Case Report

Soft tissue angiofibroma in a 13-year-old adolescent: case report and literature review

Yan Qi1,2*, Xiao-Juan Lian1*, Li-Juan Pang1,2, Hong Zou1,2, Ning Wang1,2, Jian-Ming Hu1,2, Chun-Xia Liu1,2, Wen-Jie Zhang1,2, Jin Zhao1,2, Feng Li1,2

1Department of Pathology, Shihezi University School of Medicine, Shihezi, Xinjiang, China; 2Key Laboratories for Xinjiang Endemic and Ethnic Diseases (Ministry of Education), Shihezi University School of Medicine, Shihezi, Xinjiang, China. *Equal contributors.

Received January 27, 2016; Accepted April 25, 2016; Epub June 1, 2016; Published June 15, 2016

Abstract: Soft tissue angiofibroma (STA) is a rare, benign soft tissue neoplasm recognized by the World Health Organization in 2013. STA occurs mainly in the lower extremities of middle-aged and elderly patients. Here, we report the case of a 13-year-old adolescent with STA in the left thigh. We focus on establishment of the specific pathological characteristics of STA. Grossly, the tumor was a well-demarcated, soft, painless, large lump and was partial encapsulated with a grayish-white color and firm consistency. Histologically, in areas having high cellular-ity, the tumor was composed of bland spindle-shaped tumor cells and branching small vessels. Focal tumor cells were vacuolated, including potential erythrocytes, making differential diagnosis challenging. Mitotic counts were 2-3 cells/10 high-powered fields. Occasional tumor cells had irregularly-shaped, large, multinucleate, hyperchromatic nuclei, making it difficult to distinguish between STA and low-grade malignant soft tissue tumor. We used a panel of immunohistochemical markers and showed that the tumor cells expressed FLI-1, Bcl-2, CD31, F8, vimentin and desmin. Additionally, the Ki-67 labeling index was about 5% that higher than that in other cases. STAT6 was negative, which could be used to exclude solitary fibrous tumors. CAMTA1 was negative, which could be used to distinguish STA from epithelioid hemangioendothelioma. In this report, we describe the youngest case of STA to date, broadening the pathological characteristics of STA. Most STAs and aggressive tumors have similar clinicopathological features. Thus, identification of this tumor type may prevent misdiagnosis of a variety of benign or malignant tumors.

Keywords: Soft tissue angiofibroma, benign, adolescent, differential diagnosis

Introduction

Soft tissue angiofibroma (STA) is a rare, benign, soft-tissue tumor that occurs mainly in the lower extremities of middle-aged and elderly patients [1]. STA has generally been reported in patients 37 to 73 years of age [1-9]; few studies have reported STA in adolescent patients. To make a definite diagnosis of STA is challenging because STA resembles a variety of benign and low-grade malignant soft tissue tumors, such as epithelioid hemangioendothelioma (EHE) [10], solitary fibrous tumor (SFT) [11], low-grade myxofibrosarcoma (LGFM) [12], myxoid liposarcoma (MLS) [13], and cellular angiofibroma [14].

In this report, we describe unique clinicopathological and immunohistochemical features in a case of STA. Our data may provide important insights into the differential diagnosis of STA.

Case presentation

A 13-year-old adolescent presented with a painless soft-tissue mass in the left thigh for 1 year. He was admitted to our hospital for further evaluation and treatment. He had no history of other systemic diseases. A physical examination revealed that the fixed soft tissue mass was positioned on the left side of the upper middle section of the lateral thigh. The mass measured approximately 8×8 cm and was soft, with a clear boundary. The mass could be moved slightly, was not painful, and did not alter the lower limb activity of the patient. A hypoechoic area was observed within the mass during the ultrasound examination, and com-
Computed tomography (CT) showed that the tumor was located within the subcutaneous fat clearance area of the outer edge of the left thigh. Edge blurring and abnormal signals of homogeneously enhanced areas were observed (Figure 1A and 1B). Moreover, local swelling was observed in the adjacent muscle group. No mineralization was observed by radiography or CT. The patient underwent surgery for mass resection, and biopsy of the mass suggested EHE [10]. The patient was diagnosed with a minute malignant tumor and subsequently underwent whole-bone scanning and chest x-ray. No obvious metastases were observed. Subsequent pathological examination suggested STA. Neither local recurrence nor distant metastasis was observed for 15 months after the operation.

