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Case report

Immunohistochemistry in a Spindle Cell Lesion: A Case of Cellular Dermatofibroma

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Abstract

Cellular dermatofibroma (CDF) is an uncommon hyper-cellular variant of benign fibrous histiocytoma that may clinically and histo-pathologically mimic malignant spindle cell neoplasms, particularly dermatofibrosarcoma protuberans (DFSP) and spindle cell squamous cell carcinoma (SpSCC). Accurate distinction is essential because these entities differ substantially in biological behaviour, therapeutic management, and prognosis. This study reports a diagnostically challenging case of CDF in a 56-year-old woman presenting with a gradually enlarging keratotic nodule over the extensor aspect of the left forearm. Clinically, the lesion resembled keratoacanthoma, while preliminary histopathological evaluation suggested a spindle cell neoplasm. Histopathological examination revealed a hypercellular dermal spindle cell proliferation arranged in fascicular and focal storiform patterns without significant atypia, necrosis, or atypical mitoses. No honeycomb infiltration of subcutaneous fat was identified. Immunohistochemistry demonstrated negativity for CD34, AE1/AE3, STAT6, SOX10, desmin, smooth muscle actin, caldesmon, calponin, and ERG, with focal S100 positivity. Excision followed by histopathological examinations such as correlation of histomorphological and immunophenotypic findings revealed a well-circumscribed, densely cellular dermal spindle cell lesion, and immunohistochemistry confirmed a diagnosis of cellular dermatofibroma (CD34, Pan-cytokeratin negative). This case highlights the diagnostic utility of immunohistochemistry in the evaluation of cutaneous spindle cell lesions and emphasises the importance of distinguishing CDF from malignant mimickers to prevent unnecessary aggressive surgical management.

Keywords: Cellular dermatofibroma; Dermato-fibro-sarcoma protuberans; Spindle cell lesion; Immuno-histochemistry; Dermatopathology

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Introduction

Dermatofibroma, also termed benign fibrous histiocytoma, is a common benign fibrohistiocytic tumour of the skin composed of fibroblastic and histiocytic cells and typically presents as a slowly enlarging papule or dermal nodule involving the extremities of adults[1,2]. Although conventional dermatofibroma is usually straightforward to diagnose histologically, several histological variants exhibit atypical architectural and cytological features that may closely simulate malignant spindle cell neoplasms. There are several variants of DF, distinguished by their distinct clinical and histological features (table 1)[3,4] Cellular DF is a morphological variant of DF known for its deeper involvement and recurrences[1-5.] Among these, cellular dermatofibroma (CDF) represents an uncommon variant accounting for approximately 2-5% of dermatofibromas and is characterised by increased cellularity, fascicular or storiform spindle cell proliferation, deeper dermal extension, and occasional involvement of the superficial subcutis[16-20]. This pathological distinction of CDF from malignant spindle cell tumours is of considerable diagnostic importance because of substantial overlap with entities such as dermato-fibrosarcoma protuberans (DFSP), spindle cell squamous cell carcinoma (SpSCC), atypical fibroxanthoma, solitary fibrous tumour, and cutaneous smooth muscle or neural tumours[4-11], Histologically, the hyper cellular architecture, infiltrative growth pattern, and occasional mitotic activity observed in CDF may result in over diagnosis of malignancy, particularly in limited biopsy specimens lacking adequate representation of tumour depth and architecture. Such diagnostic pitfalls may lead to unnecessarily aggressive surgical intervention and increased patient morbidity.

According to the recent World Health Organization (WHO) classification of skin tumours, cellular dermatofibroma is recognised as a benign fibro histiocytic neoplasm with locally recurrent potential. Unlike DFSP, which characteristically harbours COL1A1–PDGFB fusion, CDF lacks a defining recurrent molecular alteration, supporting its distinction from true fibroblastic sarcomas. Immunohistochemistry therefore serves as an important adjunct in the evaluation of spindle cell lesions of the skin. Cellular dermatofibroma typically lacks diffuse CD34 expression, thereby facilitating distinction from DFSP, while negative cytokeratin staining assists in excluding spindle cell epithelial malignancies. Additional markers including STAT6, SOX10, smooth muscle actin (SMA), and desmin may further aid in excluding histological mimickers depending on the differential diagnostic considerations.

