J Med Sci 2013;33(3):159-162
http://jms.ndmctsgh.edu.tw/3303159.pdf
DOI:10.6136/JMS.2013.33(3).159

Primary Angiosarcoma of the Submandibular Gland

Keng-Kuang Tsai[1,3], Chih-Kung Lin[2], Chiang-Hung Hsu[1], and Jih-Chin Lee[1*]

[1]Department of Otolaryngology-Head and Neck Surgery; [2]Department of Pathology, Tri-Service General Hospital, National Defense Medical Center, Taipei; [3]Department of Otolaryngology-Head and Neck Surgery, Tri-Service General Hospital Songshan Branch, Taipei , Taiwan, Republic of China.

Angiosarcoma of the head and neck is a rare tumor of vascular origin that occurs almost exclusively in the scalp and forehead region. Primary angiosarcomas of the submandibular gland are extremely rare. Here we report one such case. The patient was referred for evaluation of a neck mass in the right submandibular region that had rapidly enlarged within the previous half year. Computed tomography scanning showed a hypervascular tumor within the submandibular gland. Excision of the submandibular gland was attempted. The histopathology revealed characteristic features of high grade angiosarcoma, which revealed a predominant solid tumor mass with few vascular channels which composed with irregular and freely anastomosing channels lined by marked pleomorphic spindle endothelial cells. Positive CD34 and P53 expressions indicated malignant vascular origin tumor. Such a rare case of angiosarcoma occurs in the salivary gland presenting as a neck mass with variable imaging and cytological features make pre-operative diagnosis difficult. Spectrum of vascular tumors are variable, and excision biopsy should be performed to establish the diagnosis. The final diagnosis must be made according to histological examination, immunocytochemical studies and clinical behaviors.

Key words: submandibular gland, angiosarcoma, salivary gland

INTRODUCTION

Angiosarcoma (AS) is a rare and aggressive malignant neoplasm of vascular origin that predominates in the skin and soft tissue. Approximately 50% of AS tumors occur in the head and neck, although they account for less than 0.1% of head and neck malignancies.[1] Primary lesions of the salivary gland are extremely rare. When AS occurs in submandibular gland (SMG) and presents as neck mass, it is difficult to make early diagnosis due to nonspecific imaging features and variable cytological features. The diagnosis of AS is dependent on histologic studies with immunocytochemical stains.

In this article, we present the case of a 62 year-old female who developed a primary AS in the SMG. The diagnosis features, clinical approach, management and prognosis have all been documented.

Received: November 13, 2012; Revised: March 27, 2013; Accepted: April 3, 2013
*Corresponding author: Jih-Chin Lee, Department of Otolaryngology-Head and Neck Surgery, Tri–Service General Hospital, National Defense Medical Center, No. 325, Sec. 2, Cheng-gong Road, Taipei 114, Taiwan, Republic of China. Tel: + 886-2-87927192; Fax: +886-2-87927193; E-mail:asdcxzgg@gmail.com

CASE REPORT

A 62-year-old female was referred to our hospital for assessment of a right submandibular region mass that had progressively enlarged within the previous year, and developed tenderness in the past month. Antibiotic treatment had been given, under the impression of sialoadenitis. There was no significant history of illness or treatment thereof except that she had received hormone therapy for post-menstrual syndrome. On physical examination, the mass was found to be firm, with tenderness, fixed, and measuring approximately 3 cm in diameter. There were no palpable lymph nodes over the bilateral areas of the neck. The patient denied any history of irradiation or trauma of that location and there were no other significant findings on physical examination.

Ultrasonographic examination revealed a heterogeneous hypoechoic lesion about 3 cm in diameter in the right SMG. Computed tomography (CT) scanning of the neck showed a heterogeneously enhancing tumor measuring 2.9×3.3×1.9 cm in the posteromedial portion of the right submandibular gland (Figure 1). No lymphade-

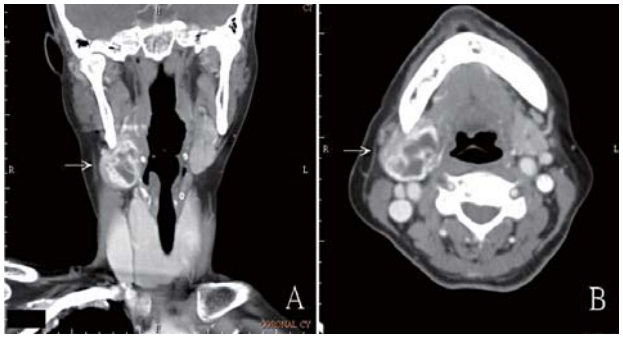

Fig. 1 Coronal (A) and axial (B) computed tomography scans demonstrate a mass located in the right submandibular region (White arrow).

