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Report

A retrospective review of 93 cases of cellular dermatofibromas

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Abstract

Background Cellular dermatofibromas (CDF) are an uncommon variant of benign fibrous histiocytomas with propensity to recur and rarely metastasize as well as demonstrate histologic similarities to more dangerous lesions.

Objectives The aim of this present study was to further describe the presentation and outcome of the cellular variant of benign fibrous histiocytomas so that it can be diagnosed and treated appropriately.

Methods A retrospective chart review was performed on all patients seen in a single hospital system in Detroit, Michigan, from 2007 to 2017. CDF was confirmed by pathology. Baseline demographics, specialty service of diagnosis and treatment, treatment modality, and outcome were collected.

Results Of the 93 qualifying patients, the average age at diagnosis was 42.65 years. The most common specialty service that diagnosed and treated patients was dermatology (38.71%). About 95.0% of CDF stained positive for Factor 13A (19/20), and 90.48% were CD34 negative (19/21). Of patients, 33.33% had recurrences of their CDF (9/27). Two patients had three or more recurrences. One patient's death was attributed to the CDF.

Conclusion CDF have a high local recurrence rate and similarities to more dangerous and malignant lesions. Patients with cellular dermatofibromas present to many subspecialty services for diagnosis and should be treated aggressively.

Introduction

Cellular dermatofibromas (CDF), also known as "cellular fibrous histiocytomas" or "atypical dermatofibromas", are an uncommon variant of benign fibrous histiocytoma (BFH; dermatofibroma), which were first described in a series of case reports in 1994.[1] Patients with CDF often present with hyperpigmented papules with central hypopigmentation (Fig. 1). While BFH rarely recurs after incomplete excision, several reports have documented the rate of local recurrence of CDF ranging anywhere from 17 to 50%.[1–3] There have also been several reports of CDF metastasizing and sometimes resulting in death.[4–8] In this retrospective study, we sought to further describe the patient demographics, clinical characteristics, treatment modalities, recurrence rates, and specialty services that most frequently encounter cellular dermatofibromas, therefore helping to facilitate early recognition and treatment of this potentially aggressive diagnosis.

Methods

A retrospective chart review was performed on all patients diagnosed with cellular dermatofibroma who were seen by the Henry

