Case Reports

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
49(3) 1–7

DOI: 10.1177/03000605211000536
journals.sagepub.com/home/imr
SAGE

Cellular solitary fibrous tumor in the mental area: a case report and literature review

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Abstract

Solitary fibrous tumors (SFTs) are rare benign mesenchymal tumors that occur mainly in the pleura. We herein report the first case of a cellular SFT located in the mental region of the head and neck in a 46-year-old woman. Facial computed tomography revealed a mass measuring 0.8 cm with clear boundaries in the right mental region. After excision of the mass, expert pathologists diagnosed a cellular SFT. To our knowledge, this is the first case of a cellular SFT identified in the subcutaneous tissue of the mental region of the head and neck. Because the postsurgical prognosis of SFTs is unpredictable, long-term follow-up and further studies are necessary to determine the characteristics of cellular SFTs in the head and neck region.

Keywords

Head and neck neoplasms, solitary fibrous tumors, STAT6 transcription factor, immunohistochemistry, mass excision, subcutaneous tissue

Date received: 20 January 2021; accepted: 12 February 2021

Introduction

Solitary fibrous tumors (SFTs) are rare benign mesenchymal tumors that were first described by Klemperer and Rabin in 1931.[1] The World Health Organization (WHO) defines SFTs as benign mesenchymal tumors because most originate from the submesothelial cells of the pleura.[2] Although SFTs were originally described in the pleura, they have been reported in

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almost every anatomic site.[3] Histological features of SFTs include bland, uniform, fibroblast-like spindle cells and branching hemangiopericytoma-like vessels.[2] The most prevalent primary site in the head and neck region is the sinonasal tract, followed by the orbit, oral cavity, salivary glands, deep tissues of the neck, and subcutaneous tissue.[4–9]

Even when SFTs are pathologically diagnosed as benign, some SFTs may recur or metastasize.[10] Therefore, these tumors are uniquely challenging to diagnose and treat. We herein report the first case of a cellular SFT arising in the subcutaneous tissue of the mental region and discuss the clinical and pathological features of SFTs of the head and neck.

Case report

A 46-year-old woman with an incidentally detected hard mass in the mental region visited Chonnam National University Dental Hospital in October 2018. The patient had undergone treatment for polyarthralgia 7 years previously, but she had no unusual symptoms during the hospital visit. Physical examination revealed unremarkable findings with the exception of a palpable mass in the mental region. Laboratory parameters were within the reference ranges. Facial computed tomography revealed a mass measuring 0.8 cm with clear boundaries in the right mental region (Figure 1). Based on a clinical diagnosis of fibroma, complete surgical removal of the tumor was performed.

On macroscopic examination, the mass had a well-defined oval shape and a diffuse fibrotic appearance. Furthermore, it was white to faint yellow in color and had mild elasticity. Microscopically, the lesion was well circumscribed with a thin-walled capsule and exhibited an SFT pattern including hypercellularity and frequent blood vessels (Figure 2(a), (b)). On high magnification, the lesion displayed high cellularity with bland, ovoid to spindle-shaped cells haphazardly arrayed in a "patternless pattern" with stromal collagen bundles arranged near variably sized ectatic vessels in a characteristic "staghorn" configuration (Figure 2(c)). One cell per 10 high-power fields (HPFs) was observed undergoing mitosis.

Immunohistochemistry revealed strong expression of vimentin, signal transducer and activator of transcription-6 (STAT6), and CD34 (Figure 3(a)–(c)). The neoplastic cells displayed uniformly negative expression of S-100 protein and transducin-like enhancer protein 1 (TLE1) (Figure 3(d), (e)). The Ki67 index, indicating the

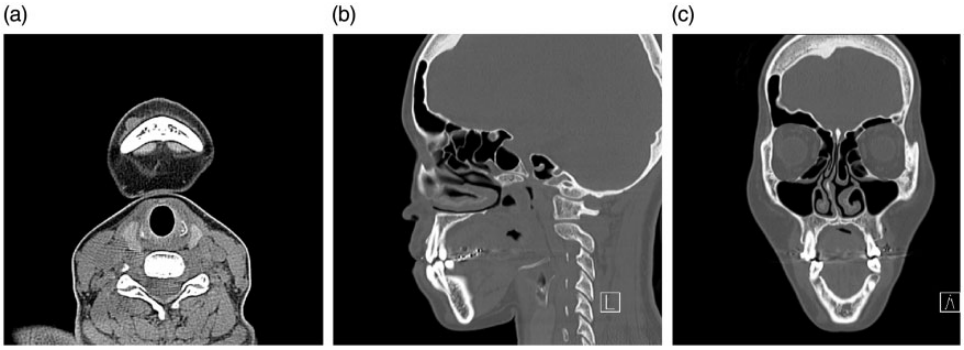

Figure 1. Facial computed tomography revealing a mass measuring 0.8 cm with clear boundaries in the right mental region as shown in the (a) axial, (b) sagittal, and (c) coronal planes.