Table 1. Antibodies used in this case

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Clone</th>
<th>Dilution</th>
<th>Source</th>
<th>Location</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vimentin</td>
<td>Mouse mAb</td>
<td>1:100</td>
<td>Gene Tech (Shanghai) Company limited</td>
<td>Cytoplasm</td>
<td>+</td>
</tr>
<tr>
<td>FLI-1</td>
<td>Mouse mAb</td>
<td>1:50</td>
<td>Dako</td>
<td>Cell nucleus</td>
<td>+</td>
</tr>
<tr>
<td>Desmin</td>
<td>Mouse mAb</td>
<td>1:100</td>
<td>Dako</td>
<td>Cytoplasm</td>
<td>Focal</td>
</tr>
<tr>
<td>Bcl-2</td>
<td>Mouse mAb</td>
<td>1:100</td>
<td>Dako</td>
<td>Cell membrane or cytoplasm</td>
<td>Focal</td>
</tr>
<tr>
<td>S-100</td>
<td>Rabbit pAb</td>
<td>1:200</td>
<td>ZSGS-BIO</td>
<td>Cytoplasm</td>
<td>Focal</td>
</tr>
<tr>
<td>CD34</td>
<td>Mouse mAb</td>
<td>1:80</td>
<td>Dako</td>
<td>Vascular</td>
<td>+</td>
</tr>
<tr>
<td>CD31</td>
<td>Mouse mAb</td>
<td>1:40</td>
<td>Dako</td>
<td>Vascular</td>
<td>Vascular +</td>
</tr>
<tr>
<td>F8</td>
<td>Mouse mAb</td>
<td>1:50</td>
<td>Dako</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>AE1/AE3</td>
<td>Mouse mAb</td>
<td>1:1000</td>
<td>Dako</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>SMA</td>
<td>Rabbit pAb</td>
<td>1:1000</td>
<td>Dako</td>
<td>Vascular</td>
<td>Vascular +</td>
</tr>
<tr>
<td>Ki-67</td>
<td>Mouse mAb</td>
<td>1:300</td>
<td>ZSGS-BIO</td>
<td>Cell nucleus</td>
<td>5%</td>
</tr>
<tr>
<td>Stat6</td>
<td>Rabbit mAb</td>
<td>1:600</td>
<td>Abcam</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>CAMTA1</td>
<td>Rabbit pAb</td>
<td>1:100</td>
<td>Abcam</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

Abbreviations: SMA, smooth muscle antibody; mAb, monoclonal antibody; pAb, polyclonal antibody; +, positive; −, negative.

Written informed consent was obtained from the patient regarding the use of the collected samples in research studies. The patient records and information were anonymized and de-identified before analysis. Human subjects in this study provided informed consent for use of their tissues for research purposes following procedures approved by the Clinical Research Ethics board of the First Affiliated Hospital, Shihezi University School of Medicine.

Materials and methods

The resected specimens were fixed in 10% buffered formalin, embedded in paraffin, sectioned at 5-μm thickness, and stained with hematoxylin and eosin. Immunohistochemical investigations were performed using a Leica
Soft tissue angiofibroma of adolescent

Pathological findings

On gross inspection, the excised mass surface was coated in tendons and measured 9×7×5 cm³. The cut surface (6.2×5.5×4.3 cm³) resembled a nodular tumor, separated from the tendons by about 0.1 cm. The cut surface was reddish-gray in color, with a slightly soft and fleshy appearance (Figure 1C). Part of the area was homogeneous.