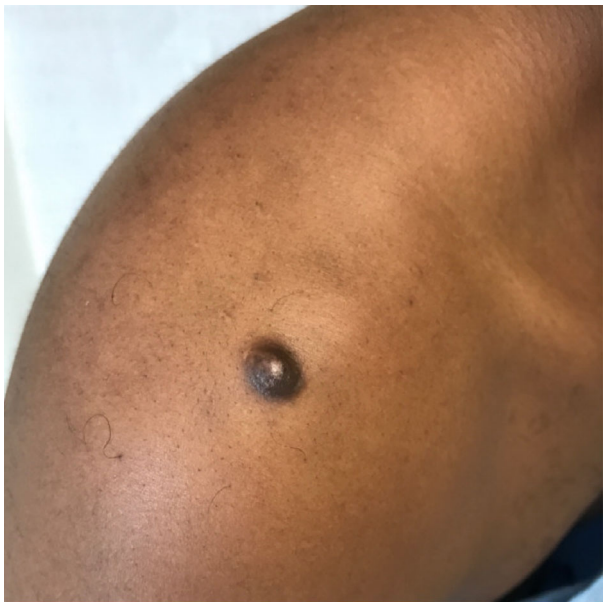

Figure 1 Cellular dermatofibroma on patient's shoulder

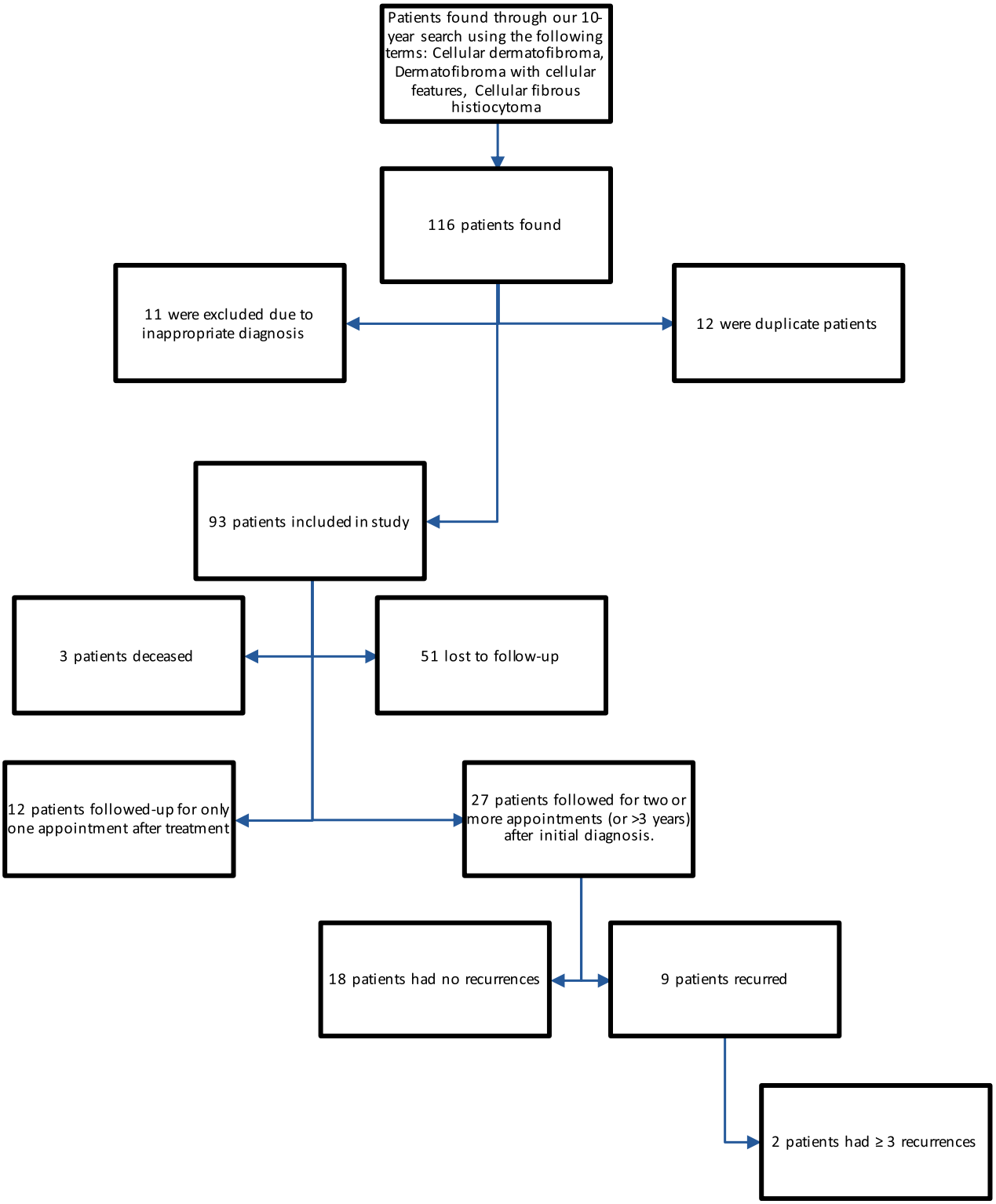

Figure 2 Flowchart of patients included in the study

Ford Health System from 2007 to 2017. The study was approved by the Institutional Review Board at Henry Ford Health System. A natural language search of the dermatopathology medical record system (Co-Path) was performed on all patients over the aforementioned 10-year period using the following keywords: "Cellular dermatofibroma", "Dermatofibroma with cellular features", and "Cellular fibrous histiocytoma." Only patients with an official pathology diagnosis of CDF were included in the study. The records of each patient were reviewed for baseline demographics, clinical characteristics, specialty service of diagnosis and treatment, treatment modality, and outcome with special attention paid to any patients with recurrence(s) of their CDF. The age of the patient was recorded at the time of the original biopsy, which confirmed the diagnosis of CDF.

