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REVIEW

Dermatofibroma: Reappraisal and Updated Review

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Abstract: Dermatofibromas (DF), also known as fibrous histiocytomas, are common benign cutaneous lesions characterized histologically by dermal proliferation of spindle-shaped fibrocytes, with the overlying epidermis often demonstrating hyperplasia with acanthosis, basal layer hyperpigmentation, and a characteristic "collarette" of epidermal hyperplasia surrounding the lesion. The etiology of DF remains debated, with theories ranging from reactive processes triggered by local trauma, such as insect bites, to spontaneous development. DF typically presents as a hyperkeratotic nodule or plaque, most often on the lower extremities, and can exhibit a wide spectrum of clinical appearances. Variants such as hemosiderotic, epithelioid, aneurysmal, and cellular DF show distinct clinical and histopathological features that may sometimes mimic malignant lesions. Dermoscopic findings can aid in diagnosis, although biopsy is often required for definitive classification. Discrepancies in the literature persist regarding the pathogenesis and classification of DF, and while DF is generally benign, rare cases of metastasizing DF have been reported. This review aims to provide an examination of DF, including its clinical manifestations, etiology, subtypes, histological features, and differential diagnoses. It also discusses dermoscopic findings, controversies in the literature, and current treatment options. A clearer understanding of its diverse presentations, along with refined diagnostic criteria, will enhance clinical management and treatment strategies.

Keywords: dermoscopy, histiocytoma, cutaneous lesions, subtypes

Introduction

Dermatofibroma (DF), also known as fibrous histiocytoma, is a common cutaneous lesion that is almost always benign and asymptomatic.[1–3] DF typically presents as firm, subcutaneous nodules measuring up to 1 cm in diameter, most commonly located on the extremities.[1] DF can occur in people of all ages, though it is mostly seen in adults and is rarely diagnosed during the first two decades of life. Dermatofibromas are usually asymptomatic but may occasionally cause pain, tenderness, or pruritus. Definitive diagnosis requires histological evaluation.[1] Histologically, DF is characterized by a dermal and, in some cases, superficial subcutaneous proliferation of spindle-shaped fibrocytes.[1,4]

The etiology of DF remains a subject of debate. Some cases seem to arise in response to local factors like inflammation or trauma, including insect bites, while others develop spontaneously without any identifiable trigger.[1,2] Despite its high prevalence, DF merits attention due to its varied clinical presentations, distinctive histological features, and tendency to be misdiagnosed as other dermatological disorders.[5]

This review provides a focused and up-to-date comprehensive examination of DF's clinical presentations, pathogenesis, subtypes, histological characteristics, dermoscopy findings, differential diagnoses, and current treatment options. Additionally, the review will include a case study that highlights a rare variant of DF. In February 2024, the terms "dermatofibroma" "fibrous histiocytoma" "common fibrous histiocytoma" and "superficial benign fibrous histiocytomas"

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were used in a PubMed literature search. Three independent reviewers selected relevant articles, ensuring a comprehensive analysis of the existing literature.

Clinical Presentation

DF is a soft tissue lesion that arises gradually as a single, 0.5 cm to 1 cm hyperkeratotic nodule with a red-yellowish brown surface.[4–6] Though it can occur anywhere on the body, it is most frequently seen on the lower extremities. Additional clinical manifestations include plaques, firm, flat, or numerous papular nodules, and a wide spectrum of coloration, ranging from pink to red.[4,6] There are rare variants of DF that can have atypical clinical presentations, such as metastasizing DFs, which, despite being considered benign, can spread. These are typically larger than common DFs, with an average diameter of 3.2 cm (range: 1–5 cm), and have the potential to metastasize to other areas of the body, most commonly the lungs.[6,7] Another rare variant, multiple eruptive DFs, accounts for fewer than 0.3% of cases. These lesions can develop rapidly in immunocompromised individuals, presenting as a plaque with a cluster of more than 15 papules accompanied by hyperpigmentation.[6,8] Polypoid or pedunculated DFs, which make up about 3% of the cases, present as brown, solid polypoid nodules with a thin pedicle.[9]

Pathogenesis

The exact etiology and pathogenesis of DF remains a topic of discussion and debate in dermatology. One popular hypothesis is that DF is a reactive process that occurs due to a local inflammatory response to some form of trauma, such as an insect bite or a ruptured hair follicle.[1,2] Support for this hypothesis comes from the frequent presence of inflammatory cells alongside fibrosis in DF lesions and the tendency for DF to progress from an initial inflammatory and cellular stage to a later stage characterized by fibrosis.[1,10] However, DF most often develops spontaneously, without any known precipitating event, which challenges this hypothesis.[1]

Alternatively, others have suggested that DF arises through a neoplastic process.[1,2,10] This hypothesis is mainly supported by the fact that DF rarely spontaneously regresses, the identification of clonality in DF through cytogenetic studies, and even rare reports of so-called "benign" metastases.[10] However, it is important to note that clonality alone does not confirm neoplasia, as it has also been observed in various other non-neoplastic conditions such as psoriasis and atopic dermatitis.[2]

It has also been hypothesized that DF may involve both inflammatory and neoplastic processes, but its exact pathogenesis remains unclear.[1]

Variants with Clinical Associations and Histopathological Features

DF and its variations exhibit a broad range of histopathological and clinical appearances. Although typical DFs are easily identified both clinically and histologically, the presence of variants can complicate diagnosis and may require biopsy confirmation. It is essential to accurately identify these variations to avoid misdiagnosing potentially malignant lesions.[5,11] Some of the recognized variants include common, epithelioid, hemosiderotic, aneurysmal, palisading, cellular, clear cell, lipidized, atrophic and angiomatoid variants.[5] A summary of clinical and histopathological features is provided in Table 1 and Figure 1.

