

## **Sclerotic fibroma-like dermatofibroma: an uncommon distinctive variant of dermatofibroma**

**M.C. González-Vela<sup>1</sup>, J.F. Val-Bernal<sup>1</sup>, M. Martino<sup>1</sup>, M.A. González-López<sup>2</sup>, E. García-Alberdi<sup>1</sup> and S. Hermana<sup>1</sup>**

<sup>1</sup>Department of Anatomical Pathology and

<sup>2</sup>Service of Dermatology Marqués de Valdecilla University Hospital, Medical Faculty, University of Cantabria, Santander, Spain

**Summary.** Dermatofibroma (DF) is a common benign cutaneous tumor with many variants based on alterations in the morphology and composition of its diverse elements. One very infrequent type is sclerotic fibroma-like DF (SF-DF). We report 7 new cases of SF-DF. In addition, their main clinicopathological and immunohistochemical features were compared with 14 unselected common DFs and with 3 sclerotic fibromas (SFs).

Microscopically, the 7 cases of SF-DFs showed an unencapsulated, well-circumscribed, hypocellular central nodule with thick collagen bundles arranged in a storiform pattern with prominent clefts. The overlying epidermis was attenuated. The periphery of this nodule was more cellular with histopathologic features of common DF. The 7 SF-DFs patients were 4 women and 3 men with a mean ( $\pm$ SD) age of 44.8 ( $\pm$ 15.5) years. These 7 patients were younger than those suffering from SFs [71.0 ( $\pm$ 17.3) years; ( $p=0.04$ )] and older than those presenting common DFs [30.5 ( $\pm$ 12.3) years; ( $p=0.03$ )]. Immunohistochemically, spindle cells in all 7 SF-DFs were negative for CD34 and CD99. On the contrary, the 3 cases of SF were positive for CD34 and CD99. All of the common DFs were negative for CD34 and only 4 (28.6%) of them were positive for CD99. In conclusion, SF-DF is an uncommon variant of DF with similar clinicopathological and immunohistochemical features. SF-DF shares certain histopathologic features with SF but they are immunophenotypically different. Therefore, both entities should be differentiated.

**Key words:** Sclerotic fibroma-like dermatofibroma, Common dermatofibroma, Sclerotic fibroma, Immunohistochemistry, Circumscribed storiform collagenoma

### **Introduction**

Dermatofibroma (DF) is a common benign skin tumor that usually occurs on the extremities, particularly the lower, of young or middle-aged adults (Niemi, 1970). Histologically, the tumor shows no sharp circumscription and is composed of varying proportions of fibrocytes, fibroblasts, myofibroblasts, histiocytes and histiocytic-like cells intermixed with variable numbers of giant cells, foamy macrophages, siderophages, lymphocytes and occasional plasma cells. The stroma is composed of many small blood vessels and variable amounts of mature collagen (Calonje and Fletcher, 1994). A wide diversity of histopathological variants of DF has been described (Calonje and Fletcher, 1994; Weedon, 2002).

Sohn et al. (2002) reported the first case of DF with sclerotic areas resembling a sclerotic fibroma (SF) of the skin. One part of the lesion was consistent with DF; another area adjacent to DF showed the characteristic pattern of a SF. The third area revealed transitional changes from DF to SF.

In this article we report 7 new cases of sclerotic fibroma-like DFs (SF-DFs) and review the literature on the matter. In addition, we examine the main clinicopathological and immunohistochemical features in comparison with 14 unselected common DFs and 3 SFs.

### **Materials and methods**

#### *Clinical material*

All cases were retrieved from the files of the Department of Anatomical Pathology at our hospital. We reviewed all consecutive cases of DFs diagnosed between January 2001 and June 2004, searching for lesions with prominent sclerotic changes. Out of 230 diagnosed DFs, there were 7 cases that showed a sclerosis pattern resembling a SF of the skin. The 3 SFs were also diagnosed at our institution; one of them has been recently reported (González-Vela et al., 2004).

### Clinical data and histopathologic study

Clinical data were obtained by reviewing the medical record file. The following variables were recorded: age, sex, tumor size, location and duration of the lesions. In all cases, sections of formaldehyde-fixed, paraffin-embedded material stained with haematoxylin and eosin were analyzed at the time of the study.