Table 1 Patient demographics and distribution of lesions

Age (years)	**42.65 ± 16.7 (range 6–85)**
Gender	
Female	51 (54.84%)
Male	42 (45.16%)
Race	
Unknown	32 (34.41%)
Caucasian	29 (31.18%)
African-American	23 (24.73%)
Hispanic	3 (3.26%)
Indian	2 (2.15%)
Arabic	2 (2.15%)
Location of cellular dermatofibroma	
Extremity	43 (46.24%)
Trunk	24 (25.81%)
Acral	12 (12.90%)
Face	7 (7.53%)
Scalp	5 (5.38%)
Neck	2 (2.15%)

Results

A total of 116 patients were identified using the described search terms. Of these, 12 were duplicate patients (because of re-excisions and recurrences) and 11 were excluded from the study because of inappropriate diagnoses, which yielded a total of 93 patients with pathology-proven cellular dermatofibromas (Fig. 2). Average age at diagnosis was 42.65 years (standard deviation [SD] = 16.7 years) (Table 1 & Fig. 3). The majority of patients were female (54.84%) and Caucasian (31.18%), with the most common location of the CDF being on the extremity (46.24%) or trunk (25.81%) (Table 1).

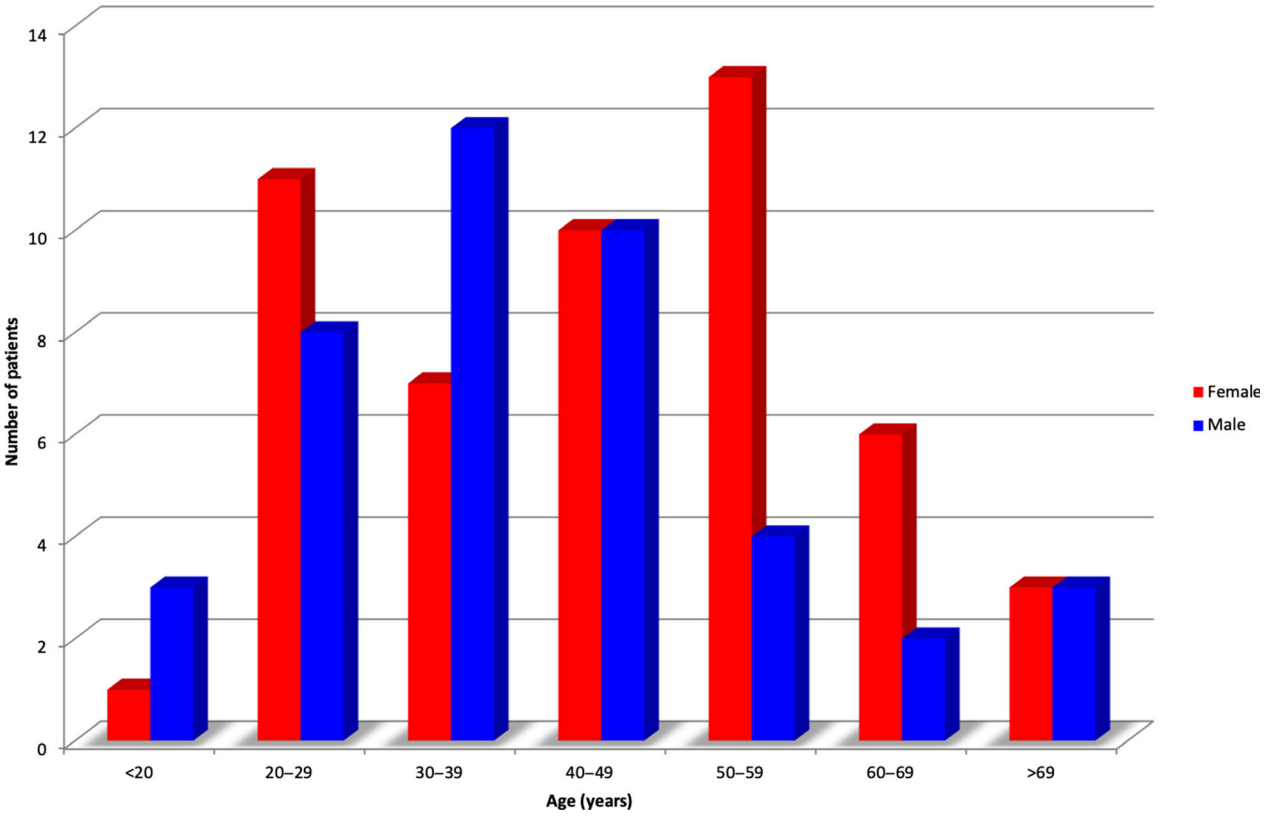

Figure 3 Age and gender of patients reviewed with cellular dermatofibromas

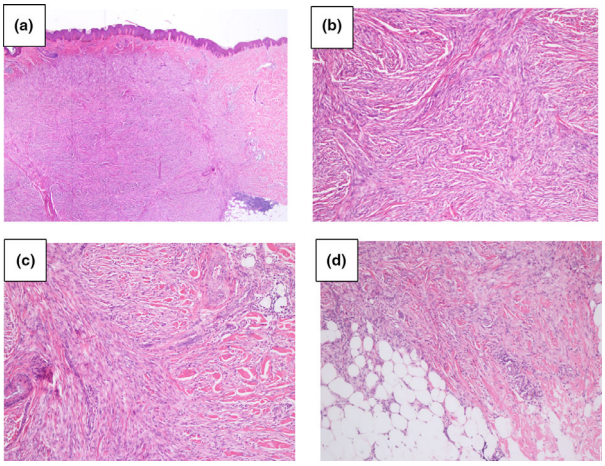

Figure 4 Histopathologic characteristics of cellular dermatofibromas. Key histopathologic findings suggestive of CDF include a large cellular collection in the dermis (hematoxylin-eosin stain [H&E], ×40) (a) with a storiform arrangement (H&E, ×100) (b). Additionally, CDF demonstrate collagen trapping normally visualized in dermatofibromas (H&E, ×100) (c). CDF can extend deep even to the subcutaneous fat but has minimal infiltration into the septae and lobules (H&E, ×100) (d)