Common DF

The most prevalent form of DF, common DF, typically presents as small, firm, hyperkeratotic nodules with a red-brown surface and often displays a characteristic "central dimple" sign when compressed laterally.[5] Histopathologically, it manifests as a non-encapsulated dermal lesion capable of infiltrating the superficial subcutaneous fat (Figure 2). The lesion contains spindle cells in short fascicles dispersed within a loose collagenous stroma, intermingled with multi-nucleated giant cells and foam cells, that tend to spare the papillary dermis creating the "grenz-zone". A diagnostic hallmark appears at the lesion's periphery, where individual collagen bundles are enveloped by lesional cells.[5,12]

Hemosiderotic DF

Hemosiderotic DF (also known as sclerosing hemangioma) poses a diagnostic challenge due to its resemblance to vascular tumors or melanomas on dermatoscopy. Additionally, hemosiderotic DF also exists on a spectrum with

Table 1 Clinical Presentation, Distinct Histopathological Features of Subtypes of DF

Subtype	Clinical Presentation	Distinct Histopathological Feature(s)	Able to be Differentiated Clinically from Common DF?
Common[12]	Reddish-brown to dark pigmented, slow-growing solitary lesion with central dimpling upon lateral compression	Proliferation of fibrohistiocytic cells with spindle cells in short fascicles, multinucleated giant cells, and foam cells with sparing of the papillary dermis (grenz-zone)	N/A
Epithelioid[5]	Red, polypoid nodule, usually on the limbs	Well-demarcated lesion composed primarily (>50%) of round or polygonal epithelioid cells with abundant eosinophilic cytoplasm, often surrounded by epidermal collarette	Yes
Hemosiderotic[13,14]	Homogenous blue to bluish-red or bluish-gray central pigmentation with fine peripheral pigment network, melanoma or vascular tumor-like pattern on dermoscopy	Proliferation of macrophages with cytoplasm rich in hemosiderin with heavy pigmentation	No
Aneurysmal[5,12]	Dark brown to red or blue (variegated coloration) papule, indolent growth followed by a rapidly growing phase caused by hemorrhage	Proliferation of histiocytes, hemosiderin-laden macrophages, and foam cells with blood-filled spaces without endothelial lining of varying sizes (slit-like to large cavities)	Yes
Palisading[15,16]	Firm, painless nodule most often occurring on the digits. Very rare variant.	Characterized by nuclear palisading, peripheral areas have features characteristic of common DF (proliferation of fibroblasts, histiocytes, foam cells), may mimic Verocay bodies.	No
Cellular[5,12]	Slow-growing solitary nodule, more likely to form on unusual sites including face/ears, hands, feet and preferentially impacts males	Prominent fascicular and focal storiform growth pattern, highly cellular and may infiltrate into the subcutis. Cells have highly eosinophilic cytoplasm.	Yes
Clear cell[17]	Clinically indistinguishable from common DF (firm, slow-growing nodule or papule that may be skin-colored or hyperpigmented)	Sheets of clear cells surrounded by thin sclerotic collagen and/or reticulin fibers, sometimes with spindle cells in storiform pattern, lymphocytic infiltrate or peripheral macrophages. No epidermal changes are seen.	No
Lipidized[5,18]	Solitary nodule, often exophytic, polypoid, and yellow in color and typically larger than common DF. Most commonly arises on the lower extremities, specifically the ankle.	Characterized by foam cell predominance and wiry stromal hyalinization, Touton-type giant cells and siderophages are frequently seen. Features co-exist with characteristics of common DF.	No
Atrophic[5,11]	Solitary patch with central depression/ umbilication, varying in color from flesh-colored to brown to erythematous	Hypocellular with dermal atrophy and predominated by sclerotic collagen	Yes

aneurysmal DF, which further complicates the differentiation between these subtypes.[5] According to Li et al, the hemosiderotic subtype of DF is more common in females and usually affects the extremities of young to middle-aged individuals, and it presents as a homogenous blue, bluish-red, or bluish-gray nodule with fine peripheral pigment network. Many cases are initially suspected to be melanoma based on dermatoscopic findings.[13,14] Microscopically,

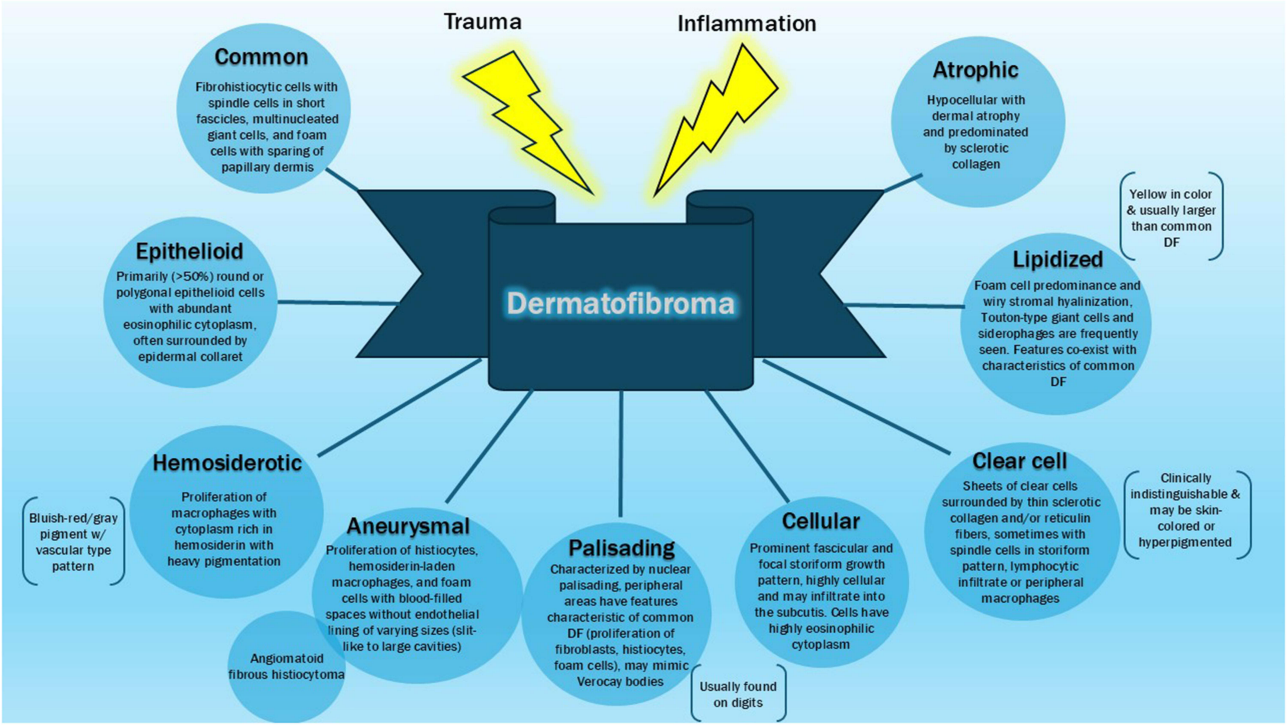

Figure 1 Graphic summary of various subtypes of dermatofibroma.