### Immunohistochemical study

Immunohistochemistry (IHC) was carried out in formalin-fixed, paraffin-embedded tissue sections by using the EnVision+ method (DAKO, Glostrup, Denmark) and a TechMate 500 automated immunostainer (BioTek, Santa Barbara, CA, USA). The following monoclonal antibodies were utilized: S100 protein (1:2000, Polyclonal, DAKO), CD34 (1:200, HPCA-1, Becton Dickinson, San José, CA, USA), CD99 (1:50, 12E7, DAKO), Vimentin (1:500, V9, DAKO), Ki67 (1:100, MIB1, Master Diagnostica, Granada, Spain) and CD68 (1:200, KP1, DAKO). An antigen retrieval technique was used for CD34, CD99, Ki67 and CD68 antibodies. Using a pressure cooker, sections were boiled for 2 minutes in 10 nmol sodium citrate buffer (pH 6.0) before staining. Diaminobenzidine (DAKO) was used as a chromogen. The slides were counterstained with Mayer's hematoxylin (Merck, Darmstadt, Germany) and dehydrated.

### Statistical study

A comparative study of the main general clinicopathological and IHC features between the 7 SF-DFs with 14 unselected consecutive common DFs and with 3 SFs was conducted.

Analysis was carried out using the STATISTICA package for Macintosh (Stat soft Inc. Tulsa, OK). Descriptive statistics were calculated for all variables. Results were expressed as mean ( $\pm$ SD). Categorical variables were compared following the chi-squared-test. Continuous variables were compared by using student's 2-tailed-t-test. Results were considered statistically significant at  $p < 0.05$ .

## Results

### Clinical findings

The main data of our 7 cases of SF-DFs, 3 SFs and 14 common DFs are summarized in Table 1. There were no statistical differences except for the age of the patients. SF-DFs occurred in patients older than did common DFs and younger than did SF. SF-DFs and common DFs were located more frequently on extremities than SFs. However, the difference did not reach statistical significance.