This clinical study herein report a diagnostically challenging case of cellular dermatofibroma presenting clinically as a keratoacanthoma-like lesion over the forearm in a 56-year-old woman, wherein detailed histopathological examination and comprehensive immune histo-chemical analysis were essential in establishing the final diagnosis.

Case report

A 56-year-old woman presented with a solitary nodular lesion over the extensor aspect of the left forearm of approximately two years' duration. The lesion had gradually increased in size, with relatively rapid enlargement and increased firmness during the preceding six months. There was no associated pain, bleeding, ulceration, or constitutional symptoms. The patient denied antecedent trauma, similar lesions elsewhere, or significant family history. Cosmetic concern was the primary reason for seeking medical attention.

Cutaneous examination revealed a well-defined dome-shaped brown dermal nodule measuring approximately 0.4 × 0.3 cm with a central keratin-filled crater over the extensor surface of the left forearm [Figure 1]. The lesion was firm in consistency and non-tender. Clinical differentials included keratoacanthoma, adnexal neoplasm, and spindle cell tumour.

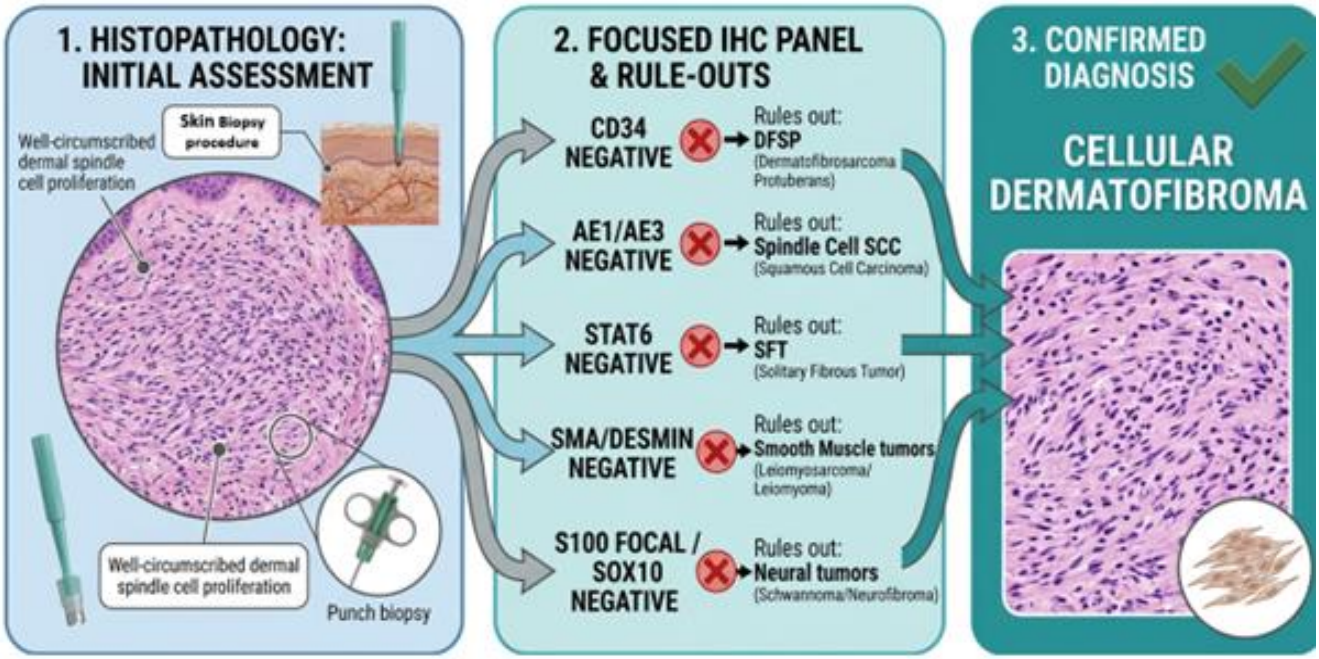

Fig 1: Diagnostic workflow for a Dermal Spindle cell lesion