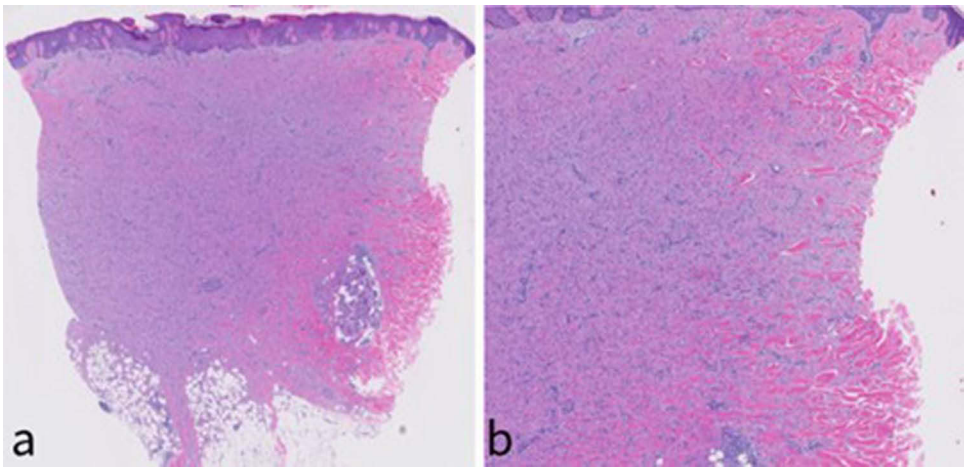

Figure 2 (**a**) Common Dermatofibroma (low power): Proliferation of fibrohistiocytic cells with spindle cells in short fascicles, multinucleated giant cells, and foam cells, with sparing of the papillary dermis (grenz-zone). (**b**) Keloidal collagen at the periphery, where individual collagen bundles are enveloped by lesional cells.

hemosiderotic DF is characterized by a prominent accumulation of intracellular and extracellular hemosiderin, detectable with iron staining, along with numerous small capillaries. Furthermore, acanthosis is frequently observed.[5,13,14,19–21] Histologically, hemosiderotic DF demonstrates multifocal interstitial hemorrhage with heavy hemosiderin deposition (Figure 3a and b).

Epithelioid DF

Wilson Jones et al first described epithelioid DF in 1989.[21] It often presents as a polypoid, erythematous lump that primarily affects the lower limbs (60%) and upper extremities (20%), with fewer cases on the trunk (10%) and head and neck (<10%). Due to its histological and clinical similarities to Spitz nevus and pyogenic granuloma, it is frequently

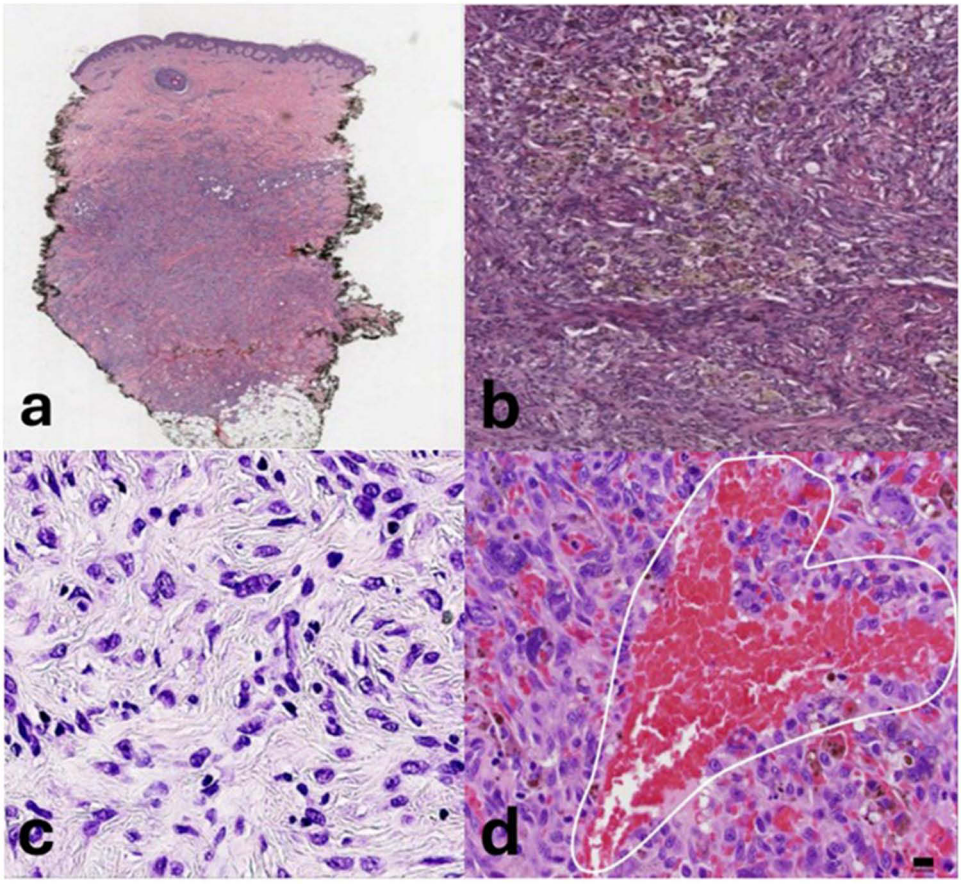

Figure 3 (**a**) Hemosiderotic DF (low power). (**b**) Hemosiderotic dermatofibroma (high power), shows multifocal interstitial hemorrhage with heavy hemosiderin deposition. (**c**) Epithelioid dermatofibroma: well-demarcated proliferation surrounded by an epidermal collarette. (**d**) Aneurysmal dermatofibroma: presence of blood-filled cystic spaces devoid of an endothelial lining, accompanied by small capillaries within the surrounding stroma, often seen within the white outlined heart-shaped area. (**c**) Reproduced from Secco L-P, Libbrecht L, Seijnhaeve E, Eggers S, Dekairelle A-F, De Roo A-K. Epithelioid Fibrous Histiocytoma with CARS-ALK Fusion: First Case Report. Dermatopathology. 2023; 10(1):25-29. https://doi.org/10.3390/dermatopathology10010003. Used under the licensing requirements of Creative Commons Attribution 4.0 International https://creativecommons.org/licenses/by/4.0/.[22] (**d**) Reproduced from Xie DY, Varughese N, Jared K, et al, (2019) AneurysmalDermatofibroma of the Earlobe: A Case Report. Dermatol Arch3(1):82-85. Used under the licensing requirements of Creative Commons Attribution 4.0 International https://creativecommons.org/licenses/by/4.0/.[23]