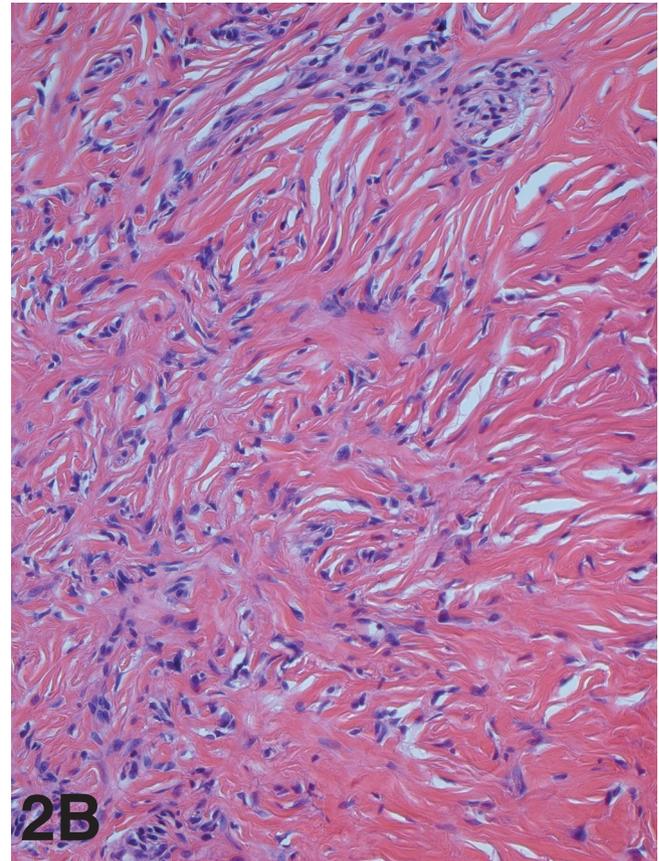
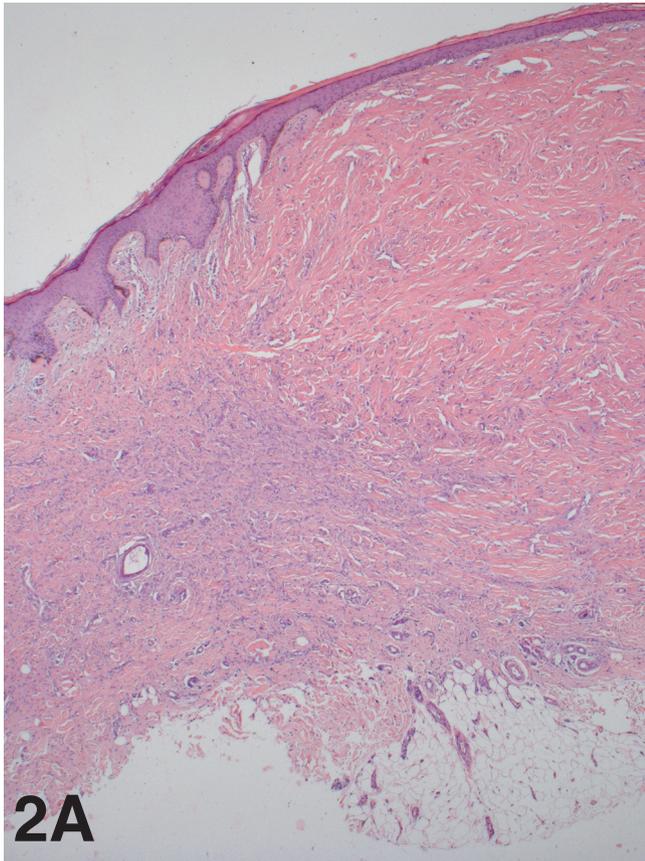
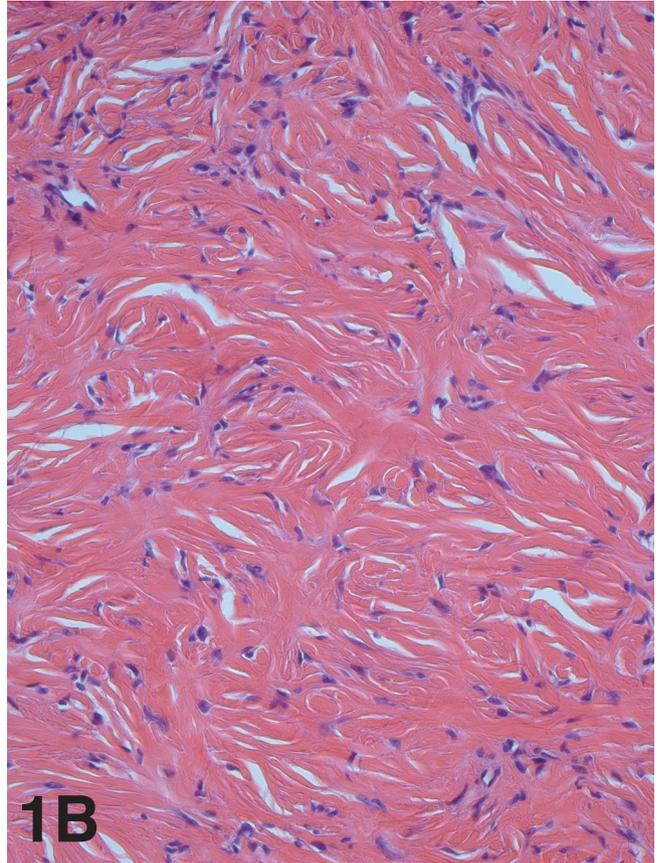
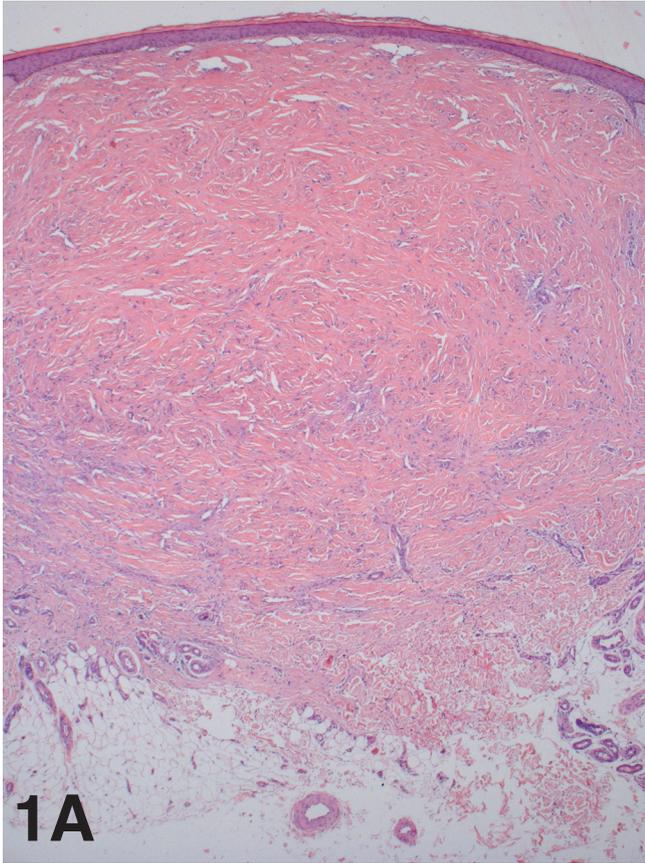
### Pathological findings

