples were fixed with 10% buffered formalin and were processed by conventional histopathological methods, using paraffin embedding, sectioning and Hematoxylin-Eosin (HE) staining. After that, the sections were deparaffinized in toluene and alcohol and then washed in PBS (phosphate saline buffer), incubated with normal serum, then incubated with primary antibody overnight. Later, washing in carbonate buffer and development in 3,3'-diaminobenzidine hydrochloride/ hydrogen peroxide and nuclear counterstain with Mayer's Hematoxylin were performed. The immunohistochemical markers that we used were AE 1/ 3, S100 protein, Vimentin, CD 34, Ki 67 and p53.

Results

We reported the case of a 53-year-old female with no significant medical history, denying any trauma or radiotherapy, who presented with a pigmented brownish painless nodule on the upper back, which had been progressively growing for 5 years, initially as a plaque-like dermal lesion and as a rapidly-growing nodule later. A dermoscopy was performed, revealing a 30 mm lesion, with

bluish structureless background without a pigmented peripheral network. The lesion was then surgically removed and the specimen was submitted for a histopathological and immunohistochemical analysis. Upon gross pathologic examination, we identified a 3/ 2/ 1.5 cm solitary protuberant grey-white dermal nodule, with a bluish shade and flecked melanin pigment. The microscopic examination of the fragments revealed a malignant tumoral proliferation, exhibiting a predominantly fascicular growth pattern, composed of plump spindle cells, with markedly pleomorphic nuclei and high mitotic rate. Few giant Touton-like cells were also observed. The tumor showed infiltrative growth and invaded into the subcutis. Interestingly, the presence of irregularly scattered dendritic cells with abundant pigment was also noted, drawing suspicion of a sarcomatous variant of Bednar tumor (**Fig. 1, 3, 4**). A Pearls stain was also executed and the presence of intratumoral hemosiderin was identified (**Fig. 2**). On the immunohistochemical study, the malignant proliferation showed intense positivity for vimentin and negative AE 1/ 3 and had faint CD 34 staining (**Fig. 6,7**), whereas the dendritic pigmented cells stayed positive for S100 protein (**Fig. 5**). Ki 67 was positive in about 15% of the cells and wild type p53 expression was noted (**Fig. 8**).



A B

Fig. 1A. Malignant mesenchymal tumor proliferation with fascicular growth-pattern and scattered pigment-laden cells (HE, 4X); B. Heavily pigmented cells intermingled within the fibrohistiocytic tumor proliferation (HE, 10X)

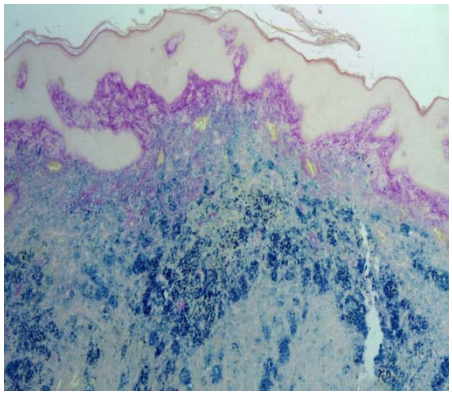


Fig. 2 Pearls stain demonstrating the presence of intratumoral hemosiderin (ob, 10X)