CDF are recognized by histopathologic features including spindle cell proliferations with storiform appearance, peripheral collagen trapping, and increased cellularity with fibrohistiocytic cells (Fig. 4). These tumors also tend to be larger than BFH and extend to the deep dermis or into the subcutis. Of the 93 patients diagnosed with CDF, 29 of them had some form of immunohistochemistry (IHC) performed on their tissue sample(s). Of those studied, 95.0% were positive for Factor 13A (19/20), and 90.48% were CD34 negative (19/21). Additionally, 94.12% were S100 negative (16/17), 100% were desmin negative (0/7), 4/4 were vimentin positive, 5/5 were CD163 positive, and 3/5 were CD68 positive (Table 2 and Fig. 5).

Margins were evaluated and commented on in 62/93 cases (67.7%). The margins were noted to be positive either lateral and/or deep in 51/62 cases (82.3%) and negative in 11/62 (17.7%). About 8/9 patients with recurrent lesions were noted to have positive lateral and/or deep margins (88.9%).

The majority of patients were seen and treated by Dermatology (38.71%). The remaining patients were treated by Plastic Surgery (19.35%), General Surgery (13.98%), Family Medicine (7.53%), Orthopedics (2.15%), Podiatry (2.15%), Internal Medicine (1.08%), and Hematology & Oncology (1.08%) (Fig. 6).

The most common treatment modality was no re-excision after the original biopsy (27.84%) followed by wide local excision (23.71%), which, when documented, had average procedure margins of 24.38 mm (range = 10–60; SD = 22.59). Other treatment modalities included re-excision (18.56%), Mohs surgery (6.19%), or surgical excision (2.06%) (Fig. 7). Re-excision was defined as a procedure with margins less than 10 mm (average = 3.93; range = 2.0–6.0; SD = 1.33), and surgical excision was defined as a treatment when the patient was taken to the operating room and put under general anesthesia. Of the patients that had recurrences (9), five had been treated via re-excision, one via Mohs micrographic surgery, one via wide local excision, and two had no re-excision after the original biopsy.