misdiagnosed as one of these entities.[12,24,25] Histologically, epithelioid DF presents as a well-demarcated proliferation surrounded by an epidermal collarette in the papillary and superficial reticular dermal areas (Figure 3c). By definition, at least 50% of the lesion consists of rounded or polygonal epithelioid cells with abundant eosinophilic cytoplasm and round to oval nuclei containing small eosinophilic nucleoli. Small vascular structures may be seen surrounding the epithelioid cells, and mild nuclear pleomorphism can be present.[5,12]

Aneurysmal DF

Aneurysmal DF constitutes approximately 1.7% of all DF types and is often associated with local trauma.[26] Its distinctive features, including rapid growth, variegated coloring, and potential for multiple lesions, necessitate a thorough evaluation to exclude more serious differential diagnoses such as malignant melanoma, and Kaposi sarcoma.[12,27,28] Histologically, a key diagnostic indicator of aneurysmal DF is the presence of blood-filled cystic spaces that lack an endothelial lining, along with small capillaries within the surrounding stroma (Figure 3d).[5,12] It is also noteworthy that aneurysmal DF is considered the final stage in the evolution of hemosiderotic DF, with the latter serving as a precursor.[5] Thus, a distinction is not always made between the two subtypes. Another unrelated tumor that is often confused with aneurysmal DF is angiomatoid fibrous histiocytoma, which will be discussed in detail later in this review article.[29]

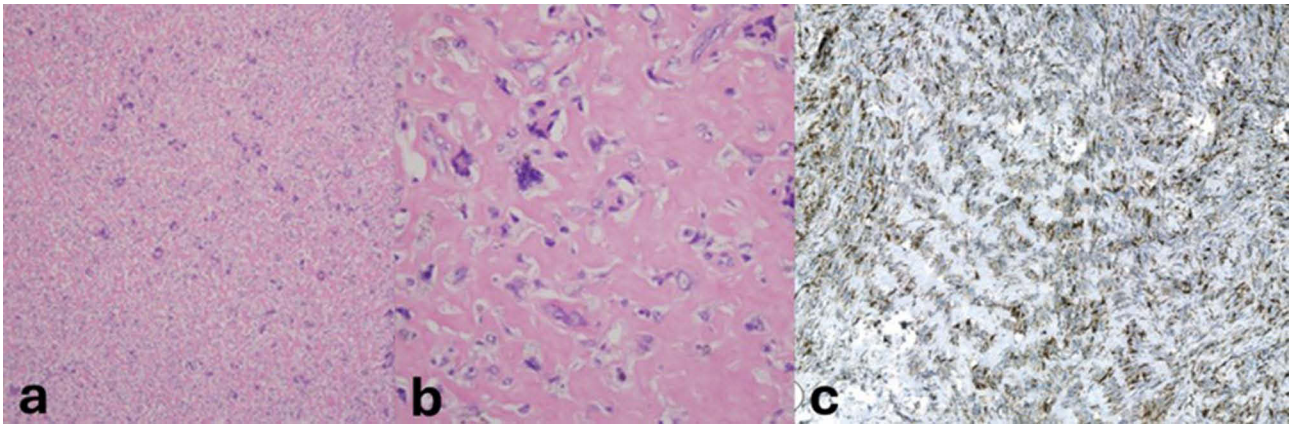

Figure 4 (**a**) Cellular Dermatofibroma: bland dermal proliferation of plump fibroblasts mixed with foamy histiocytes. (**b**) Cellular Dermatofibroma: close view of A. (**c**) Palisading Dermatofibroma: prominent palisading of nuclei. (**c**) Reproduced from Kok YB, Demirkesen C. Dermatofibroma with Verocay Body-Type Palisading Features and a Brief Discussion on Potential Schwannoma Mimickers of the Skin.Turk Patoloji Derg. 2023;39(3):218-220. Used under the licensing requirements of Creative Commons Attribution 4.0 International https://creativecommons.org/licenses/by/4.0/.[33]

Cellular DF

Cellular DF constitutes less than 5% of all DFs.[30] In a study of 216 cases, Gaufin et al found that the upper limb (41%) is the most common site of involvement, followed by the lower limb (39%).[31] While predominantly affecting the limbs, cellular DF have also been seen in atypical sites such as the back, chest, ears, and face.[12] Although rare, cases of cellular DF metastasizing to the lungs or local lymph nodes have been documented in the literature.[5]

Histologically, cellular DF exhibits a dense fibrohistiocytic proliferation arranged in fascicles, with lesional cells frequently displaying eosinophilic cytoplasm that can extend into the subcutis (Figure 4a and b). Hyperkeratosis and basal cell hyperpigmentation are commonly observed.[5,31] Due to histologic and immunopathologic overlap, it is critical to distinguish between DF and dermatofibrosarcoma protuberans (DFSP). DFSP, an uncommon soft tissue sarcoma, is characterized by local aggressiveness, a high recurrence rate following wide local excision, and a low metastatic potential. The absence of focal classical DF areas at the periphery is a key histological feature that distinguishes DFSP from cellular DF.[32]

Palisading DF

Palisading DF is a rare variant that poses significant diagnostic challenges. Typically, these lesions measure less than 20 mm in diameter and commonly manifest on acral sites.[15]

Histologically, palisading DF mirrors all the hallmark features of common DF. However, it also showcases regions of nuclear palisading (Figure 4c), a distinguishing feature that expands the differential diagnosis to include other tumors with a similar histologic arrangement. Among these are cutaneous and soft tissue tumors exhibiting a palisading pattern, such as palisaded encapsulated neuroma and schwannoma. Unlike these entities, which express S-100 protein (Calcium-binding proteins that regulate cell growth and inflammation and serve as markers for neural injury and melanoma) and are encapsulated, palisading DF lacks encapsulation and is S-100 negative.[15,16,34]