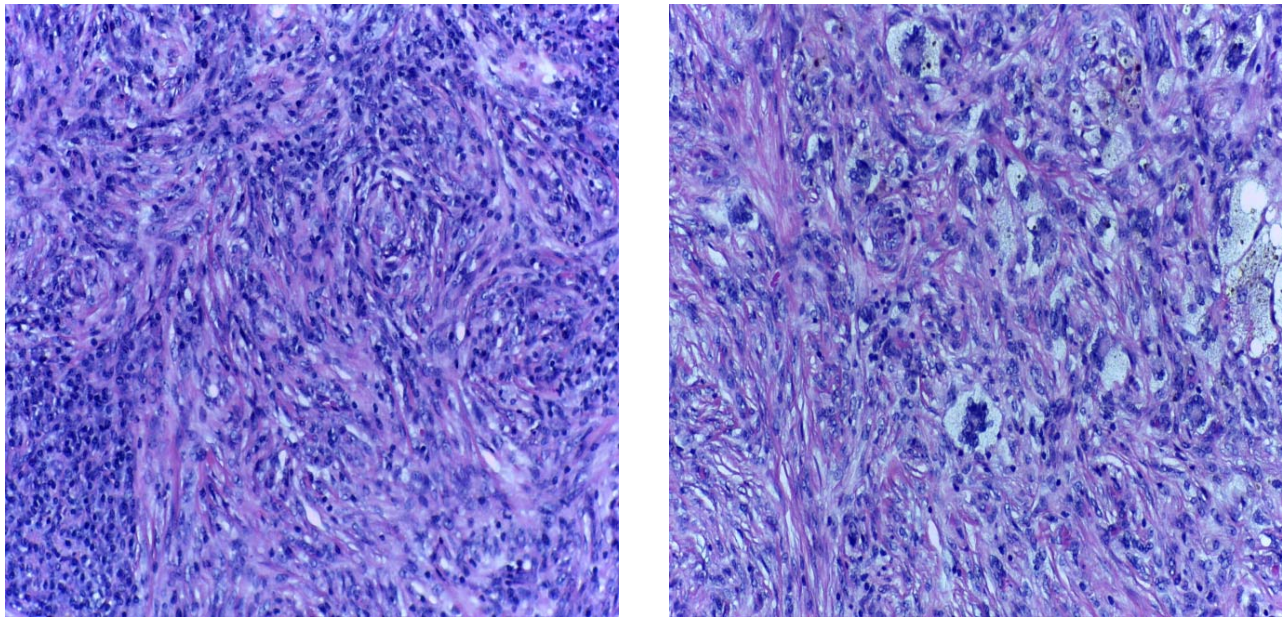


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Fig. 3A. Atypical spindle cells proliferation with fascicular architecture (HE, 20X); B. Note the presence of Touton-like giant cells within the tumor proliferation (HE, 20X)

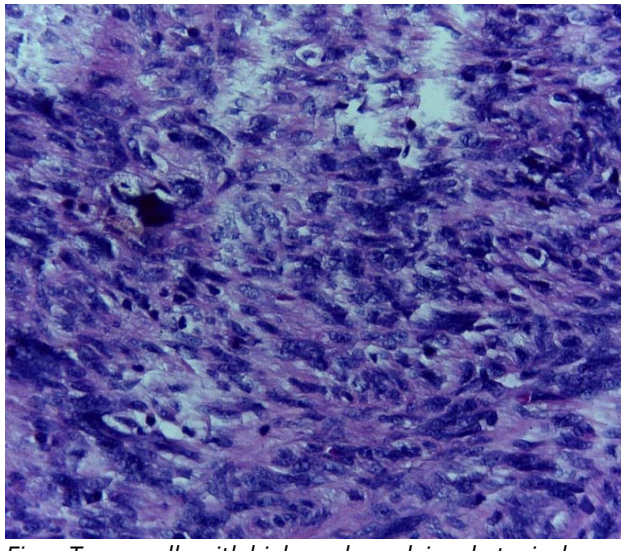

Fig. 4 Tumor cells with high grade nuclei and atypical mitotic figures (HE, 40X)

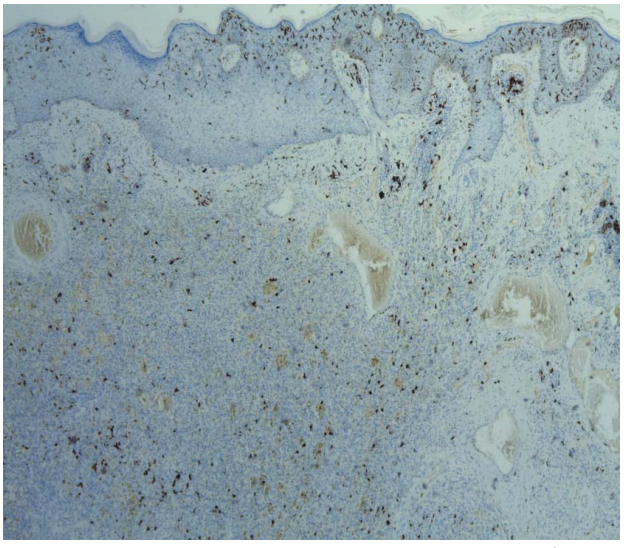

Fig. 5 Positive S100 staining in pigmented cells, confirming their neuroectodermal differentiation (S100, 10X)