Table 2 The number of patients with immunohistochemistry findings on the samples that were studied

	Positive	Negative	Total studied
Desmin	0	7	7
Factor 13A	19	1	20
CD34	3 (1 indeterminate)	19	21
Vimentin	4	0	4
S100	1	16	17
CD163	5	0	5
CD68	3	2	5
EMA	1	3	4
CD1a	0	2	2
CD31	0	2	2
Cytokeratin	0	9	9
BCL2	1	0	1
Smooth muscle actin	1	2	3
CD10	3	0	3
Factor 8	0	1	1
M181	3 (all low)	0	3
SMA	4	1	5
MelanA	0	2	2
Beta Catenin	1	1	2
AE1/AE3	0	3	3
Sox10	0	3	3
HMB45	0	1	1
CD99	1	0	1
PGP 9.5	1	0	1
HHF35	0	1	1
Pan keratin	0	1	1
KP-1	0	1	1

Of the original 93 patients included in our study, three passed away during the study timeframe. One death was attributed to the underlying CDF as there was sarcomatous extension into the chest wall with recurrent bleeding. The other two deaths were attributed to unrelated causes: acute myocarditis with respiratory distress syndrome (one) and natural passing (one). Fifty-one patients never followed up after diagnosis or treatment with the primary service that cared for their CDF. Of the 27 patients that did follow-up with their primary service for two or more appointments or over the span of two or more years, nine had recurrences of their CDF (33.33%). The average recurrence occurred at 14.56 months after original treatment (range = 1–60; SD = 15.59). Two patients had three or more recurrences. The most striking feature that was noted on the evaluation of recurrent cases was positive deep and/or lateral margins, which was found in 8/9 cases.

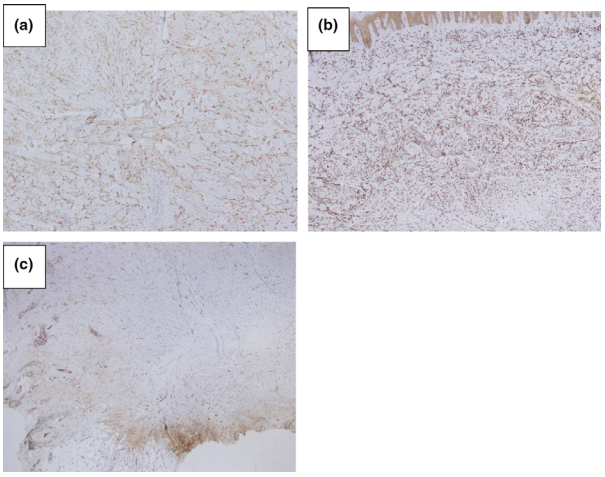

Figure 5 Cellular dermatofibroma immunohistochemistry (IHC) stains. IHC stains frequently employed to identify cellular dermatofibromas include positive factor XIIIa (×40) (a) and positive CD163 (×40) (b). CD34 is often used to differentiate CDF from dermatofibrosarcoma protuberans (×40) (c); however, at times this stain can be positive deeply near the fat

Discussion

Cellular dermatofibromas (CDF) constitute approximately 5% of all benign fibrous histiocytomas (BFH; dermatofibroma), the most common cutaneous spindle cell neoplasm.[9] Although the exact etiology of all dermatofibromas is unknown, they are thought to represent both a reactive and/or neoplastic process.

CDF are most commonly found on the extremities, but they can also develop on the face, ears, scalp, hands, and feet.[10] Females are affected slightly more frequently than males, especially those in their middle age.[9] While cutaneous dermatofibromas are generally considered a benign tumor, the cellular variant has been reported to have a significant tendency for recurrence after local excision and was found to recur in 33.33% of cases in the present study. Furthermore, because this study had a significant proportion of patients who were lost to follow-up (55.67%), the recurrence rate of CDF may be even higher than what we have reported.