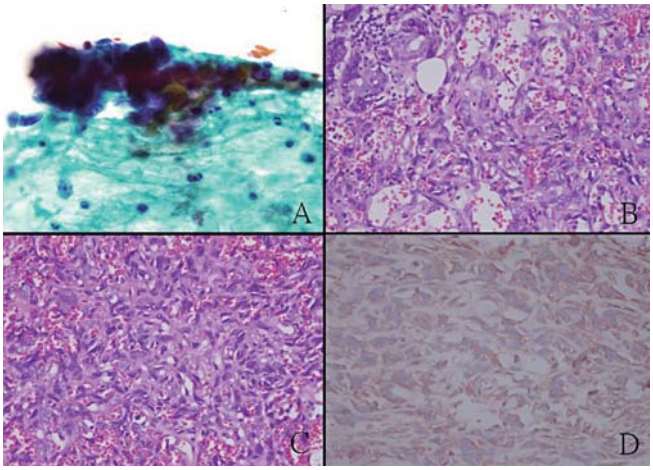

Fig. 2 Fine needle aspiration cytology reveal abnormal epithelioid cells and occasional nuclear grooving (A, 100×). Photomicrograph of the tumor shows a predominant solid tumor mass with few vascular channels (B, 100×) and irregular and freely anastomosing vascular channels lined by marked pleomorphic spindle endothelial cells at low-power field (Hematoxylin-Eosin stain) (C, 100×). Tumor cell stained positively with CD-34 (D, 200×).

nopathy was found. A preoperative fine needle aspiration (FNA) cytology report revealed abnormal epithelial cells with suspicion of malignancy.

Excision of the SMG was attempted and effected. The lesion was excised completely intra the right SMG. There was no adherence to skin or adjacent mandible. Grossly, the tumor was red in color and firm in consistence. The cut surface of the main tumor showed a hemorrhagic mass measuring 3×3×2.5 cm in size. Histopathological examination revealed dense clumps of irregular, pleomorphic anaplastic cells and focal vascular lumens formation as well as abortive lumen lined with single or a few pleomorphic cells and contained red blood cells in some of them. In addition, some atypical mitoses are also noted. According to those histopathological features, the tumor was graded as high grade. Immunohistochemical stains revealed positive immunoreactivities for CD-34, and focal positives for Vimentin and over-expression of P53, but negatives for cytokeratin, S100, Actin, and factor VIII (Figure 2). A final diagnosis of angiosarcoma of the submandibular gland (T1bN0M0, stage I) was established.

Sequential radiotherapy on the tumor bed (total 6000 cGy) and right regional lymph nodes (total 5000 cGy, covering right neck level II, III, and IV) was done. The patient was followed up for 12 months and remained free of apparent tumor recurrence.

DISCUSSION

AS is a rare and aggressive vascular malignancy. When an AS occurrs in head and neck, more then 50% of patients arise from the scalp and forehead.[1] Primary lesions of the salivary gland are extremely rare. The majority of AS occur in the head and neck, with a mean patient age of 63 and a slight male predilection. Oral and salivary gland AS, however, tend to occur earlier.[1-2] The tumorigenesis of the vascular tumors is still undetermined. Actinic damage from sun exposure, previous radiation exposure, and local trauma with connective tissue damage often have been suggested as possible predisposing factors.[3] They usually present as an enlarging mass and produce symptoms due to inflammation, compression of adjacent structures, or bleeding.[4] About 50 percent of the patients with head-and-neck AS have previously been misdiagnosed as having infection, hematoma, or other tumors such as lipoma, basal cell carcinoma, and lymphoma.[1] Delays in diagnosis are common and may be attributable to a lack of clinical awareness and the protean clinical nature of AS.[3]