Clear Cell DF

Wambacher-Gasser et al described clear cell DF, identifying six cases of this novel variant. Since then, only 14 additional cases have been reported in the literature.[35,36] Clinically, clear cell DF presents as a nodule, most often located on the lower extremities, and is challenging to distinguish from common DFs.[36]

Histologically, this variant retains typical DF features while exhibiting sheets of clear cells with vesicular nuclei in the reticular dermis, sometimes extending into the subcutaneous tissue. Notably, clear cell DF lacks epidermal changes, a feature that can assist in differentiating it from other entities.[5]

Given the presence of clear cells, clinicians should consider both benign and malignant differentials when evaluating a lesion suspected to be clear cell DF. Relevant differentials include metastatic renal cell carcinoma, xanthogranulomatous reactions, melanoma, and clear cell sarcoma.[35,36]

Lipidized DF

Lipidized DF was first identified by Iwata et al.[18] Typically found on the ankles, this variation manifests as a solitary yellow nodule that is well-circumscribed. Due to its predilection to form on the ankles, lipidized DF has sometimes been informally referred to as "ankle-type" DF.[5] Patients with this variant are typically older, male, and often present in their fifth or sixth decade of life, compared to those with common DF. Lipidized DF also tend to be larger in size than common DF.[18,37]

Histologically, lipidized DF is characterized by abundant sclerotic collagen bundles surrounding foamy macrophages (Figure 5).[5]

Atrophic DF

Atrophic DF is another rare benign variation. Clinically, it appears as a single, asymptomatic, depressed patch with a central umbilication; however, some patients may experience discomfort or observe lesion enlargement.[39] Interestingly, patients with atrophic DF typically do not recall a history of trauma or insect bites– a contrast to those with common DF. According to Cohen et al, this variety is more commonly seen above the waist (72%), with only 28% of tumors found on the legs or buttocks. Additionally, there is a notable 5:1 female-to-male ratio in cases of atrophic DF.[11]

Histologically, atrophic DF shows dermal atrophy, which is characterized by conspicuous sclerotic collagen and low cellularity.[5]

Controversies and Reappraisal of the DF Subtypes

Over the years, numerous variants of DF have been described in the literature. Due to differing clinical and histological findings, diagnostic confusion often arises.[40]

Aneurysmal DF vs Angiomatoid Fibrous Histiocytoma

Aneurysmal DF frequently raises clinical suspicion for hemangioma due to its similar histological features, including epidermal hyperplasia and lateral collagen entrapment.[29] However, it is often mistaken for angiomatoid fibrous histiocytoma, an unrelated tumor. Both aneurysmal DF and angiomatoid fibrous histiocytoma are superficial lesions with blood

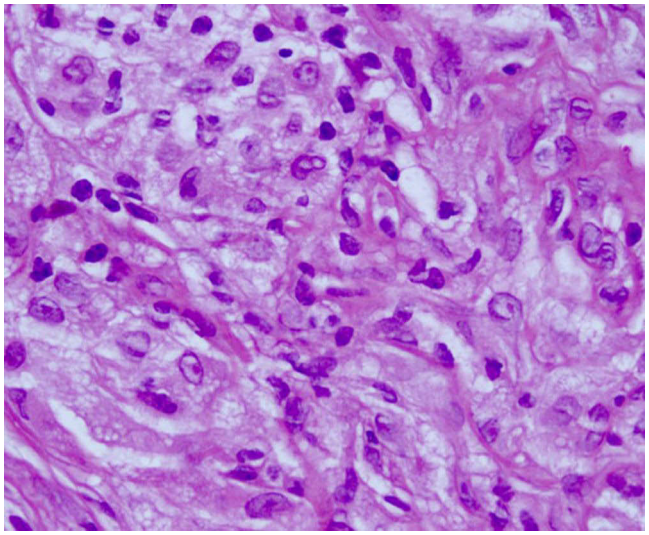

Figure 5 Lipidized Dermatofibroma: presence of foamy macrophages. Reproduced from Uzuncakmak TK, Oba MC, Sar M, Kutlubay Z. Dermoscopy of lipidized dermatofibromas. An Bras Dermatol. 2023;98(3):387-390. Used under the licensing requirements of Creative Commons Attribution 4.0 International https://creativecommons.org/licenses/by/4.0/.[38]

spaces, which contributes to diagnostic confusion.[41] Enzinger et al first proposed angiomatoid fibrous histiocytoma as a variation of malignant fibrous histiocytoma, distinguishing it from typical fibrous histiocytoma by its tendency to occur in significantly younger individuals and more superficial locations.[42] Costa's investigation found that wide excision improved prognosis for angiomatoid fibrous histiocytoma, leading to its classification as a separate entity.[43]

Angiomatoid fibrous histiocytoma is a tumor that occurs in the subcutaneous tissue of children and young adults and has the potential to spread to lymph nodes.[41] It is usually painless and presents as a subcutaneous soft tissue mass. On gross examination, angiomatoid fibrous histiocytoma lesions are firm, often multicystic and multinodular, and may exhibit areas of hemorrhage.[41] The tumor demonstrates indolent behavior and is classified as a tumor of "uncertain differentiation" with intermediate potential for malignancy.[41] This subtype has a relatively good prognosis, and treatment is primarily surgical.[41]

Histologically, angiomatoid fibrous histiocytoma lesions exhibit a pseudohematous hemorrhagic sac cavity, a mixture of spindle cells and ovoid cells, and the presence of mitotic figures (Figure 6a–c).[44] The tumors may also have lymphoplasmacytic infiltrate and intralesional hemorrhage.[41] While aneurysmal DF often presents with blood spaces and hemorrhage, it is characterized by a more heterogeneous cell population that includes giant cells and hemosiderin-laden macrophages. Notably, aneurysmal DF lacks the lymphoplasmacytic infiltrate, which can help distinguish between the two.[41]