Microscopically, the 7 cases of SF-DFs showed a well-demarcated, non-encapsulated and eosinophilic dermal nodule (Fig. 1A). The central area of the nodule was composed of hypocellular hyalinized collagen bundles arranged in a characteristic storiform pattern with prominent clefts (Fig. 1B); similar to what is described in SF of the skin. The overlying epidermis was attenuated. Adjacent to this sclerotic area, the tumor showed a fibrohistiocytic proliferation with variable amounts of mature collagen consistent with DF (Fig. 2A). The fibroblasts at the periphery of the lesion were intercalated between thickened collagen bundles (Fig.

**Table 1.** Comparative study between sclerotic fibroma-like dermatofibroma (SF-DF), common DF and sclerotic fibroma (SF).

	SF-DF (N= 7)	COMMON DF (N= 14)	SF (N=3)
<i>General clinicopathological data</i>			
Mean age ( $\pm$ SD)	44.8 ( $\pm$ 15.5) *	30.5 ( $\pm$ 12.3)	71 ( $\pm$ 17.3)
Sex; female/male (%)	4/3 (57.1%)	9/5 (64.3%)	2/1 (66.7%)
Mean ( $\pm$ SD) tumor size	9.7 mm ( $\pm$ 4.2)	7.6 mm ( $\pm$ 2.6)	7 mm ( $\pm$ 1.73)
<i>Anatomical location</i>			
Head and neck	0	0	2 (66.7%)
Trunk	1 (14.3%)	2 (14.3%)	0
Extremities	6 (85.7%)	12 (85.7%)	1 (33.3%)
<i>Immunohistochemical study**</i>			
Vimentin	7/7 (100%)	14/14 (100%)	3/3 (100%)
MIB-1	0/7 (0%)	0/14 (0%)	0/3 (0%)
S100 protein	0/7 (0%)	0/14 (0%)	0/3 (0%)
CD68	7/7 (100%)	14/14 (100%)	0/3 (0%)
CD34	0/7 (0%)	0/14 (0%)	3/3 (100%)
CD99	0/7 (0%)	4/14 (28.6%)	3/3 (100%)