A punch biopsy has been performed for histopathological evaluation. The lesion was unusually firm and adherent to the surrounding tissue, making excision technically difficult and raising suspicion for a deeper spindle cell process. Histopathological examination demonstrated a well-circumscribed but non-encapsulated hyperactive cellular dermal spindle cell proliferation composed of elongated spindle-shaped cells arranged in intersecting fascicles and focal storiform whorls. The tumour cells exhibited bland elongated nuclei with fine chromatin and inconspicuous nucleoli. Mitotic activity was infrequent (<one mitosis/10 high-power fields), and atypical mitotic figures, necrosis, marked pleomorphic, and significant cytological atypia were absent. The lesion remained confined to the dermis without extension into the subcutaneous fat. Characteristic honeycomb infiltration of adipose tissue was not identified. Epidermal dysplasia, keratin pearl formation, and overt epithelial differentiation were absent. [Fig: 2-4]

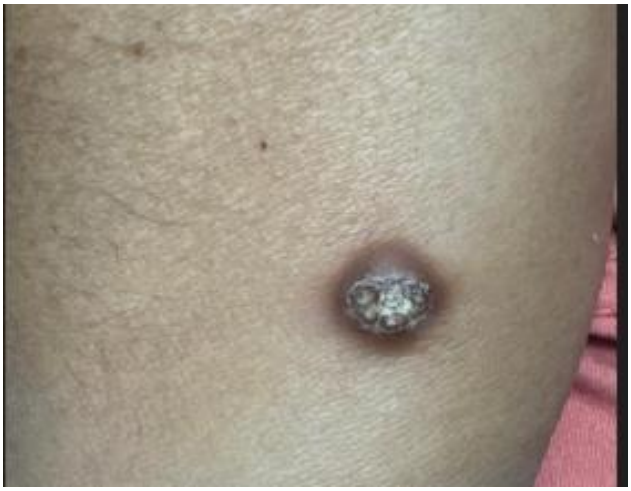

Figure 2: Clinical photograph showing a dome-shaped, firm dermal nodule with central keratin-filled crater on the left forearm.

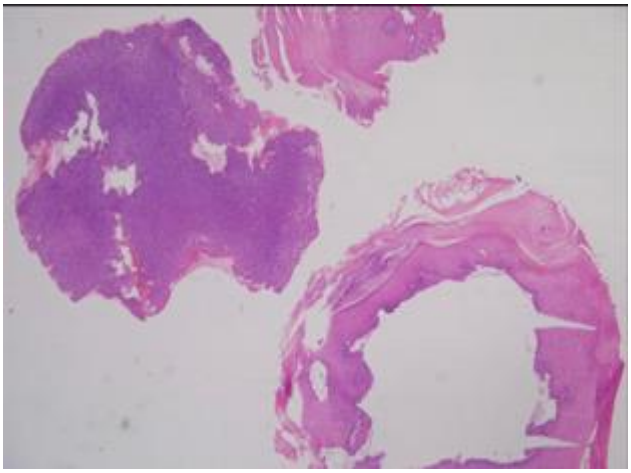

Figure 3: Low-power photomicrograph showing a well-circumscribed, densely cellular dermal spindle cell lesion (H&E, ×10).