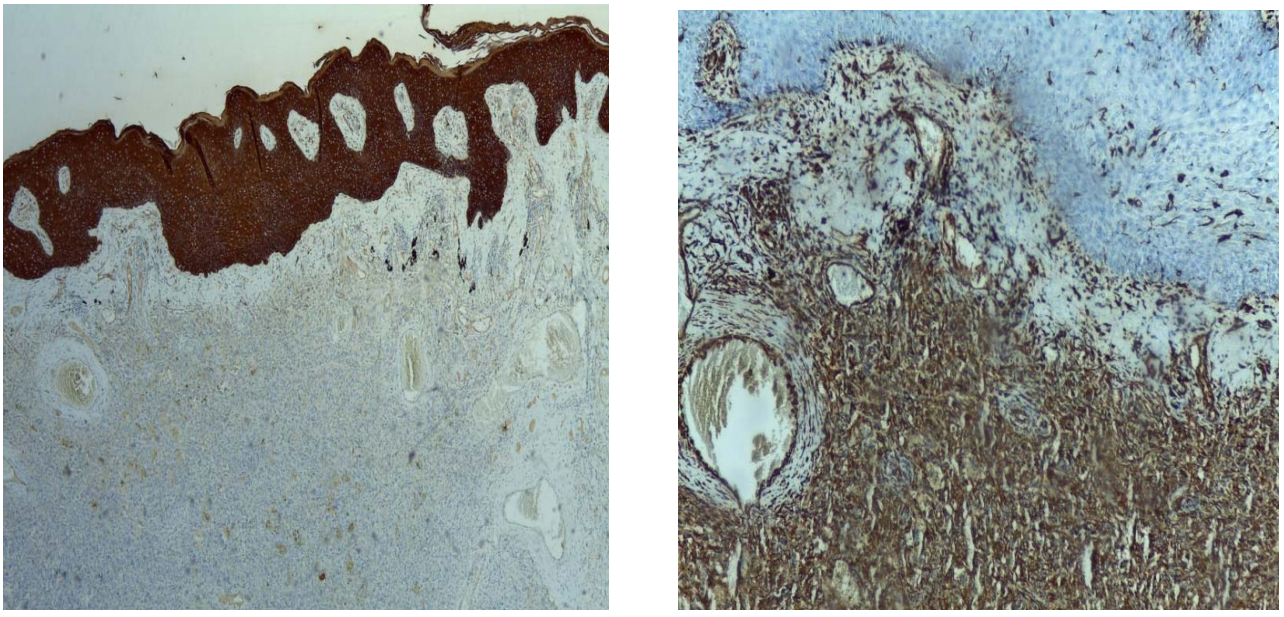

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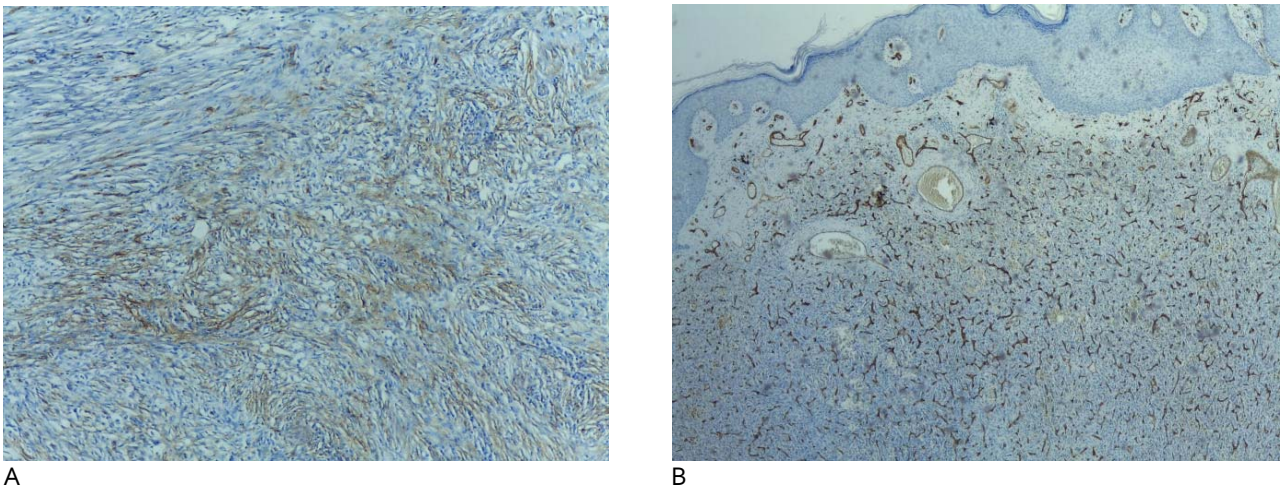
Fig. 6A. AE 1/ 3 negative staining in tumor cells (AE 1/ 3 10X); ***B****. Diffuse intense vimentin staining (Vim, 10X)*



A B

Fig. 7A. CD 34 weakly positive in tumor cells (CD 34, 10X); B. Diminished and absent expression of CD 34 in tumor areas with fibrosarcomatous transformation (CD 34, 4X)

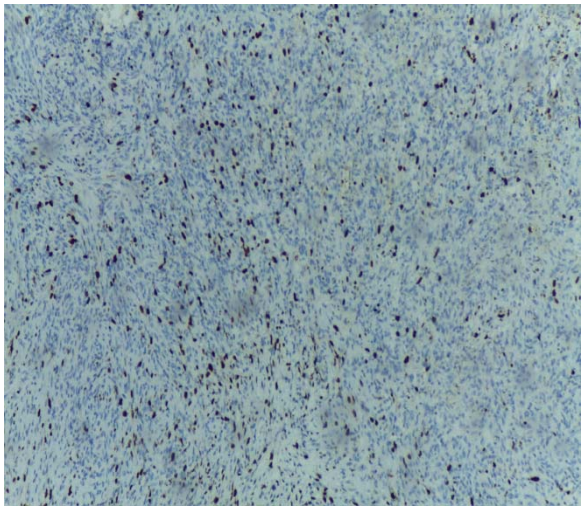


Fig. 8 Ki 67 index positive in 15% of tumor cells (Ki 67, 10X)

Following the complete surgical resection of the tumor and the histopathological diagnosis, the patient was placed under surveillance and received further oncological care.

Discussions

Bednar tumor is an exceptionally rare cutaneous neoplasm, accounting for approximately 1-5% of all cases of dermatofibrosarcoma protuberans, being regarded as a pigmented morphological variant of the fibrohistiocytic skin tumor [**1,3**]. Its genetic features, as well as the clinical presentation and histological characteristics are similar to those of ordinary dermatofibrosarcoma protuberans, but its histological hallmark is the presence of scattered dendritic cells that contain melanin [**1,3,12**]. In most of the cases, these lesions clinically present as slowly-growing plaques or subcutaneous nodules, as it was also documented in our patient's case [**7,8**]. The number of melanin-containing cells can vary and, as a result, black discoloration can be observed in lesions with many pigment laden cells, whereas other tumors only have microscopically detectable melanin [**12**]. In our case, an abundant quantity of pigment was observed, both on gross examination and on microscopic analysis.

Dermatofibrosarcoma protuberans and its variants, including its pigmented counterpart, Bednar tumor, are considered tumors of intermediate malignancy, as they deeply infiltrate the dermis and subcutis and have a high local recurrence rate, especially correlated with conservative surgical excision [**13**]. In addition, some patients can develop distant metastasis, especially involving the lungs [**1**]. Metastatic disease usually occurs several years after the diagnosis of the primary tumor and is strongly associated with multiple local recurrences [**1,14**] and tumor size [**15**]. There is an increased awareness that fibrosarcoma or even pleomorphic sarcoma can arise from such low-grade malignant skin tumors [**4,5,15**]. This implies a more aggressive clinical behavior of the lesion, and it appears that these patients have a higher risk of developing distant metastases [**13,15,16**]. Moreover, they can be associated with an increased oncological treatment resistance and require special attention [**16**].