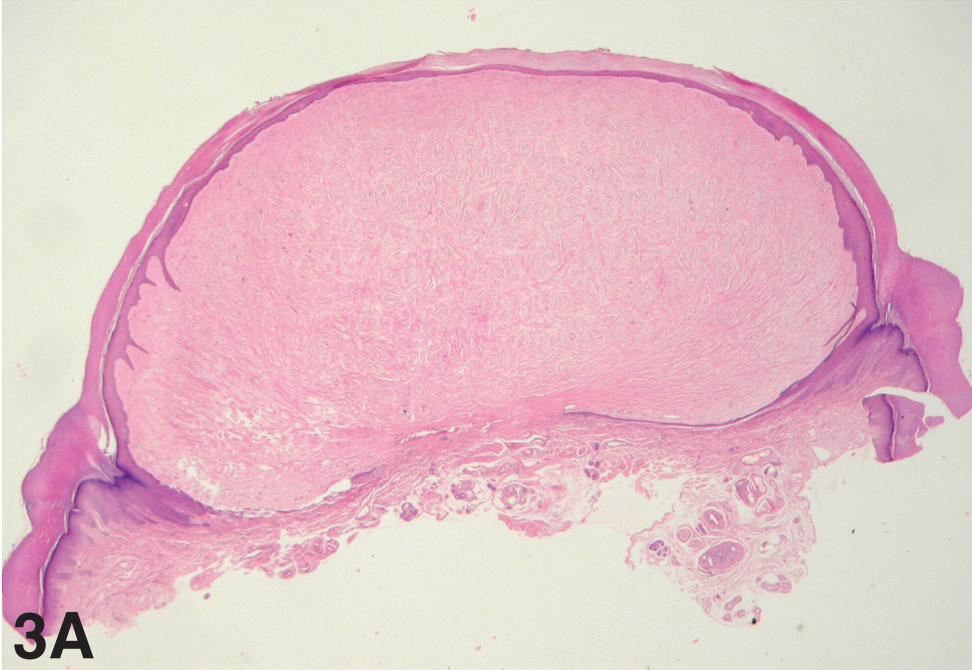
\*: patients with SF-DFs were older than common DFs ( $p = 0.03$ ) and younger than SF ( $p = 0.04$ ); \*\*: expressed as number of positive cases/number of total cases (percentage) .



**Fig. 1. A.** Dermatofibroma with prominent central sclerotic change. **B.** Higher magnification reveals thick eosinophilic staining collagen bundles separated by prominent clefts.

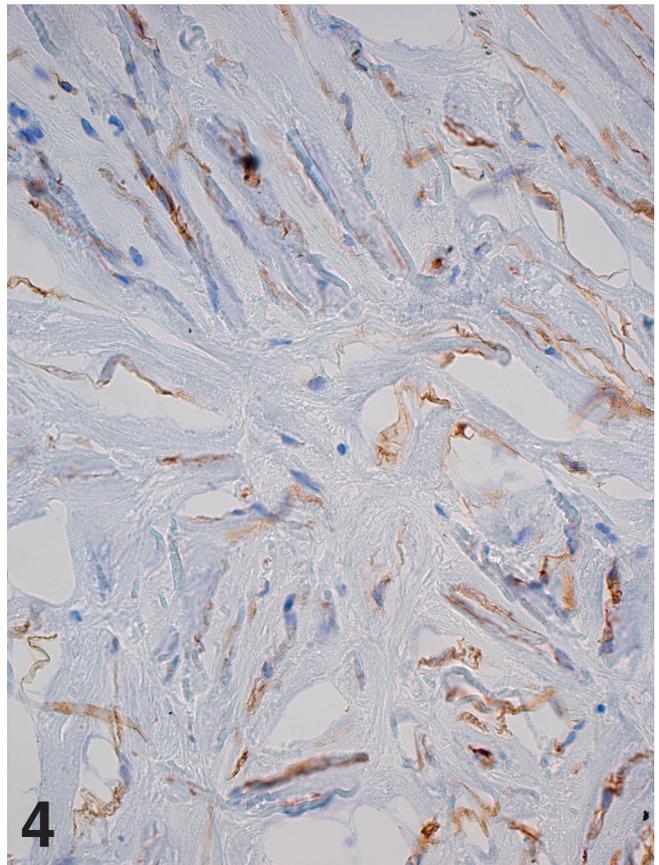
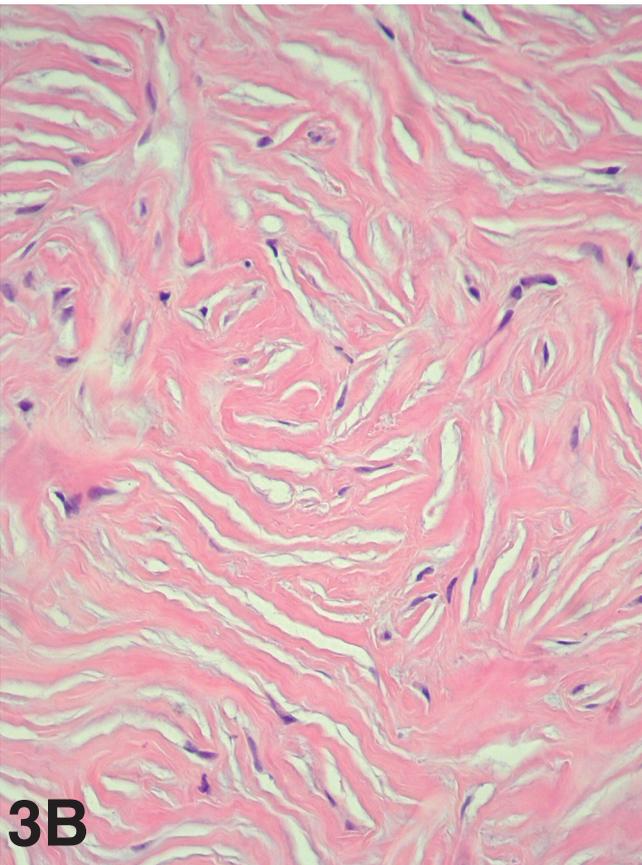
**Fig. 2. A.** The periphery of the lesion shows a fibrohistiocytic proliferation. **B.** The fibroblasts are interspersed between collagen bundles.