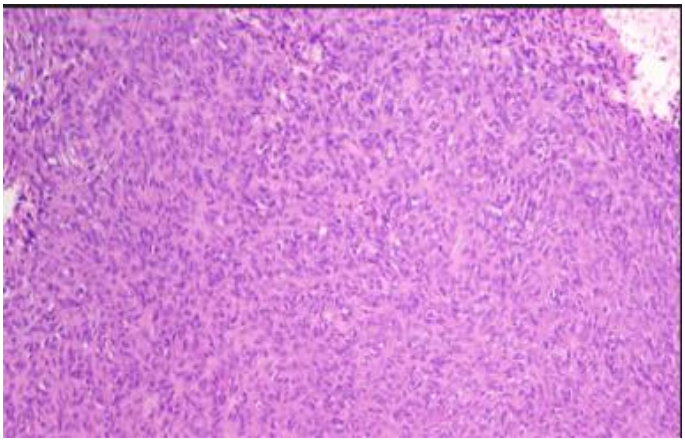

Figure 4: Intermediate-power view demonstrating fascicular spindle cell arrangement with bland nuclear features (H&E, ×40).

Given the histomorphological overlap with malignant spindle cell neoplasms, a broad immunohistochemically panel was performed. Tumour cells were negative for CD34, AE1/AE3, STAT6, SOX10, SMA, desmin, caldesmon, calponin, and ERG, while focal S100 positivity was observed[9]. The absence of diffuse CD34 expression and lack of subcutaneous honeycomb infiltration effectively excluded DFSP[7,8,21]. Negative pan cytokeratin staining ruled out spindle cell squamous cell carcinoma[11], whereas STAT6 negativity excluded solitary fibrous tumour. The absence of smooth muscle markers excluded smooth muscle neoplasms including leiomyosarcoma[6,11]. Although focal S100 positivity was present, the lack of diffuse staining and concurrent SOX10 negativity argued against neural differentiation[9]. Correlation of clinical, histopathological, and immunophenotypic findings established the diagnosis of cellular dermatofibroma[16,17]. Complete surgical excision was advised because of the lesion's hyperactive cellular nature, cosmetic reasons and recognised local recurrence potential. The patient remains under regular follow-up with no evidence of recurrence after six months. [Table 1, 2]

Table 1. Variants of Dermatofibroma

Variant	Clinical Features	Histopathologic Features	Key References
Common fibrous histiocytoma (classic DF)	Firm papule / nodule, commonly on lower limbs	Storiform spindle cells, epidermal hyperplasia, collagen trapping	1–3
Hemosiderotic DF	Brown to bluish lesion	Hemosiderin deposition, siderophages	1,3
Cellular DF	Larger, firm nodule	Hypercellular spindle cells, fascicular pattern	1–5
Aneurysmal DF	Rapidly enlarging, bluish lesion	Blood-filled spaces, multinucleated giant cells, hemosiderin	1–3,12
Epithelioid DF	Nodular lesion	Epithelioid cells arranged in sheets / nests	1,13
Lipidized DF	Yellowish papule / nodule	Foam cells, hyalinized collagen	2,14
Clear cell DF	Skin-colored nodule	Clear cytoplasm (glycogen-rich cells)	3,15
Atrophic DF	Depressed / atrophic lesion	Thinned dermis, decreased collagen	3,9
Palisading DF	Firm nodule	Palisading arrangement of spindle cells	2,4
Keloidal DF	Firm, scar-like lesion	Dense hyalinized collagen bundles	2,3
Granular cell DF	Small nodule	Granular eosinophilic cytoplasm	2,3
Myxoid DF	Soft papule / nodule	Myxoid stroma with abundant mucin	2,3
Lichenoid DF	Pigmented papule	Lichenoid lymphocytic infiltrate	2,3
Balloon cell DF	Skin-colored nodule	Ballooned vacuolated cells	2,3
Signet-ring cell DF	Rare nodular lesion	Vacuolated cells with peripheral, crescentic nuclei	2,3