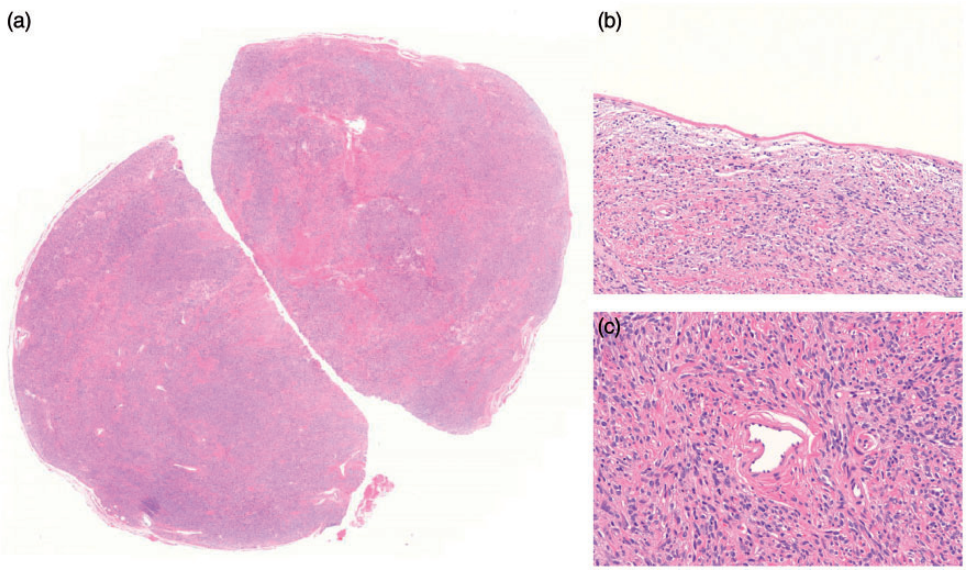

Figure 2. Microscopic findings of the cellular solitary fibrous tumor. (a) The tumor specimen shows high cellularity with a well-demarcated boundary (hematoxylin–eosin staining; magnification, 10×). (b) The tumor is well circumscribed with a thin-walled capsule (hematoxylin–eosin staining; magnification, 100×). (c) The tumor is composed of bland, spindled-shaped cells in a "patternless pattern," with variably intervening dense fibrous stroma and dilated and branching thin-walled staghorn-shaped vessels (hematoxylin–eosin staining; magnification, 200×).

proliferation of tumor cells, was <2% (Figure 3(f)). Based on the histological and immunohistochemical results, the tumor was diagnosed as a cellular SFT. After surgical excision of the tumor, no recurrence was observed during the 28-month follow-up (until January 2021).

Discussion

SFTs have rarely been reported in the subcutaneous area of the head and neck region. Of the 88 cases of SFTs arising in the head and neck region summarized by Smith et al.,[11] SFTs in subcutaneous tissues of the head and neck region were found in only 7 cases, with 3 cases involving the cheek, 2 cases involving the eyelids, 1 case involving the external auditory canal, and 1 case involving the chin. Table 1 summarizes the clinicopathological characteristics of all eight cases of SFTs in the subcutaneous tissue of the head and neck region (including the present case). The median patient age at diagnosis was 45.1 years (range, 17–64 years). The tumor size ranged from 0.6 to 6 cm. Based on the limited number of cases, SFTs appear to occur slightly more frequently in female patients than in male patients (1.7 vs. 1.0, respectively).

Among the eight cases of subcutaneous SFTs, five (62.5%) were of the cellular type, three (37.5%) involved atypia, and two had a mitotic count of 4 per 10 HPFs. None of the cases showed epithelioid cytomorphology (excluding one case lacking cytomorphological data). Excluding two cases that were lost to follow-up, recurrence was noted in only one case of cellular SFT (2 mitotic cells per 10 HPFs) without atypia or epithelial features 11 months after the surgery. The median follow-up

