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Case Report

Pseudoangiomatous spindle cell lipoma: a case report and literature review

Shuai Chen[1*], Zhi-Hong Cui[2*], Ren-Ya Zhang[1]

[1]*Department of Pathology, Affiliated Hospital of Jining Medical University, Jining, Shandong Province, P. R. China;* [2]*Department of Pathology, The Second People's Hospital of Jining, Jining, Shandong Province, P. R. China.* [*]*Equal contributors.*

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Abstract: Spindle cell lipoma (SCL) is a benign lipomatous and fibroblastic neoplasm, mainly appearing among middle-aged and older men. Pseudoangiomatous spindle cell lipoma (PASCL), a variant of this tumor, is extremely rare. To the best of our knowledge, only 21 cases of PASCL have been reported so far. This study reports a case of a 63-year-old male patient diagnosed with lipoma by B-ultrasonography. Histopathologic analysis suggested that the mass was a myxoid SCL with a pseudoangiomatous pattern. Immunohistochemistry stains for CD34, CD31, Vimentin, Bcl-2, S-100, CD99, D2-40, Fli-1, and ERG were performed. It was found that tumor cells, lining the cleft-like spaces resembling vascular structures, were diffusely positive for CD34, Vimentin, Bcl-2, and CD99 and focally positive for S-100, while endothelial cell markers CD31, D2-40, Fli-1, and ERG were negative in these spindle cells. The patient was followed up for 26 months after surgical resection without any local recurrence or any metastasis. PASCL is a rare benign adipocytic tumor, with a high rate of clinical misdiagnosis. Its exact diagnosis should be based on combined consideration of clinical characteristics, B-ultrasonography, CT imaging, and pathological features.

Keywords: Pseudoangiomatous spindle cell lipoma, immunohistochemistry, CD34, ERG, D2-40

Introduction

Spindle cell lipoma is a rare subcutaneous benign lipomatous neoplasm, first described in 1975 by Enzinger and Harvey [1]. It often occurs in the neck and shoulder region of middle-aged to older men [2-4]. Pseudoangiomatous spindle cell lipoma (PASCL) is a rare variant subtype of spindle cell lipoma, with an obscure pathogenesis. Average onset age and tumor size are 52 years and 3 cm, respectively [5]. Until now, only 21 cases PASCL have been reported [6]. This study presents another case of myxoid SCL with a pseudoangiomatous pattern. Histologically, it was like those reporting SCL, composed of bland spindle cells, ropey collagen, and adipocytes with myxoid stroma. An explicit diagnosis was obtained by combining common pathological results with histopathology and immunohistochemistry. Additionally, a review of relevant literature was conducted, aiming to raise the diagnostic level of SCL and provide a basis for treatment and prognosis of PASCL.

Case report

Clinical history

A 63-year-old man, presenting with a mass in the neck for 10 years, without obvious incentive and discomfort, arrived at the Department of General Surgery on August 4, 2015. The mass had slowly increased, accompanied by pain. Physical examination confirmed that there was a mass of about 3.0×2.0×1.0 cm in the neck. It had a smooth surface and it was soft and mobile. Tumor ultrasonography demonstrated that it was neck lipoma. In a case like this, it is difficult to differentiate the origin of the tumor without pathologic evidence. The patient underwent surgery and its pathologic characteristics were explored.

Materials and methods

Tumor samples were fixed in 10% formaldehyde (formalin) and embedded in paraffin for pathological study. Sections (4 μm) were cut from