Immunohistochemistry can be used to detect desmin and EMA expression, which aids in the accurate diagnosis of angiomatoid fibrous histiocytoma. Aneurysmal DF is typically desmin negative, while angiomatoid fibrous histiocytoma shows desmin positivity in about 50% of cases.[41] Fluorescence in situ hybridization (FISH) is another diagnostic tool for recognizing the EWSR1 gene, which is expressed in angiomatoid fibrous histiocytoma.[29]

Hemosiderotic DF vs Aneurysmal DF

Another diagnostic challenge in diagnosing specific subtypes of DF is distinguishing between hemosiderotic and aneurysmal DF. Both subtypes are characterized by extensive involvement of the subcutis and prominent acanthosis.[5] Additionally, they share clinical similarities with melanoma, often leading to diagnostic confusion. Hemosiderotic DF is thought to represent a precursor stage in the evolution of aneurysmal DF, yet distinctive features allow differentiation between the two.[5,40] Clinically, while both subtypes exhibit a vascular tumor-like or melanoma-mimicking appearance, aneurysmal DF is notably characterized by a rapidly growing phase, presumably due to hemorrhage into the lesion.[12] Histologically, both types contain hemosiderin-laden macrophages and capillary proliferation, but aneurysmal DF additionally features blood-filled cystic spaces without endothelial lining, providing a clear histopathologic distinction between these two subtypes on the same spectrum.[12]

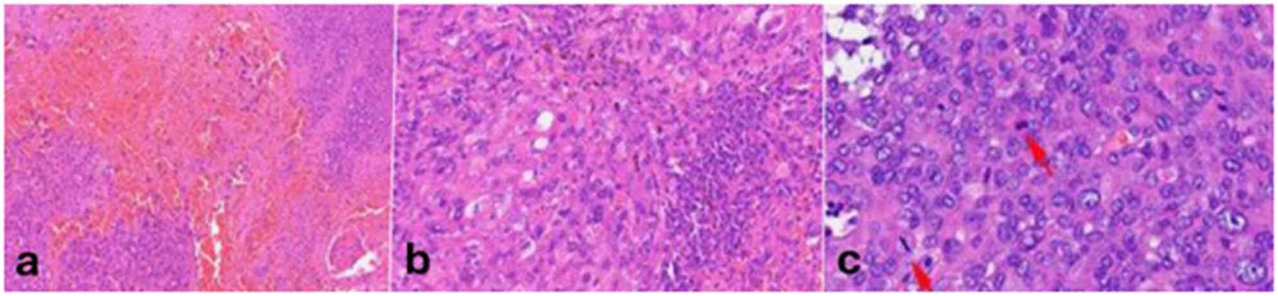

Figure 6 (**a**) A pseudohematous hemorrhagic sac cavity within the tumor. (**b**) Fat spindle cells and ovoid cells. (**c**) A mitotic figure is visible within the tumor, as indicated by the arrows. Image 6a reproduced from Feng D, Li Y, Li Z, et al. Angiomatoid fibrous histiocytoma with EWSR1-CREB1 gene fusion occurs in lungs and ribs with systemic multiple metastases: a case report and review of the literature. Front Oncol. 2025;14:1420597. Used under the licensing requirements of Creative Commons Attribution 4.0 International https://creativecommons.org/licenses/by/4.0/.[45] . Image 6b reproduced from Devi CA, Nargund A, Patil Okaly GV, Amirtham U. Angiomatoid Fibrous Histiocytoma, A Great Mimicker -A Short Series of 3 Cases with EWSR1 Fusion. Iran J Pathol. 2023;18(1):108-115. Used under the licensing requirements of Creative Commons Attribution 4.0 International https://creativecommons.org/licenses/by/4.0/.[46]

Perforating DF

Perforating DF is an uncommon variant that has not been widely recognized as a distinct subtype in dermatology, dermatopathology, or pathology. To date, there have only been three cases of perforating DF reported in the literature to date. Clinically, two cases presented with solid, erythematous crateriform nodules with central ulceration, while the third appeared as a hyperkeratotic erythematous papular lesion. Surprisingly, histological examinations of all three cases demonstrated spindle cell fascicles, collagen bundles, and elastic fibers "perforating" the epidermal layer. Despite the limited number of reported cases, their consistent clinical and histological findings suggest that perforating DF may represent a distinct clinico-pathological entity, manifesting as a crateriform nodule that closely resembles a -keratoacanthoma.[47–49]

Dermoscopic Features

Although most DF can be diagnosed based on their clinical appearance, differentiation from similar lesions, such as dysplastic nevi or malignant melanoma, can sometimes be challenging. In such cases, dermoscopy serves as a valuable diagnostic tool.[50,51]

The literature has defined four primary dermoscopic structures of DF: pigment network, core white scar-like patch, white network, and homogenous pigmentation.[50]

The pigment network, which resembles melanocytic patterns, is caused by hyperpigmentation in the rete ridges rather than melanocytic growth in the basal layer (Figure 7a).[17,50]