DF: Dermatofibroma. References: 1. Weedon D. Skin Pathology. 5th ed. 2021; 2. Calonje E. McKee's Pathology of the Skin. 5th ed. 2020; 3. Sangüeza OP, Requena L. Dermatofibroma. Semin Diagn Pathol. 1998; 15: 19–27; 4. Mentzel T et al. Am J Dermatopathol. 1997; 19: 534–542; 5. Zelger B et al. J Cutan Pathol. 1993; 20: 326–334; 9. Ackerman AB. Histologic Diagnosis of Neoplastic Skin Diseases. 2018; 12. Fetsch JF et al. Am J Surg Pathol. 1991; 15: 64–72; 13. Kaddu S, Kindl S et al. J Cutan Pathol. 1996; 23: 382–386; 14. Requena L et al. J Cutan Pathol. 1991; 18: 322–327; 15. Zelger B et al. Am J Surg Pathol. 1992; 16: 980–985.

Table 2. Differential Diagnosis of a Spindle Cell Lesion of the Skin

Differential Diagnosis	Key Features	IHC Profile (Typical)	Findings in This Case	Diagnostic Interpretation
Dermatofibrosarcoma protuberans (DFSP)	Infiltrative growth in dermis "honeycomb" pattern, subcutis involvement	CD34 positive	CD34 negative	Ruled out (no CD34 expression and no subcutis involvement)
Spindle cell Squamous Cell Carcinoma (SpSCC)	Spindle cells with epithelial differentiation, keratinization	Cytokeratin (AE1/AE3, CAM5.2) positive	Cytokeratin negative	Ruled out (absence of epithelial markers)
Solitary Fibrous Tumor (SFT)	Patternless architecture with staghorn vessels	STAT6 positive, CD34 positive	STAT6 negative	Ruled out (STAT6 negativity)
Neural Tumor (Schwannoma / Neurofibroma)	Spindle cells with wavy nuclei, may show Verocay bodies	S100 and SOX10 diffuse positive	S100 focal and weak	Not supportive of neural origin (focal S100 only)
Smooth Muscle Tumor (Leiomyoma / Leiomyosarcoma)	Intersecting fascicles of spindle cells with eosinophilic cytoplasm	SMA, Desmin positive	SMA negative, Desmin negative	Ruled out (no smooth muscle differentiation)
Cellular Dermatofibroma	Dermal spindle cells in storiform or fascicular pattern, collagen trapping	CD34 negative, Factor XIIIa positive	CD34 negative, Factor XIIIa positive	Matches – Final diagnosis supported

IHC: Immunohistochemistry; SMA: Smooth muscle actin; S100: Protein S100; SOX10: Sex determining region Y-box 10; STAT6: Signal transducer and activator of transcription 6; CD34: Cluster of differentiation 34.

Mitotic figures were rare, estimated at less than one per 10 high-power fields (HPF), with no atypical mitoses identified. The lesion measured approximately 0.4 x 0.3 cm on gross examination and was confined to the dermis with no extension into the subcutaneous fat. Imaging (ultrasound or MRI) was not performed. Ceroscopy was not performed preoperatively; however, its incorporation into the workup of ambiguous dermal nodules could have aided preoperative differentiation. [Fig: 5]

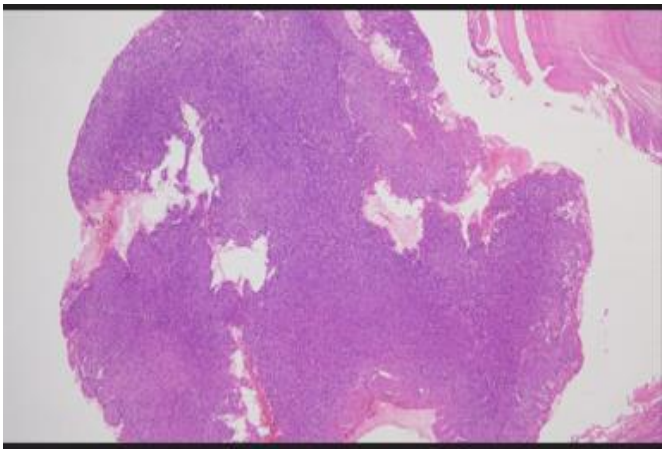

Figure 5: High-power view showing uniform spindle cells without atypia or abnormal mitoses (H&E, ×100).