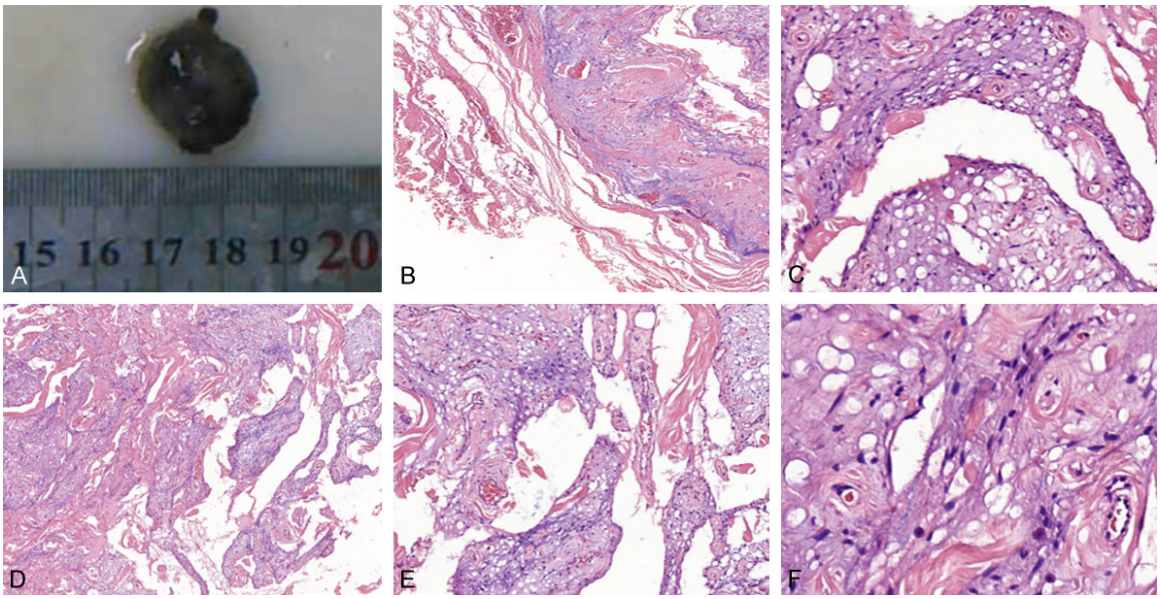

Figure 1. Pathologic findings of a pseudoangiomatous spindle cell lipoma (PASCL). A. Gross appearance of the neck PASCL. The mass was gray-brown oval with clear boundary, measured 2.0×1.5×1.0 cm with partial capsule. B. The tumor was of partial fibrous capsule (HE, ×40). C. The tumor was composed of bland spindle cells, cord-like collagen fibers, and mature fat cells (HE, ×200). D. The collagenous stroma with myxoid background showed irregular branching cleft-like vascular spaces lined by flattened cells (HE, ×40). E. The collagenous stroma with myxoid background showed irregular branching cleft-like vascular spaces lined by flattened cells (HE, ×100). F. The tumor had sporadic mast cells (HE, ×400).

each paraffin block for histopathological examination and immunohistochemical (IHC) stains. Diagnosis of PASCL occurring in the patient was confirmed, via review of 4 mm hematoxylin and eosin-stained sections by two pathologists with expertise in soft tissue pathology. This case was also analyzed with additional IHC stains. Clinical characteristics, including patient age, sex, and location of the tumor were recorded.

Immunohistochemistry analysis was performed in representative tumor sections, as previously described. A series of primary antibodies were used: CD34 (MAB-0034, QBEnd/10), CD31 (MAB-0031, JC70A), Vimentin (MAB-0735, MX034), Bcl-2 (MAB-0014, 8C8), S-100 (MAB-0585, 4C4.9), Actin (Smooth Muscle) (SMA, Kit-0006-2, 1A4), D2-40 (MAB-0567, D2-40), Fli-1 (MAB-0649, G146-222), Ready-to-use; Maixin Bio, Fujian, China; ERG (AR0283, SD-309), and Ready-to-use; Ascend Bio, Guangzhou, China. All operations were performed in strict accordance with instructions. Proper positive and negative controls were performed simultaneously for all applied antisera.

Pathological findings

The gross specimen, originally situated on the neck with a clear boundary, consisted of a gray-brown oval nodular structure (**Figure 1A**). It measured about 2.0×1.5×1.0 cm with a gray-white cut surface and partial capsule (**Figure 1B**). Microscopic examination showed that the parenchyma of the tumor was composed of bland spindle cells, cord-like collagen fibers, and mature fat cells (**Figure 1C**). Spindle cells were mild, without pleomorphism or nuclear mitoses, and arranged in parallel arrays with a "school of fish appearance". The collagenous stroma with myxoid background showed irregular branching cleft-like vascular spaces lined by flattened cells (**Figure 1D**), forming the so-called pseudoangiomatous characteristic, without obvious red blood cells (**Figure 1E**). Scattered mast cells were also observed around the spindle cells (**Figure 1F**).