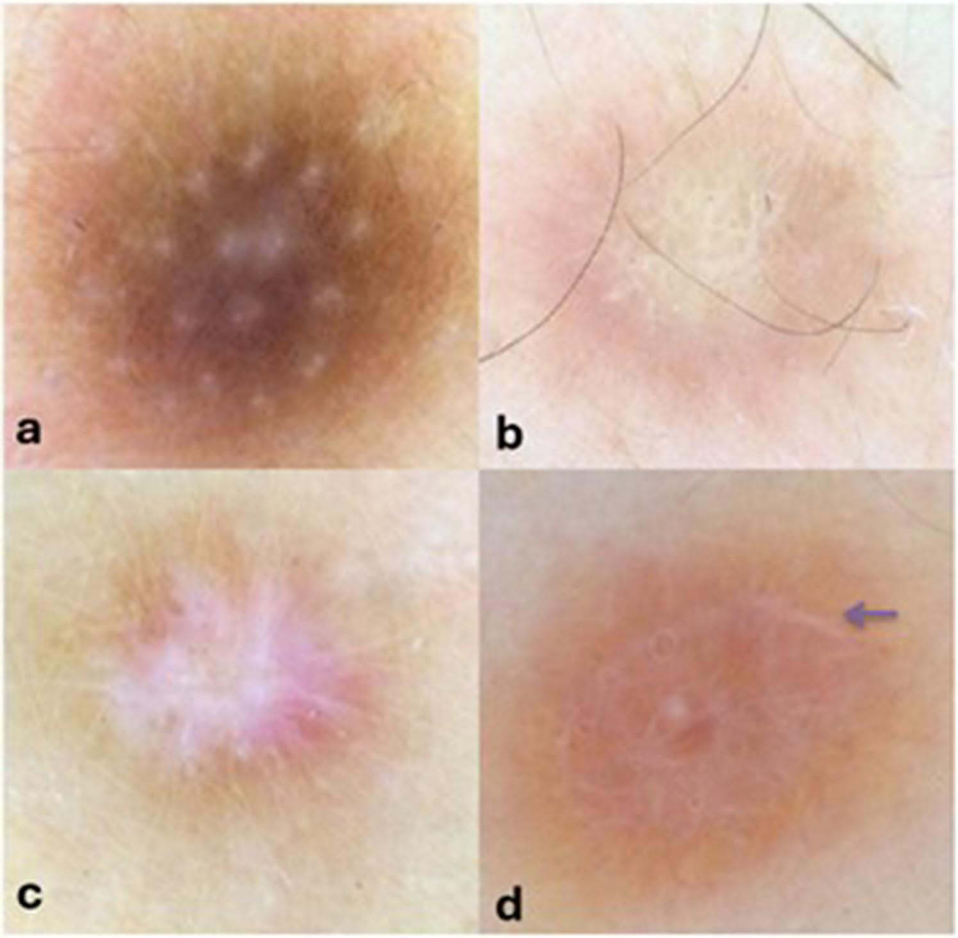

Figure 7 (**a**) Dermatofibroma on dermoscopy illustrating peripheral pigment network. (**b**) Central scar-like white patch. (**c**) Discrete peripheral network and star like white patch. (**d**) Homogeneous pigmentation with white structures forming a ring (black arrow). Reproduced from Kelati A, Aqil N, Baybay H, Gallouj S, Mernissi FZ. Beyond classic dermoscopic patterns of dermatofibromas: a prospective research study. J Med Case Rep. 2017;11(1):266. Published 2017 Sep 20. used under the licensing requirements of Creative Commons Attribution 4.0 International https://creativecommons.org/licenses/by/4.0/.[52]

Another key dermoscopic feature of DF is an irregular, well-demarcated central white scar-like area (Figure 7b). This feature is particularly important to differentiate from melanomas, dysplastic nevi, and Spitz nevi.[17,50]

Furthermore, Zaballos et al discovered a novel dermoscopic structure termed the white network, consisting of a pattern of brown holes intersected by white lines (Figure 7c). It's considered a variant of the traditional white scar-like patch.[17,40–44,47–50]

Homogeneous pigmentation is another dermoscopic feature observed in either the peripheral or central areas of the lesion (Figure 7d). This characteristic has been noted across multiple DF variants.[17,40–44,47–50]

Despite efforts to classify these features, studies have yet to reach a consensus regarding their prevalence in DF.[50] Nonetheless, a solid understanding of these four classic dermoscopic patterns enhances clinicians' ability to confidently distinguish DF from other skin lesions that may appear similar on gross examination.

Immunohistochemistry

The primary immunohistochemical markers used to diagnose DF include factor XIIIa (FXIIIa), CD34, D2-40, ERG, and IGFBP7.[53–56] Certain markers are particularly useful for distinguishing DF from other fibrohistiocytic lesions, especially dermatofibrosarcoma protuberans (DFSP) (Figure 8a and b).[53]

FXIIIa is typically strongly positive in dermatofibroma and negative in dermatofibrosarcoma protuberans (DFSP), while CD34 shows the opposite pattern—focally positive or negative in dermatofibroma and diffusely positive in DFSP. This reciprocal staining is the most reliable means of distinguishing the two entities.[53,57] D2-40 and IGFBP7 are also frequently positive in dermatofibroma but not in DFSP, offering additional diagnostic value.[55,56] ERG demonstrates nuclear positivity in most dermatofibromas and is negative in DFSP and hypertrophic scars.[54] Markers like Ki-67 (MIB-1) and phosphohistone-H3 can assess proliferative activity—typically low in dermatofibroma and higher in malignant fibrohistiocytic tumors—but are less specific diagnostically.[58,59]

Differential Diagnosis

Diagnosing DFs can be complicated due to the wide range of dermatologic conditions that share overlapping clinical features. A biopsy remains the most reliable method for confirming DF and ruling out alternative diagnoses. Table 2 highlights key conditions to consider in the differential diagnosis.[4]

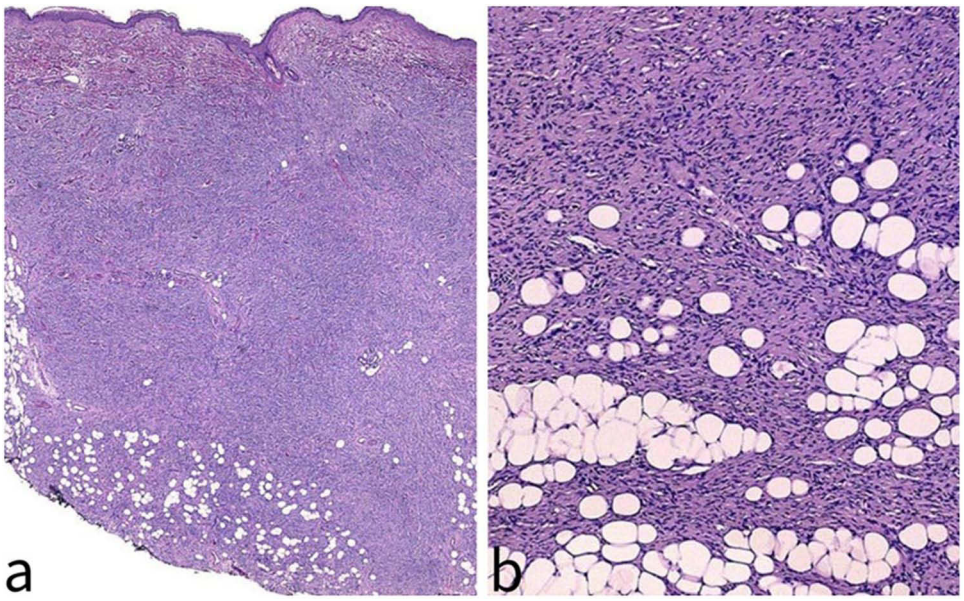

Figure 8 (**a**) Dermatofibrosarcoma protuberans (DFSP) low power, protuberant densely cellular proliferation of cells extending from an attenuated epidermis throughout the dermis and into the panniculus and fibrous septa. (**b**) The spindle cells infiltrate between adjacent collagen bundles and invade the adventitial collagen around adnexa, form fascicles of storiform, radiating and whorling patterns.