Histopathologically, DFSP usually consists of a monomorphous spindle cell proliferation with a storiform growth pattern and little mitotic activity. The histopathological diagnosis of fibrosarcomatous variant of dermatofibrosarcoma protuberans requires several criteria and it can often be challenging, especially considering the rarity of such cutaneous lesions [**1,14**]. The microscopic findings usually consist of a highly cellular malignant mesenchymal proliferation, composed of plump spindle cells, with pleomorphic nuclei with granular chromatin and variable nucleoli. The cells are usually arranged in fascicles, rather than in whorls and do not display a storiform growth-pattern, like in dermatofibrosarcoma protuberans. There is an increased mitotic activity and atypical mitoses/ mitotic figures are present [**14**]. In our patient's case, a similar microscopic aspect was identified, but the presence of pigment laden cells was also observed, raising suspicion of a Bednar tumor with fibrosarcomatous transformation. A Perls stain was initially performed, in order to highlight the nature of the pigment. Perls staining was positive in some, but not all pigmented cells, therefore proving the presence of both intratumoral haemorrhage (hemosiderin) and of another type of pigment, which was indeed melanin. The specimen was later submitted for immunohistochemical analysis. The expression of S100 protein was identified in the pigmented cells, confirming their neuroectodermal differentiation, whereas the

fibrohistiocytic malignant proliferation was S100 negative. The loss of CD34 immunoreactivity was also noticed, indicating a fibrosarcomatous transformation of a Bednar tumor, as reported by other studies as well [**1**]. The proliferation index Ki 67 was positive in 15% of tumor cells and the expression of p53 was wild type.

The histopathological differential diagnosis of DFSP includes various spindle cells neoplasms such as dermatofibroma, solitary fibrous tumor, spindle cell lipoma, schwannoma, synovial sarcoma, spindle cell melanoma or sarcomatoid carcinoma. Extensive immunohistochemistry analysis usually suffices for establishing the correct diagnosis, but in rare cases, molecular analysis can be required [**1,6,17**]. Molecular studies have demonstrated that DFSP displays a characteristic t(17;22)(q22;q13) leading to the formation and overexpression of the fusion gene COL1A1-PDGFB, and subsequently to activation of PDGF receptor [**1,16,17**].

The treatment of dermatofibrosarcoma protuberans comprises a wide surgical excision, with negative margins, as conservative excision is now considered one of the main causes of local tumor recurrence [**13**]. However, a promising alternative in the surgical treatment of skin malignancies is Moh's microsurgery during which thin layers of tumoral tissue are gradually removed and analyzed, so that the entire invaded skin is removed [**18,19**]. Due to the activation of PDGF receptor, oncological therapy with Imatinib mesylate is considered an effective treatment at present. In addition to this, DFSP is sensitive to radiotherapy and patients with large, recurrent, or inoperable tumors can benefit from radiation therapy [**17,18**].

Conclusion

DFSP is a rare skin malignancy and cases displaying melanin pigment and/or fibrosarcomatous transformation are even more exceptional, making them difficult to diagnose and treat. Our reported case of DFSP turned out to be both a pigmented version and one undergoing fibrosarcomatous differentiation, which is associated with a more aggressive behavior. Therefore, special attention is required to obtain complete surgical excision and to provide a complete histopathological diagnosis in order to achieve the best outcome for the patient.

Conflict of Interest statement

Authors state no conflict of interest.

Informed Consent and Human and Animal Rights statement

Informed consent has been obtained from all individuals included in this study.

Authorization for the use of human subjects

Ethical approval: The research related to human use complies with all the relevant national regulations, institutional policies, is in accordance with the tenets of the Helsinki Declaration, and has been approved by the review board of General University Hospital, Alicante, Spain.

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Disclosures

None.

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