The majority of patients with recurrent CDF were treated with either re-excision or Mohs micrographic surgery (6/9 patients), both of which have narrow margins of up to 10 mm. Furthermore, 8/9 recurrent cases were found to have positive deep and/or lateral margins. These findings suggest that a larger excision greater than 10 mm may be a more appropriate treatment modality. This information is relevant to all medical specialties as 61.29% of the patients in this study were diagnosed and treated by providers who did not practice dermatology.

In the literature, there have been a total of 11 documented cases involving CDF metastasizing to organs such as the lungs, lymph nodes, soft tissues, and liver.[8] Although we did not have any patients with distant metastases in our retrospective study, we cannot be certain that this did not occur in the patients who were lost to follow-up. Additionally, while we did not encounter any patients with distant metastases, one patient's death was thought to be because of aggressive local tumor growth resulting in acute hemorrhage, anemia, and thrombocytopenia.

There are several features that help to distinguish the CDF variant from the BFH. These include an average larger size (2 cm vs. 0.8 cm), higher cellularity, increased mitotic rate, possible presence of focal necrosis, limited cellular polymorphism, and common extension into the superficial fascia.[9,11] Because of these features, CDF may initially be misdiagnosed as dermatofibrosarcoma protuberans (DFSP) or leiomyosarcoma. Immunohistochemistry stains can be employed to help

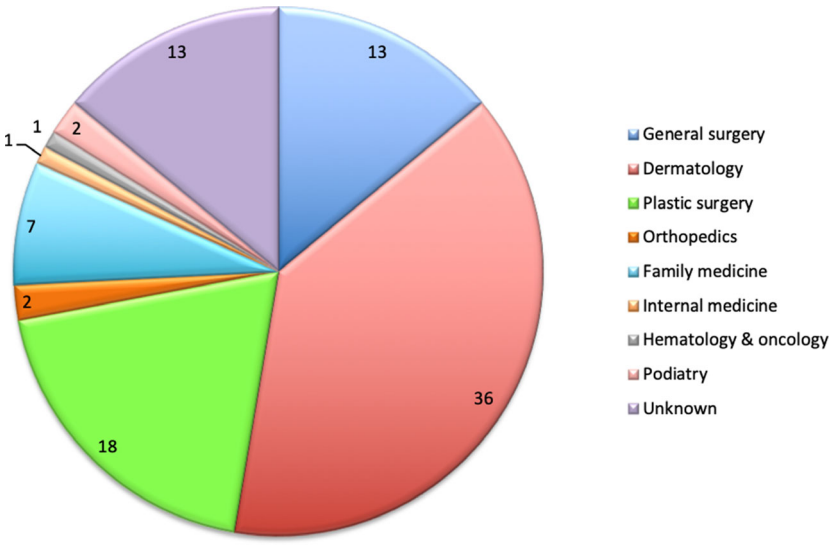

Figure 6 Distribution of the specialties that diagnosed and treated patients with cellular dermatofibromas