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**Fig. 3. A.** Sharply circumscribed hypocellular and eosinophilic dermal nodule. **B.** The tumor is composed of thick collagen bundles arranged in a storiform pattern.

**Fig. 4.** Diffuse cytoplasmic reactivity for CD34 in sclerotic fibroma.



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2B). The epidermis was acanthotic showing basal hyperpigmentation.

Histopathologic examination of the SF showed a well-demarcated, non-capsulated, round, hypocellular and eosinophilic nodule (Fig. 3A). The nodule was composed of hyalinized sclerotic collagen bundles arranged in a whorled pattern. Prominent clefts between collagen bundles were observed (Fig. 3B).

### Immunohistochemical findings

The IHC results are summarized in Table 1. All the cases of the 3 groups were positive for vimentin and negative for MIB-1 and S100 protein. Positivity for vimentin was observed in more than 80% of tumor cells in SFs and SF-DFs. Between 50-80% of tumor cells in DFs were immunoreactive for vimentin. The 3 SFs were negative for CD68 and positive for CD34 (Fig. 4) and CD99. On the contrary, both SF-DFs and common DFs were positive for CD68 and negative for CD34. CD68 positive cells were more numerous in DFs than in SF-DFs, but their percentage in relation to the total number of tumor cells was variable. CD99 was negative in all SF-DFs, while 4 out of 14 common DFs were immunoreactive for CD99. These 4 labeled cases had between 5-20% of tumor cells positive. CD99 positive cells were predominantly found at the tumor periphery. However, there was no significant difference between DFs and SF-DFs with respect to the immunoreactivity for CD99.

### Discussion

Sclerotic fibroma (SF) is an uncommon fibrocytic neoplasm that occurs sporadically as a solitary lesion and in multifocal form in patients with Cowden's disease

(Weary et al., 1972; Rapini and Golitz, 1989). This lesion shows a distinctive histological and architectural pattern (Metcalf et al., 1991). Histologically, it is characterized by a well-circumscribed dermal nodule composed of sparse spindle cells with alternating hyalinized bundles of collagen arranged in a storiform pattern (Rapini and Golitz, 1989). The histogenesis of this lesion remains uncertain. Thus, some authors even have advanced the possibility that SF may represent the end-point of a pre-existing lesion such as DF (Rapini and Golitz, 1989; High et al., 2004). On the contrary, other dermatopathologists support the idea that SF is a distinct clinicopathologic entity (Cohen et al., 1999; Requena et al., 1991).

We report 7 new cases of SF-DFs and review the literature (Pujol et al., 1996; Sohn et al., 2002; Mahmood et al., 2003; High et al., 2004), (Table 2). Although SF-DF bears histopathological resemblance to SF, the latter displays a uniform pattern (sclerotic) and a sharp circumscription of the whole lesion (Metcalf et al., 1991). SF tends to evolve as expansive masses which push aside the normal dermal collagen, unlike SF-DF in which the proliferating cells interpose between the collagen bundles at the periphery of the lesion. SF-DF could be regarded as an inflammatory process while in contrast, SF could be considered a benign neoplasia or hamartoma.

IHC may be very useful in differential diagnosis. CD34 and CD99 were negative in our 7 cases of SF-DF and positive in the 3 cases of SF. These findings are similar to the results of a previous study (Mahmood et al., 2003). On the contrary, High et al. (2004) showed negativity for CD34 in both SF and SF-DF.