Microscopically, the tumor consisted of spindle-shaped tumor cells and thin-walled branching small vessels (Figures 2 and 3). Under low-power examination, the tumor was well demarcated and partially surrounded by a fibrous capsule of variable thickness (Figure 2A). The region containing the tumor cells showed nodular growth (Figure 2B). The tumor was hypercellular, with the tumor cells often exhibiting storiform, short fascicular, and occasionally swirling arrangements (Figures 2C and 3D). High magnification images showed that the tumor cells were polygonal, with eosinophilic cytoplasm and oval to stellate nuclei (Figure 2D). Nuclear fission (Figure 2E) and inclusion bodies were observed in the intranuclear area. F. Occasional tumor cells had irregularly-shaped, large, multinucleate, hyperchromatic nuclei. A and B. Original magnification 100×; C and D. 200×; E and F. 400×.

Figure 2. Microscopic features. A. The tumor was well demarcated and partially surrounded by a fibrous capsule of variable thickness. B. The tumor cells showed nodular growth. C. The tumor was much more cellular, with lesional cells frequently showing short fascicular, storiform, and occasionally swirling arrangements. Numerous small, thin-walled, branching vessels were evenly distributing throughout the lesion. D. The tumor cells were polygonal, with eosinophilic cytoplasm and oval to stellate nuclei. E. Nuclear fission was observed in the intranuclear area. F. Occasional tumor cells had irregularly-shaped, large, multinucleate, hyperchromatic nuclei. A and B. Original magnification 100×; C and D. 200×; E and F. 400×.

Bond-Max System. The antibodies, clones, working dilutions, and their commercial sources are listed in Table 1. SFT tissue was used as the positive control for signal transducer and activator of transcription 6 (STAT6). EHE tissue was used as the positive control for calmodulin-binding transcription activator 1 (CAMTA1).
Soft tissue angiofibroma of adolescent

Figure 3. A. On high magnification, focal tumor cells were vacuolated, including potential erythrocytes. B. The extracellular matrix was comprised primarily of abundant collagens. C. Occasionally, the extracellular matrix contained loose myxoid areas. D. The transition of the hypocellular areas to more cellular areas was gradual. A and B. Original magnification 400×; C and D. 200×.

Discussion

STA is a distinct fibrovascular neoplasm first described by Marino-Enriquez and Fletcher in 2012 [1]. The cause and pathogenesis of STA are still unknown, and the sources of tumor cells are unknown. STA is characterized by spindle-shaped tumor cells and a complex vascular network [1]. From reports published to date, the ratio of female to male patients with STA is 1.76. Notably, all cases of STA have been reported to be benign, with no reports describing metastasis; however, four patients were found to have local recurrence [1].

In most patients, STA presents as a painless mass located in the soft tissues of the lower or upper limbs, often adjacent to joint-related structures; therefore, such tumors are easily detected. Tumors arising in the wrist joint sometimes present with functional limitations [1], and tumors in the soft tissues of the abdominal wall, chest wall, iliac crest, and left posterior neck region are extremely rare [1, 3]. These tumors generally range from 1.2 to 12 cm in diameter [1].

Cytogenetic analysis of STA has revealed that the t(5;8)(p15;q13) chromosomal translocation results in the fusion of two transcription-associ-
Soft tissue angiofibroma of adolescent

Furthermore, a three-way t(5;8;8)(p15;q13;p11) chromosomal translocation has also been discovered [15], and a recent case was reported to carry an alternative fusion gene, i.e., -GTF2I/NCOA2 [2]. In addition, fluorescent in situ hybridization (FISH) has demonstrated the recombination of NCOA2 [4]; this method can be used for diagnosing STA. However, a substantial subset of STAs is negative for the fusion gene [2]. To the best of our knowledge, the current case is the youngest reported case of STA to date (Table 1). The major clinical features of previously reported cases are presented in Table 2. Similar to STAs arising in other age groups, the STA in the patient in our case was well demarcated.