Immunohistochemistry

IHC staining revealed that the monomorphic spindle cells were positive for CD34, Vimentin, and Bcl-2, while these cells failed to stain with

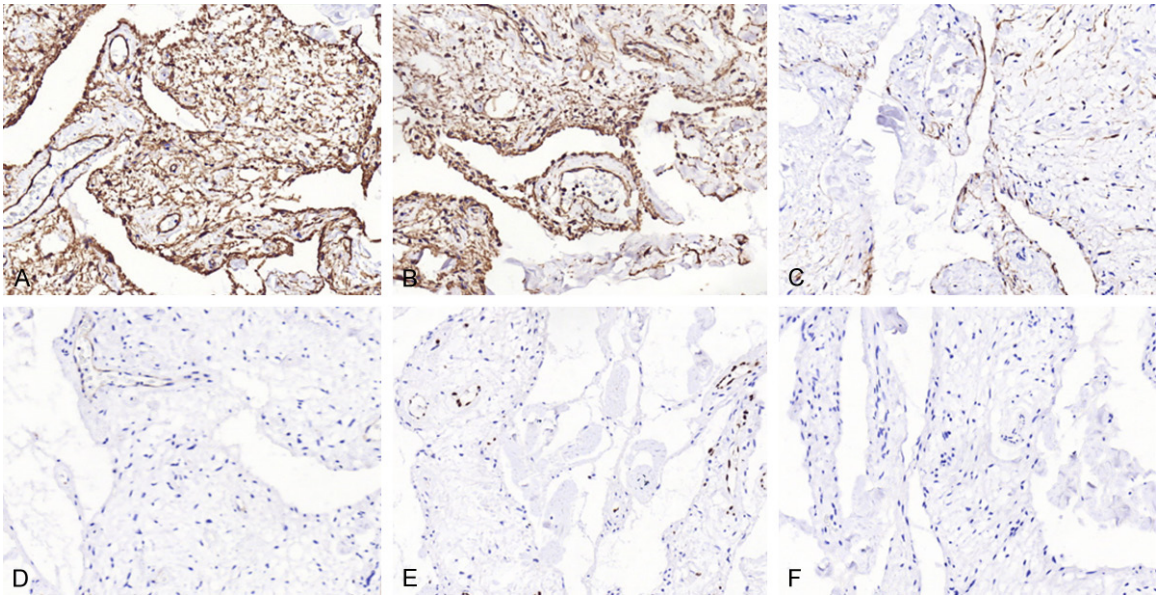

Figure 2. Immunohistochemical stains of PASCL. A. Strong and diffuse immunoreactivity for CD34 (×200). B. Strong and diffuse immunoreactivity for Vimentin (×200). C. Focal S-100 positivity (×200). D. Negative for CD31 (×200). E. Negative for ERG (×200). As a positive internal control, ERG was positive in the endothelial cells of real vessels. F. Negative for D2-40 (×200).

endothelial cell markers CD31, D2-40, Fli-1, and ERG (**Figure 2**). However, adipose cells were positive for S-100 and spindle cells were focally positive for S-100 (**Figure 2C**). Therefore, given the histologic appearance and immunohistochemical profile, this lesion was classified as pseudoangiomatous spindle cell lipoma.

Clinical follow-up

PASCL are all benign tumors and partial resection can cure them. In this case, the patient had a good prognosis, without tumor palindromia and other discomfort. The patient was followed up for 26 months.

Discussion

Spindle cells lipoma (SCL) is a distinct histological variant of lipoma derived from prelipoblastic mesenchymal cells. It is common in middle-aged men and is prone to arise in subcutaneous regions of the upper back, neck, and shoulders. There are many variant subtypes, such as plexiform, fibrous, vascular type, lack of fat type, and pseudoangiomatous type [7-11]. PASCL is a rare variant subtype of spindle cell lipoma. Only 21 cases have been reported in domestic and foreign literature [6]. In 1994, Hawley et al. first described the clinical features of 5 cases PASCL, mainly distributed in the shoulders and necks of middle-aged men [12]. Currently, there are 7 cases and 4 cases reported in these two sites, respectively, while the cheek, chest, chin, elbow, finger, and scapular area have also been reported [12-16]. The present study referred to 21 cases and summarized them (see **Table 1** for details and references).