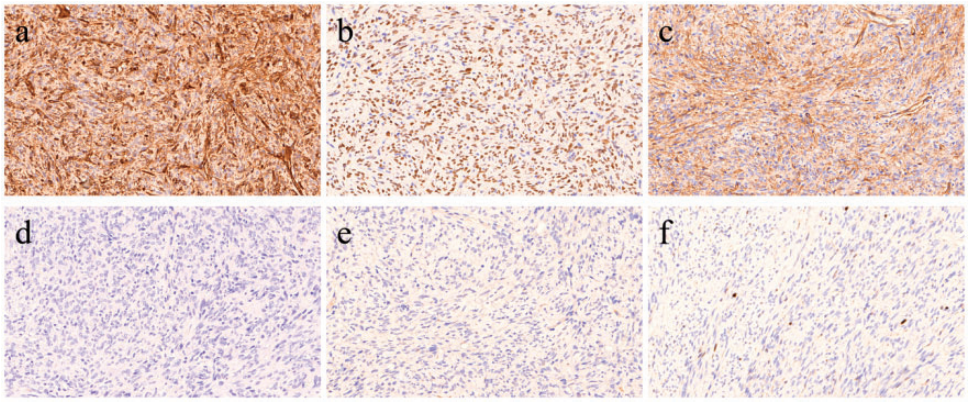

Figure 3. Immunohistochemical findings of the cellular solitary fibrous tumor. (a) The tumor cells are positive for vimentin (magnification, 200×). (b) The tumor cells show nuclear expression of signal transducer and activator of transcription-6 (STAT6) (200×). (c) Immunostaining for CD34 shows positive results (magnification, 200×). The tumor cells are negative for (d) S-100 and (e) transducin-like enhancer protein 1 (TLE1) (magnification, 200×). (f) The Ki67 labeling index is <2% (magnification, 200×).

Table 1. Clinicopathologic features of solitary fibrous tumors in the subcutaneous tissue of the head and neck region.

Case	Sex	Age (years)	Size (cm)	Morphology	Atypia	Epithelioid	Mits/10 HPFs	Rec status	Time to rec (months)
1	F	17	3	Cellular	Y	N	7	NED	3.5
2	F	31	0.6	Cellular	N	N	2	NED	43.2
3	M	26	0.7	Classic	N	N	1	NED	6.3
4	F	49	6	Cellular	Y	N	1	LTF	LTF
5	M	64	3.2	Cellular	N	N	2	Rec	11
6	M	64	3.2	Classic	Y	N	6	LTF	LTF
7	F	64	3.2	Classic	N	Not mentioned	0	NED	12
Current case	F	46	0.8	Cellular	N	N	<1	NED	28

Mits/10 HPFs, mitoses per 10 high-power fields; M, male; F, female; Rec, recurrence; NED, no evidence of disease; LTF, lost to follow-up.

time in the remaining five patients with no evidence of recurrence was 18.6 months (range, 3.5–43.2 months).

The pathological characteristics of SFTs include ovoid or spindle-shaped fibroblastic cells arranged in a storiform or haphazard patternless pattern. These cells are separated by keloid-like collagen bundles and branching of staghorn-shaped vessels resembling a hemangiopericytoma-like pattern.[12] SFTs are classified into two pathological categories: classic SFTs and cellular SFTs. Classic SFTs predominantly show low to moderate cellularity of spindle cells interspersed within the collagen matrix. In contrast, cellular SFTs exhibit dense hypercellularity of ovoid to spindle-shaped cells and a patternless distribution with little stroma.[11] In our case, the hypercellular fibrillary neoplasm had ovoid to short

spindle-shaped cells arranged in no particular pattern; thus, it was diagnosed as a cellular SFT.

The overall differential diagnosis of SFTs is quite broad because such tumors may be misdiagnosed as other spindle cell neoplasms (such as dermatofibrosarcomas or synovial sarcomas), mesenchymal lesions (such as hemangiopericytomas or fibrous histiocytomas), smooth muscle tumors (such as leiomyomas or leiomyosarcomas), neural tumors (such as schwannomas or nerve sheath tumors), or other benign soft tissue tumors (such as perineuriomas or cellular angiofibromas).[13] However, immunohistochemical tests for CD34 and STAT6 may be useful to distinguish SFTs from histological mimics because consistent CD34 expression has been reported in SFTs.[14] In a multi-institutional study by Smith et al.,[11] 80 of 88 SFT specimens were positive for CD34. In another study, CD34 expression was also identified in approximately 90% to 95% of typical SFTs.[15] The specificity of this marker is low because it is also expressed in other tumor types that may be confused with SFTs, including spindle cell lipoma, soft tissue perineurioma, and dermatofibrosarcoma protuberans.[13]

To address the need for a more specific marker, Chmielecki et al.[16] and Robinson et al.[17] introduced *NAB2-STAT6*, a novel pathognomonic gene, as a genetic hallmark of SFTs. Several clinical studies have shown that the nuclear expression of STAT6 can be useful for distinguishing SFTs from histological mimics in the head and neck, gynecological tract, and prostate.[14,18] Doyle et al.[19] analyzed 231 cases of soft tissue tumors, and 59 of 60 SFTs exhibited nuclear expression of STAT6. However, only strong and diffuse nuclear staining of STAT6 is highly specific for SFTs.