STA can easily be misdiagnosed as a variety of benign and low-grade malignant soft tissue tumors. Therefore, it is necessary to identify features unique to STA that can be used to distinguish STA from other benign and low-grade malignant soft tissue lesions, including EHE, SFT, LGFM, MLS, and cellular angiofibroma. Because the biological behaviors of these tumors differ, the treatment and prognosis of these diseases are not completely the same.

In the present case, STA was misdiagnosed as EHE, a low-grade malignant soft tissue tumor [10]. Misdiagnosis could be explained by the polygonal or spindle-shaped tumor cells, particularly the presence of vacuolated focal tumor cells, including potential erythrocytes, and the nodular growth of tumor cells, features that are similar to EHE. However, in the cytoplasm of EHE tumor cells, vacoulization or the presence of lumen containing one or multiple erythrocytes is commonly observed, and the tumor cells are arranged in nests and pseudoglandular structures, with unclear cell boundaries, distinct from STA. Detection of the fusion gene WWTR1-CAMTA1 in EHE has high diagnostic value [16]. In addition, the immunohistochemical marker CAMTA1 is useful for diagnosing EHE [17]. Thus, based on our histopathological and immunohistochemistry findings, STA could be readily distinguished from EHE.

Our case was similar to cases of SFT [11], which may exhibit aggressive behaviors with or without malignant histologic features [18]. The tumor is composed of spindle-shaped cells, multinucleated giant cells, and a variable
Table 2. Review of reported cases of angiofibroma of soft tissue (cases from 8 previous publications and the current case)

<table>
<thead>
<tr>
<th>Author</th>
<th>sex</th>
<th>Age (years)</th>
<th>Size (cm)</th>
<th>Location</th>
<th>Mitotic Count</th>
<th>Treatment</th>
<th>FU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marino-Enriquez et al [1].</td>
<td>F (∗25) and M (∗12)</td>
<td>6-86 (median 47)</td>
<td>1.2-7.2 (mean 4.3)</td>
<td>Lower extremity (∗23) Upper extremity (∗5) Back (∗3) Others (∗6)</td>
<td>&lt;1/10 hpf in 28 cases, up to 4/10 hpf in 9 cases</td>
<td>SE (∗29) Amputation (∗1)</td>
<td>Recurrence (∗4, 9, 12, 36 and 120 m)</td>
</tr>
<tr>
<td>Arbajian et al [2]. F</td>
<td>41</td>
<td>NA</td>
<td>NA</td>
<td>Thigh</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Edgar et al [3]. M (∗2)</td>
<td>62 and 68</td>
<td>7 and NA</td>
<td>Right thigh and left posterior neck region</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Zhao et al [4]. M (∗2)</td>
<td>54 and 57</td>
<td>2 cm and 2.8</td>
<td>Upper arm (∗2) Upper arm region (∗2)</td>
<td>NA</td>
<td>SE</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Lee et al [5]. F</td>
<td>37</td>
<td>9.1</td>
<td>Right foot</td>
<td>Left foot</td>
<td>NA</td>
<td>SE</td>
<td>NED and NA</td>
</tr>
<tr>
<td>Song et al [6]. M</td>
<td>51</td>
<td>2.2</td>
<td>Right thigh</td>
<td>Absent</td>
<td>SE</td>
<td>SE</td>
<td>NED</td>
</tr>
<tr>
<td>Fukuda et al [7]. F</td>
<td>73</td>
<td>9.5</td>
<td>Left thigh</td>
<td>Absent</td>
<td>SE</td>
<td>SE</td>
<td>NED</td>
</tr>
<tr>
<td>Schoolmeester et al [8]. F</td>
<td>54</td>
<td>1.9</td>
<td>Right knee</td>
<td>NA</td>
<td>SE</td>
<td>SE</td>
<td>NED</td>
</tr>
<tr>
<td>Sugita et al [9]. F (∗2) and M (∗2)</td>
<td>27-70 (median 44)</td>
<td>2-9.5 (mean 6.2)</td>
<td>Upper arm (∗2) Upper arm region (∗2)</td>
<td>NA</td>
<td>SE (∗3) WE (∗1)</td>
<td>NED</td>
<td></td>
</tr>
<tr>
<td>Lian et al. (current case)</td>
<td>M</td>
<td>13</td>
<td>8.0</td>
<td>Left thigh</td>
<td>2-3/10 hpf</td>
<td>SE</td>
<td>NED</td>
</tr>
</tbody>
</table>