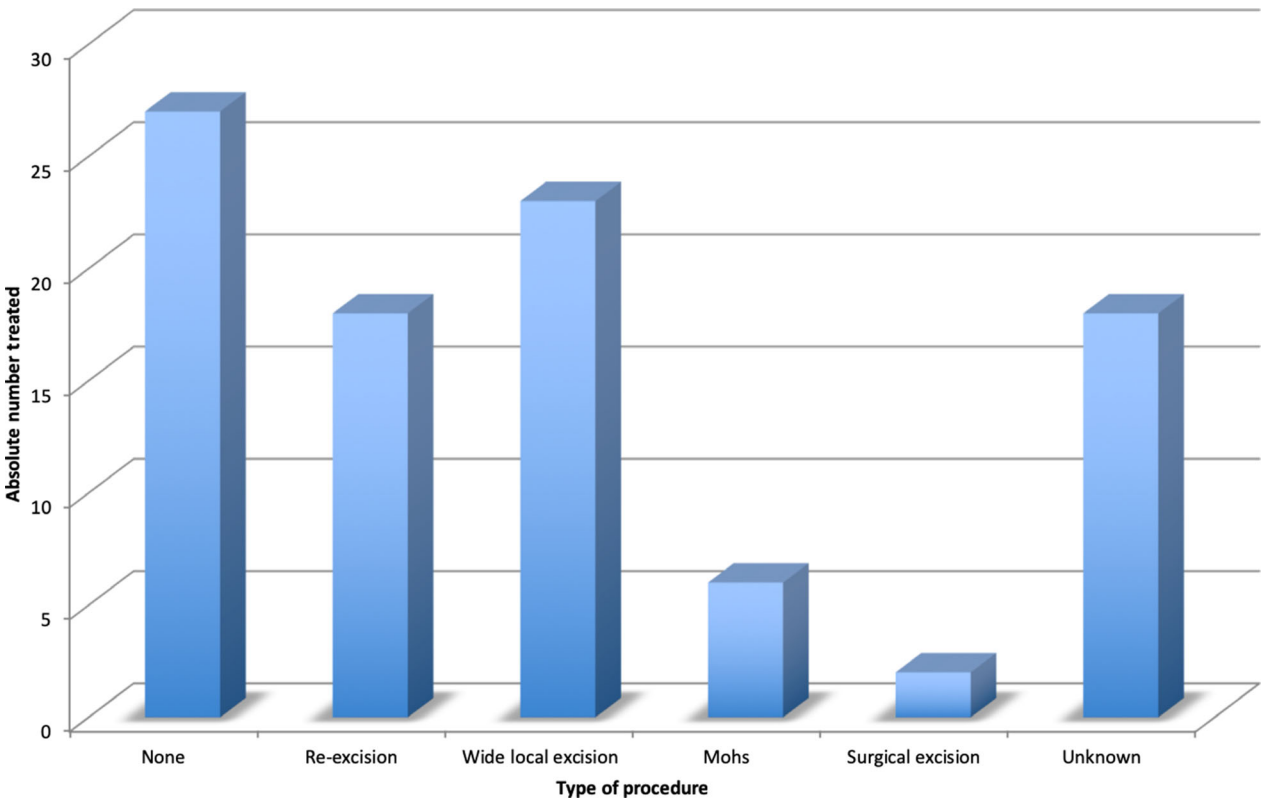

Figure 7 Absolute number of patients treated by modality

differentiate between these similar-appearing lesions. CDF have been found to predominately stain positive for factor 13a, whereas DFSP more commonly express CD34 (Fig. 3).[12,13] An additional IHC stain that can be helpful in distinguishing CDF from DFSP is CD163, which is a marker for monocytes, macrophages, and histiocytes. Our findings were consistent with what has been shown in the literature, in that of the CDF that were stained with IHC, 95.0% were positive for factor 13a, 90.48% were CD34 negative, and 100% were positive for CD163. We propose using factor 13a, CD34, and CD163 as the initial stains for lesions concerning for CDF on histology.

Although this review provides important characteristics about the uncommon cellular variant of BFH, there were several limitations. The retrospective nature of this study relied on providers to document all clinical findings, treatment, and recurrence in the patients' charts. Only 24.7% of patients had immunohistochemistry performed on their CDF biopsy, and the stains used were not standardized. Furthermore, there were a large proportion of patients that were lost to follow-up, which affects our reported recurrence rate and lack of metastasis.

Conclusion

Given the available literature and the results of this review, it is appropriate to counsel patients with CDF on the high local recurrence rate and similarities to more aggressive and malignant lesions. This study did not identify any key clinical or histology features to differentiate the recurrent cases from those that did not recur; however, the cases that recurred tended to have positive lateral and/or deep margins, which highlights the importance of complete excision. For these patients, the authors recommend re-excision of the lesion with margins >10 mm and close follow-up. Additional data and studies are needed to better define specific treatment recommendations for these lesions.

Acknowledgments

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