Discussion

Cellular dermatofibroma is an uncommon variant of dermatofibroma characterised histologically by increased cellularity, fascicular spindle cell proliferation, and a greater tendency for deeper extension compared with conventional dermatofibroma[5,16,21]. Histopathology of cellular DF can resemble certain malignant spindle cell tumours such as DFSP, SpSCC, solitary fibrous tumor, neural or smooth muscle tumours (Table 2)[4,6,10,11]. This overlap highlights the importance of integrating IHC with routine histopathological assessment to avoid diagnostic pitfalls[6,20 and 21]. Despite its benign biological behaviour, CDF remains one of the most diagnostically challenging fibro histiocytic lesions because of substantial overlap with malignant spindle cell neoplasms. Awareness of this entity is therefore important for both dermatologists and dermatopathologists to prevent diagnostic misinterpretation and overtreatment. Cellular DF often presents as a firm dermal nodule, but its dense cellularity, stipiform-to-fascicular patterns, and occasional extension into the deeper dermis may raise suspicion for DFSP [4, 5]. DFSP typically shows diffuse CD34 positivity and infiltrates the sub cutis in a honeycomb pattern [7,8,21]. In contrast, cellular DF remains predominantly confined to the dermis and is CD34-negative[5, 7]. In the present case, the absence of subcutaneous infiltration and negative CD34 staining were key distinguishing features.

Among the differential diagnoses, DFSP represents the most important histopathological consideration owing to similarities in spindle cell morphology. DFSP, however, typically demonstrates diffuse strong CD34 positivity and infiltration of the subcutaneous fat in a characteristic honeycomb pattern.[7 ,8] neither feature was identified in the present case. The lesion remained confined to the dermis and lacked CD34 immunoreactivity, thereby strongly favouring CDF. Furthermore, unlike CDF, DFSP is characterised by the COL1A1-PDGFB fusion gene and demonstrates locally aggressive behaviour with a high propensity for recurrence if incompletely excised.

Despite the cellularity and fascicular growth pattern, several features definitively exclude DFSP in this case. DFSP characteristically demonstrates diffuse, strong CD34 positivity and infiltrates the sub-cutis in a honeycomb pattern neither of which was present. The lesion was entirely confined to the dermis. STAT6 negativity further excludes solitary fibrous tumour (NAB2-STAT6 fusion). Small biopsy specimens may be misleading due to sampling limitations and inability to assess full architectural extent; this case illustrates that definitive diagnosis may require complete excision for adequate histological evaluation. Although cellular DF is a benign entity, it carries a higher recurrence potential than classic DF, reported in up to 26% of cases in some series, and may rarely exhibit locally aggressive behaviour including subcutaneous extension. This recurrence risk justifies complete excision with adequate margins and structured clinical follow-up, as recommended in the management of this case[16-20]. The

pathogenesis of cellular DF is not fully elucidated. Current evidence favours a reactive fibro-histiocytic proliferation triggered by local trauma or inflammation, rather than true neoplasia[23, 24]. Clonal analyses have yielded heterogeneous results; some studies demonstrate polyclonality, supporting a reactive aetiology. The absence of recurrent driver mutations distinguishes cellular DF from true fibroblastic neoplasms such as DFSP8,[23, 24].