Table 2 Key Differential Diagnoses for Dermatofibromas

Differential Diagnosis	Clinical Features	Histological Features
Dermatofibrosarcoma protuberans (DFSP)[1,2,60]	Slow-growing, pink or purple painless plaque	Spindle cells in storiform pattern with "honeycomb" entrapment of subcutaneous fat, more involvement of the subcutis, more proliferative
Kaposi sarcoma[1,2,61]	Pink-purple patches or papules that progress to ulcerated nodules	Weaving fascicles of spindle-shaped cells containing degenerated erythrocytes
Basal cell carcinoma[1,62]	Pearly papules, sometimes with rolled borders or induration	Nodular, superficial, and morpheaform subtypes
Keloid scar[4,63]	Firm, rubbery nodules ranging in color from flesh-colored to erythematous or hyper-pigmented	Whorls of keloidal collagen
Prurigo nodularis[4,64]	Pruritic flesh-colored to pink nodules on extensor surfaces, typically in patients with history of chronic pruritus	Thick orthohyperkeratosis with irregular epithelial hyperplasia
Atypical fibroxanthoma[4,65]	Red nodule or plaque	Dermal tumor with spindle architecture, atypical mitotic figures, and pleomorphism
Keratoacanthoma[4,66]	Rapidly growing dome-shaped tumor with a central keratin plug	Proliferation of well-differentiated but enlarged and atypical keratinocytes with eosinophilic cytoplasm
Neurilemmoma[4,67]	Palpable asymptomatic mass, sometimes painful if compressing the affected nerve	Well-circumscribed, with degenerative changes, compact spindles, macrophages, and collagen fibers
Pilomatrixoma[4,68]	Firm, flesh-toned or pearly nodules, often asymptomatic	Well-demarcated islands of epithelial cells of varying appearance
Juvenile xanthogranuloma[4,69]	Firm papules or nodules, typically yellow-orange or brown, commonly asymptomatic	Well-demarcated dense infiltration of histiocytes with scattered lymphocytes, plasma cells, eosinophils
Melanocytic nevus[4,70]	Pigmented macule or papule	Proliferation of pigmented melanocytes
Blue nevus[4,70]	Bluish papule, macule, or nodule	Melanoma with dendritic melanocytes with mitoses and necroses
Leiomyoma[4,71]	Nodules varying in color from skin-toned to pink, red, or red-brown, sometimes painful	Bundles of collagen interweaved with bundles of smooth muscle cells with eosinophilic cytoplasm and "blunt-ended cigar-shaped" nuclei
Malignant melanoma[4,72]	Lesion with asymmetry, irregular border, variable color, diameter >6 mm, and elevated surface (ABCDE)	Atypical proliferation of melanocytes
Mastocytoma[4,73]	Non-tender yellowish-brown pigmented macules, papules, or nodules	Dermal infiltrate of mast cells with eosinophils and dermal edema, primarily in the papillary dermis
Spitz nevus[4,74]	Rapidly growing red, dome-shaped papule	Epidermal changes including hyperkeratosis, parakeratosis, and giant cells
Squamous cell carcinoma[4,75]	Lesions on sun-exposed areas of skin varying in color from flesh-colored to erythematous, sometimes with scale, ulceration, or crusting	Irregular nests, cords, or sheets of neoplastic keratinocytes with dermal invasion

Abbreviations: DF, Dermatofibroma; DFSP, Dermatofibrosarcoma Protuberans; FISH, Fluorescence in situ hybridization.

Management

The vast majority of DF are benign lesions with an excellent prognosis. While metastasis and rapid growth are uncommon, most DF remain stable over time. Notably, spontaneous regression has been documented in some cases.

While most DF are benign, it is crucial to watch out for specific clinical indications that could suggest an alternative diagnosis. These include abnormally large lesions with rapid growth, lymphadenopathy, or other signs concerning for malignancy.[4]

Treatment is typically not indicated for the majority of DF. In many cases, reassurance is sufficient rather than surgical excision, as the resulting scar may be more cosmetically noticeable than the original lesion. Treatment may be indicated for symptomatic or cosmetically bothersome lesions. The most effective method for such cases is complete surgical excision. While cryosurgery and superficial shaving are alternative options, their recurrence rates tend to be higher.[4]

Numerous treatment modalities have been documented in the literature with encouraging outcomes, including fractional 1540-nm erbium glass laser, Mohs micrographic surgery, pulsed dye laser, carbon dioxide laser with topical steroids, and intralesional steroid injection. However, clinical data supporting these approaches remain limited due to a lack of robust studies.[4,76–79]

Limitations

Our review is constrained by the limited literature on DFs. Additionally, the distinction between various histologic variants remains challenging due to overlapping features and the lack of a universally accepted classification system. Furthermore, while most cases of DFs are benign, rare cases of locally aggressive or recurrent lesions warrant further investigation to determine optimal management strategies. Lastly, there is a paucity of large-scale studies exploring the genetic and molecular underpinnings of DFs, highlighting the need for further research about their pathophysiology and potential therapeutic targets.

Conclusion

DF is a common benign skin lesion that is usually asymptomatic but can present with clinical and histological manifestations. Although the exact cause of DF remains debated, evidence suggests that factors like local trauma and inflammatory responses play a role in its onset. The existence of several variants complicates diagnosis and highlights the importance of histological confirmation to differentiate DF from malignant mimickers. Dermoscopy and recognition of unique histological markers are valuable tools in this process.

Although most DFs do not require treatment, those that are symptomatic or aesthetically concerning may warrant intervention. The mainstay of treatment for symptomatic DFs remains surgical excision, but minimally invasive approaches such as cryosurgery and laser therapy have shown potential. Nonetheless, the lack of substantial clinical evidence supporting these alternative treatments underscores the need for further research.

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