Abbreviations: FU, follow-up; Lower extremity includes foot, ankle, popliteal fossa, knee, thigh, lower leg; Upper extremity includes the wrist, arm and forearm. Others include the shoulder, pelvic cavity, breast, inguinal area, pectoralis muscle and abdominal wall. F, female; M, male; SE, simple excision; WE, wide excision; NA, not available; NED, no evidence of disease.
degree of collagenous stroma and vasculature, resembling common cytological features and the patternless architecture of STA. A recent report revealed that SFTs exhibit nuclear expression of STAT6, whereas the other tumors are negative for STAT6 [9]. Consistent with this finding, the SFT in this case was positive for STAT6, whereas the STA tissue was negative for STAT6, providing a convenient method for differentiating SFT from STA.

Aggressive LGFM is most likely to be confused with STA because it shares many features with STA, including location, clinical manifestations, and pathological entities. However, the tumor is composed of diffuse fusiform cells and abundant fibromyxoid stroma, and the fusiform tumor cells are arranged in a multi-nodular pattern, with indistinct cell margins [12]; these histopathological characteristics are not observed in STA, providing another feature for distinguishing STA from LGFMs. Moreover, LGFM exhibits significant FUS-CREB3L2 or FUS-CREB3L1 translocation, facilitating a definite diagnosis of LGFM [19].

MLS and STA both have a spindle-shaped cell population and delicate arborizing capillaries [13]. However, the presence of lipoblasts with eccentrically located, small, elongated nuclei and abundant intracytoplasmic vacuoles can be used to distinguish MLS from STA. Furthermore, MLS shows significant FUS-DDIT3 or EWSR1-DDIT3 translocation [20].

Cellular angiofibroma [14] should also be ruled out during diagnosis. Cellular angiofibroma usually occurs in the vulvar or inguinoscrotal region. In addition, the numerous small- to medium-sized thick-walled vessels and the absence of significant nuclear atypia and abnormal mitoses in cellular angiofibroma are different from those in STA. Thus, STA could be easily distinguished from cellular angiofibroma by these distinctive clinicopathological characteristics.

The treatment of choice for STA is simple total excision, which is usually curative, and no reports have described the occurrence of metastasis after complete excision. However, four cases of recurrence have been reported in the literature. These reports confirm the benign nature of STA [1].

Conclusion

STA is an extremely rare type of benign soft-tissue tumor that has rarely been reported in pediatric patients. Pre-operative diagnosis and differentiation from other soft-tissue tumors are challenging. Histological and IHC findings can be used to confirm the diagnosis. If economic and technical conditions allow, detecting NCOA2 split signals on FISH is useful for confirming the diagnosis of STA, because this may exclude other histologically similar fibrovascular tumors.

Acknowledgements

This work was supported by grants from the National Natural Science Foundation of China (No. 81202120) and the Outstanding Youth Science and Technology Talent Cultivation Plan of Shihezi University (2015ZRKXJQ07) and Research Project of High Level Talents of Shihezi University (No. RCZX201549).

Disclosure of conflict of interest

None.

Address correspondence to: Drs. Feng Li and Jin Zhao, Department of Pathology, Shihezi University School of Medicine, Shihezi, Xinjiang, China; Key Laboratories for Xinjiang Endemic and Ethnic Diseases (Ministry of Education), Shihezi University School of Medicine, North 4th Road Shihezi, Xinjiang 832002, China. Tel: 86-993-2057125; Fax: 86-993-2057136; E-mail: lifeng7855@126.com (FL); 1505108219@qq.com (JZ)

References