More recently, molecular analyses of *NAB2-STAT6* have been used to confirm SFT diagnoses; thus, this approach may have prognostic value. STAT6 is a member of the STAT family of cytoplasmic transcription factors regulating gene expression. STAT signaling is critical for normal cellular processes (such as regulation of cell differentiation, growth, and embryonic development).[20] *NAB2* acts as a transcriptional repressor by interacting with the early growth response family of transcription factors.[21] However, *NAB2* gains an activation domain when fused to *STAT6*, and overexpression of the fusion gene *NAB2-STAT6* causes translocation to the nucleus, where it acts as a transcriptional activator and increases cell proliferation.[17] This gene fusion is considered the primary pathogenic event in SFT development.[17] Because *NAB2* and *STAT6* are in close proximity on chromosome 12q13, conventional fluorescence *in situ* hybridization may produce false-negative results; therefore, it is not considered an ideal diagnostic tool.[13] Nuclear STAT6 expression detected by immunohistochemistry and *NAB2-STAT6* fusion detected by reverse transcription-polymerase chain reaction are considered more useful methods to confirm SFTs. In our case, immunohistochemical staining for STAT6 produced intense and diffuse nuclear staining, confirming the diagnosis of an SFT. In addition, the tumor was immunohistochemically positive for vimentin and CD34. Furthermore, the Ki67 index was $<2\%$; therefore, a benign SFT was diagnosed.

Approximately 80% of patients with SFTs have benign SFTs and are asymptomatic; however, a significant fraction of patients may have SFTs that display malignant behavior.[22] The tumor location is highly associated with disease-specific death, and patients with large (≥ 8 cm) tumors in the chest or abdominal/retroperitoneal cavity have the highest mortality risk.[23] However, it is difficult to accurately predict the prognosis of head and neck SFTs because the criteria used to determine

tumor behavior are controversial on account of the rarity of these tumors.

According to the WHO, hypercellularity, increased mitotic activity (>4 mitotic cells per 10 HPFs), cytological atypia, tumor necrosis, and infiltrative margins in SFTs can be risk factors for malignancy.[24] Our case had none of the above factors and the mitotic activity was low (1 mitotic cell per 10 HPFs), suggesting the possibility of benign features. However, Table 1 shows that the tumor in Case 1 exhibited 7 mitotic cells per 10 HPFs had no recurrence, whereas the tumor in Case 5 exhibited cellular features and 2 mitotic cells per 10 HPFs (in accordance with the WHO guidelines for benign tumors) had recurrence. Other studies have also supported the observation that the biological behavior of SFTs is not strictly dependent on tumor size and mitotic count; thus, even SFTs that are considered benign based on histology may aggressively recur.[25]

The gold standard treatment for SFTs is surgical resection.[26] Demicco et al.[26] analyzed 110 patients with SFTs after surgery and reported that the overall 5- and 10-year patient survival rates were 89% and 73%, respectively. Our patient was diagnosed with a benign cellular SFT, and no recurrence was observed for 28 months after surgery. It is important to track disease progression in patients, and long-term follow-up is necessary to understand the disease behavior.

In conclusion, we have herein reported the first case of a cellular SFT arising in the subcutaneous tissue of the mental region of the head and neck. Further extensive studies are required to fully understand the biological potential and clearly define the clinical behavior of head and neck SFTs. The postsurgical prognosis for this disease is unpredictable, and long-term observation and follow-up are therefore required to determine its nature.

Declaration of Conflicting Interests

The authors declare that there is no conflict of interest.

Ethics

The Ethics Committee of the Dental Hospital of Chonnam National University waived the requirement for ethical approval and documentation for this study (IRB No. CNUDH-EXP-2020-008) because the patient in this case report sustained minimal harm, all of the patient's information was de-identified, and none of the patient's genetic information (e.g., DNA data) was used. Written consent for treatment was obtained from the patient before surgery. To increase the accuracy, transparency, and usefulness of this case report, this study was performed in compliance with the CARE guidelines.[27]

Funding

This work was supported by National Research Foundation of Korea (NRF) grants funded by the South Korean government (MSIT) (No. 2019R1A5A2027521 and NRF-2018R1D1A1B 07047482) and a grant from Chonnam National University Hospital Biomedical Research Institute (BCRI19027).

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