Histologically, PASCL has the structural components of classic spindle cell lipoma: mild spindle cells, ropey collagen, and mature adipocytes. In addition, the special structure of PASCL includes some vascular-like spaces or branching cleft-like spaces formed by flattened spindle cells, with villiform myxoid connective tissue projections. In Hawley's report, flattened spindle cells lining the cleft-like spaces, resembling vascular structures, did not show CD31, CD34, or Factor VIII-related antigen immunoreactivity. The authors posited that the pseudoangiomatous pattern seemed to be the result of myxoid degeneration of the stroma [12]. In 2007, Zamecnik et al. [14] found the ultrastructure of vascular endothelium in fissure-like structures of three PASCL. These were positive for endothelial markers D2-40 and CD34. Analogous to Zamecnik's results, spindle cells of the branching cleft-like spaces from the

Table 1. Clinical features of 21 reported cases of PASCL and the immunophenotype of cells lining cleft-like spaces

No.	Information Literatures	Age (y)	Sex	size (cm)	Site	Positive IHC of spindle cells	Negative IHC of cells spindle cells
1	Hawley et al., 1994	71	M	16	Shoulder	none	CD31, fVIII, CD34
2		76	M	5	Cheek	none	CD31, fVIII, CD34
3		51	M	3	Shoulder	none	CD31, fVIII, CD34
4		54	M	5	Neck	none	CD31, fVIII, CD34
5		39	F	5	Neck	none	CD31, fVIII, CD34
6	Richmond et al., 1995	64	F	4	Neck	CD34	CD31, fVIII
7	Zamecnik et al., 2007	74	M	2	Nuchal	CD34, CD31, fVIII, D2-40	None
8		45	M	1.5	Chest	CD34, D2-40	CD31, fVIII
9		57	M	0.5	Subscapular	CD34, D2-40	CD31, fVIII
10	Billings et al., 2007	N/A	N/A	N/A	N/A	N/A	N/A
11	Zouaidia et al., 2011	76	M	4	Cheek	N/A	N/A
12		42	M	2.5	Finger	N/A	N/A
13		39	M	2	Neck	N/A	N/A
14		49	M	1.5	Chin	N/A	N/A
15		72	M	3	Shoulder	N/A	N/A
16		33	M	5	Elbow	N/A	N/A
17	Dong et al., 2013	62	M	8	Neck	CD34	N/A
18	Forcucci et al., 2013	70	M	1	Neck	N/A	N/A
19	Bhat et al., 2016	30	F	1	Thumb	CD34	None
20	Marks et al., 2017	49	F	1.5	Shoulder	CD34	CD31, D2-40, Fli-1, ERG
21	Panagopoulos et al., 2017	35	F	6	Left elbow	CD34, CD31	D2-40, MDM2
22	Present case*	63	M	2	Neck	CD34	CD31, D2-40, Fli-1, ERG

y: years, cm: centimeters, M: male, F: female, N/A: Not available, *Current case.

present case also expressed CD34 (**Figure 2A**), but more specific expression of CD31, D2-40, Fli-1, and ERG (Fli-1 and ERG play a crucial role in the formation of endothelium and have a high degree of specificity and sensitivity compared to CD34) were negative (**Figure 2D**, **2F**). Results suggested that these slit-like structures were not real blood vessels. In view of the abovementioned immunohistochemical results and positive expression of CD34 in the stroma of spindle cell lipoma, it was considered that these cleft-like pseudovascular structures may have been caused by atrophy of stromal cells. This is consistent with the original view of Hawley et al. [12] that pseudovascular structures are the result of degenerative stromal cells. Certainly, in view of the paucity of related cases, mechanisms of PASCL should be further explored. Briefly, the lesion showed limited anomalous structures or cell pleomorphisms, with no mitoses and necrosis, supporting the present diagnosis. Moreover, immunohistochemical staining revealed that the monomorphic spindle cells were positive for CD99, Bcl-2, and S-100, which requires further confirmation (**Figure 2C**). However, as Mentzel et al. reported, these may be the diagnostic pitfalls of SCL [17]. Therefore, whether these immunophenotypes are specific manifestations requires more accumulating cases.