On the other hand, IHC shows similar staining characteristics in SF-DF and common DF. Both tumors were always negative for CD34 and only occasionally

**Table 2.** Main findings of published cases of sclerotic fibroma-like dermatofibroma.

CASE/ AUTHOR	AGE/SEX	LOCATION	SIZE (mm)	LESION DURATION (years)	HISTOPATHOLOGICAL FINDINGS location of sclerotic changes	IMMUNOHISTOCHEMICAL STAINS	
						Positive	Negative
1/ Sohn	36/M	Lower leg	10	10	center	Factor XIIIa,	S100
2/ Mahmood	43/M	Neck	7	Several	center	Factor XIIIa,	S100, CD34, CD99, MIB1
3/ High	49/F	Thigh	ND	ND	center	Factor XIIIa, Procollagen I	S100, CD34, MIB1
4/ High	42/F	Lower leg	ND	ND	center	Factor XIIIa, Procollagen I	S100, CD34, MIB1
5/ High	54/M	Thigh	ND	ND	center	Factor XIIIa, Procollagen I	S100, CD34, MIB1
6/ Pujol	23/M	Face	4	Several	periphery and deep area	Factor XIIIa, Vimentin	S100
7/ Pujol	36/M	Back	12	Several	periphery and deep area	Factor XIIIa, Vimentin	S100
8/ present	40/F	Lower leg	9	Several	center	Vimentin, CD68	S100, CD34, CD99, MIB1
9/ present	52/M	Abdomen	6	2	center	Vimentin, CD68	S100, CD34, CD99, MIB1
10/ present	45/M	Lower leg	6	Several	center	Vimentin, CD68	S100, CD34, CD99, MIB1
11/ present	27/F	Lower leg	4	Several	center	Vimentin, CD68	S100, CD34, CD99, MIB1
12/ present	67/M	Lower leg	10	Several	center	Vimentin, CD68	S100, CD34, CD99, MIB1
13/ present	58/F	Lower leg	10	Several	center	Vimentin, CD68	S100, CD34, CD99, MIB1
14/ present	25/F	Lower leg	12	Several	center	Vimentin, CD68	S100, CD34, CD99, MIB1

F: female; M; male; ND: No data.

common DF was positive for CD99. To the best of our knowledge, reactivity for CD99 in common DF has not been described before.

Because of the large numbers of CD34-reactive cells only in SF, we consider them to be the main cells and not merely entrapped cells. Positivity for CD34 in SF had already been previously described (Hanft et al., 2000). CD34 was originally characterized as a bone-marrow progenitor cell antigen (Civin et al., 1984). It has been identified on a small number of other normal cell types and on a variety of tumors (van de Rijn and Rouse, 1994). In normal human skin a minority of the interstitial cells expresses CD34, being more numerous in the reticular dermis and around adnexal structures (Nickoloff, 1991). The CD34 positivity in SF and the negativity in SF-DF suggest a distinct histogenesis.

SF-like changes may well be able to be considered a distinct reaction pattern that may also be seen focally in a wide variety of other inflammatory, neoplastic and hamartomatous conditions (High et al., 2004). This common sclerotic reaction pattern could be explained as a result of common pro-sclerotic cytokine secretion that increases the collagen synthesis by fibroblasts. It has been proposed that cutaneous DF arises from dermal dendrocytes that represent bone marrow derived monocytes/macrophages, which could provide the pro-sclerotic cytokines secretion.

Keloidal dermatofibroma (Kuo et al., 1998) also exhibits a superficial circumscribed area of sclerotic change under an atrophic epidermis in an otherwise ordinary dermatofibroma. However, the collagen fibers are irregularly oriented, thick, brightly eosinophilic, i.e., show a keloidal change. This change could be viewed as secondary and imposed by a traumatic injury to a pre-existing dermatofibroma.

In summary, SF-DF and common DF show similar clinicopathological and immunophenotype features. Thus, SF-DF could represent a later, more sclerotic stage of DF. On the other hand, the immunohistochemical profile from SF-DF and common DF are different from SF. Finally, SF-DF shares certain histopathologic features with SF but they are immunophenotypically different. Therefore, both entities should be differentiated.

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