The focal S100 positivity seen in some cases of DF may mimic neural tumors, however the lack of diffuse S100 positivity and SOX10 negativity can help to exclude these entities.9 Spec is an important differential due to its spindle-shaped tumor cells, but cytokeratin expression is essential for its diagnosis. The negative AE1/AE3 staining in this case helped exclude SpSCC[10]. Spindle cell squamous cell carcinoma constitutes another important differential diagnosis because of its spindle-shaped morphology and occasional keratoacanthoma-like clinical appearance. However, the absence of epidermal dysplasia, keratinisation, and pan cytokeratin expression excluded epithelial differentiation in the present case. Similarly, STAT6 negativity excluded solitary fibrous tumour, while negative SMA, desmin, caldesmon, and calponin staining excluded smooth muscle neoplasms[9, 25]. Although focal S100 positivity was observed, this finding has been described in a subset of dermatofibromas and should not be misinterpreted as evidence of neural differentiation.[9] the lack of diffuse S100 staining together with SOX10 negativity effectively excluded schwannian neoplasms.

The present case additionally highlights the limited biopsy sampling in the evaluation of spindle cell lesions of the skin. Small or superficial biopsy specimens may inadequately demonstrate tumour architecture and depth, thereby contributing to potential over diagnosis of malignant spindle cell neoplasms. Complete excision with adequate histopathological sampling may therefore be necessary in selected diagnostically ambiguous lesions. Although cellular dermatofibroma is considered benign, recurrence rates higher than those observed in conventional dermatofibroma are have been reported, particularly in incompletely excised lesions.[5] rare cases demonstrating locally aggressive behaviour and extension into the superficial sub cutis have also been described. Complete excision and periodic follow-up are therefore advisable in hyperactive cellular variants.

The present case underscores the importance of integrating histomorphological findings with focused immunohistochemically analysis in the evaluation of cutaneous spindle cell lesions. Accurate classification is essential because the therapeutic implications differ substantially between benign fibro-histiocytic proliferations and malignant spindle cell neoplasms requiring aggressive surgical management.

Conclusion

Cellular dermatofibroma is an uncommon benign fibro-histiocytic neoplasm that may closely mimic malignant spindle cell tumours clinically and histo-pathologically. These tumours are often characterised by increased cellularity and a fascicular growth pattern[5, 17-20]. This case highlights the importance of immune-histochemical approach when evaluating spindle cell lesions of the skin. Relying solely on the morphology of the lesion and histopathology may lead to misdiagnosis and unnecessary aggressive surgical intervention. Careful clinic-pathological correlation supplemented by targeted immunohistochemistry is necessary for accurate diagnosis. Recognition of distinguishing features such as absence of diffuse CD34 expression, lack of subcutaneous honeycomb infiltration and negative epithelial and smooth muscle markers is uniquely significant in differentiating CDF from its malignant mimickers. Accurate diagnosis prevents unnecessary aggressive treatment and ensures appropriate patient management.

Three clinical imperatives emerge from this case: IHC is not supplementary but essential in cellular spindle cell lesions of the skin as morphology alone is insufficient; misdiagnosis as DFSP carries tangible consequences including unnecessary wide excision, sentinel node mapping, and imatinib

therapy; and complete excision with structured follow-up is warranted even for confirmed cellular DF given its recurrence potential[16-20]. Dermoscopy and imaging should be incorporated into workup protocols where available. Systematic documentation of collagen trapping, epidermal hyperplasia, and inflammatory infiltrate will enhance reporting quality in spindle cell lesions.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has provided consent for clinical information and images to be reported in the journal. The patient understands that names and initials will not be published and due efforts will be made to conceal identity, although anonymity cannot be guaranteed.

Author Contributions

Ruben Bhasin: Conceptualization, methodology and data collection, manuscript preparation.

Naaz Sharma: Data collection and analyses, literature review, manuscript review.

Sangeeta Mitra: Conceptualization, methodology, complete manuscript preparation, critical revision, and supervision.

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Conflicts of interest

There are no conflicts of interest.

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