In addition, Panagopoulos and Jessica et al. used FISH technique, finding that there was 13q14 partial chromosome deletion in PASCL [6, 18]. However, partial loss of the 16q chromosome or monoallelic loss of the 13q chromosome and a ring chromosome has been associated with SCL [19, 20]. Bartuma et al. also found that *C13orf1* was expressed at significantly lower levels in SCL, compared to the control common lipoma [20]. Recently, Uehara et al. found that Rb1 and FOXO1 genes, encoded by 13q14 region in SCL, cellular angiofibroma (CAF), and mammary-type myofibroblastoma (MFB), showed low expression compared to solitary fibrous tumors with a normal 13q chromosome. They found increased expression of oxidative stress markers 8-hydroxy-2'-deoxyguanosine (8-OHdG) and 4-hydroxy-2-nonenal (4-HNE), due to activation of MAPK p38 path-

ways in SCL. This result may provide more theoretical basis for further revealing the pathogenesis of PASCL [21].

Differential diagnosis of PASCL involves elastofibroma, solitary fibrous tumors (SFT), mammary-type myofibroblastoma, angiolipoma, cellular angiofibroma, angiomyolipoma, and myxoid liposarcoma. Compared with PASCL, elastofibroma is commonly found at the female scapula and grossly appears more fibrous. Microscopically, it is made up of collagen and elastic fibers admixed with adipose tissue. Thus, an elastin stain, such as Verhoeff-Van Gieson (VVG), can highlight the elastin fibers to differentiate from PASCL. Solitary fibrous tumors reveal monomorphous spindle cells with a disordered pattern, few mature adipose tissues, and irregularly spaces representing staghorn-like vessels, similar to PASCL. However, they are often located at a deeper lesion and diffusely express CD99 and STAT6. Mammary-type myofibroblastoma, is often found in the breast parenchyma, the groin area, or along the milk line. Microscopically, it is composed of bland spindle cells, expressing diffuse desmin, with haphazardly arranged thick bundles of collagen. It has outstanding areas of adipocytes with abundant mast cells. Cellular angiofibroma usually involves the groin/pelvic area and appears as a rubbery gray to pink nodule. It is composed of short spindle cells along with numerous small to medium-sized thick-walled hyalinized vessels [22, 23]. Some tumors with desmin and smooth muscle actin negativity contain a minimal amount of adipose tissue [23]. Compared with PASCL, angiomyolipoma also contains spindle cells and mature adipocytes separated by a vascular patch. It does not express CD34 and occurs mainly on the trunk and extremities of children or adolescents. Myxoid liposarcoma is histologically characterized by the proliferation of short spindle cells with uniform ovoid nuclei and different sizes of lipoblast, embedded in the myxoid matrix with plexiform vasculatures. It prefers to locate in soft tissues of the extremities and is accompanied by a specific translocation t(12;16)(q13-14;p11).

In summary, PASCL is an uncommon variant of SCL. It can be a delusive entity for pathologists, mainly composed of spindle cells lining the cleft-like spaces, with a pseudoangiomatous pattern. Despite the undefined cause of cleft-like spaces in PASCL, this study proved that cleft-like spaces in PASCL were not real vessels, according to immunohistochemistry. In the future, with increasing cases and application of advanced molecular techniques, the pathogenesis of PASCL may become more obvious.

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Disclosure of conflict of interest

None.

Address correspondence to: Ren-Ya Zhang, Department of Pathology, Affiliated Hospital of Jining Medical University, 89 Guhuai Road, Jining 272029, Shandong Province, P. R. China. Tel: +86-537-2903217; Fax: +86-537-2903281; E-mail: hzzhang_1964@163.com

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