When AS occurs in the neck, most patients first present as having an asymptomatic mass.[1] Diagnostic workup usually encompasses imaging studies followed by FNA cytology. Grey scale sonography and CT imaging features were nonspecific to AS but were characteristic for hypervascular tumors. Most lesions were ill defined, heterogeneous, and had variable degrees and patterns of enhancement on contrast-enhanced CT study.[5] Doppler color flow imaging provided valuable information on the vascular malformations and Bernathova reported detected venous tumor vessel flow characteristic of breast AS.[6] The effectiveness of the tool needs more experiments to

evaluate.

The role of FNA in diagnosing rare primary malignant soft tissue tumors such as AS has not been clearly defined. One review of the FNA cytology of soft tissue tumors of 43 patients suggests that the correct specific diagnosis was given in only 21% of the cases.[7] The diagnosis of AS can be suggested by FNA when vasoformative features are present, but a definitive diagnosis of AS is often difficult to render due to a paucity of diagnostic cells and variable cytological features. Multiple aspirations are often needed in order to obtain diagnostic material when AS is suspected, but hematoma or bleeding after a FNA biopsy for AS in intra-abdominal organs, breasts and thyroids has been reported, and this procedure has even been argued to be a hazardous procedure in cases of AS of the liver.[8] Typical cytologic features of vasoformation such as intracellular red blood cells, well-formed vessels, attempts at lumen formation, and intracytoplasmic lumens are variably present. Due to high false rate of cytological studies and possible critical complications of FNA, we consider excision biopsy is more suitable for patients who had neck mass suspected AS.

Cutaneous vascular tumors included angiosarcoma and Kaposi's sarcoma. Histopathologically, the angiosarcoma is characterized by multiple vascular channels of different sizes lined by endothelial, atypical cells, disposed on one or more layers. The atypical endothelial cells are more protuberant than normal cells, pleomorphic, with pale, light eosinophilic cytoplasm and voluminous and hyperchromatic nuclei. Lymphocytic infiltrate is present. Tumor cells show an alveolar or fasciculate pattern. Kaposi's sarcoma is also a mesenchymal tumor characterized by the proliferation of spindle-shape cells, usually in a directional streaming pattern, neoangiogenesis, inflammation with fibrosis and hyperemia (extravasated erythrocytes and hemosiderin storage). In this case, the tumor was characteristic with a predominant solid tumor mass with few vascular channels rather then hyperemia and absent of extravasated erythrocytes and hemosiderin storage. The vascular channels composed with irregular and freely anastomosing channels lined by marked pleomorphic spindle endothelial cells with lymphocytic infiltrate. Those histopathological findings revealed the tumor was in favour of a high grade AS.

Histologic studies are the mainstay of diagnosis of AS, but, perplexedly, AS often have different characteristics within a single tumor.[1] Regarding vascular origin tumors, to distinguish between benign hemangioma, polymorphous hemangioendothelioma, and AS are dependent on the degree of vascular differentiation and malignant behaviors. The vascular differentiation are defined by the description of pleomorphism, mitoses, proportion of solid areas, spindle cell component and epithelioid cell component.[1] Malignant hemangioendothelioma is a distinctive variant of low-grade AS, characteristic with well-differentiated cells morphology. Sharon considered epithelioid endothelial cells may be seen in benign vascular tumors and rarely in AS.[9] In Aust study, 75% of AS revealed none to mild degree epithelioid cell component, and majority presented with adnexal structures invasion(83.3%).[1] In the SMG location, the most common AS morphology is less-differentiated cells with high proportion of undifferentiated solid areas.[2] With the aid of immunocytochemical stains, diagnoses of AS can be obtained more accurately and definitively. CD34, a marker for vascular endothelial cells and pericytes showed positive in this case. Besides, over-expression P53, hallmark of cancer cell, offered strong evidence of malignancy. In addition to the histopathological findings, positive staining with CD34 and P53 also support our diagnosis.

Angiosarcoma of the soft tissue is a high-grade sarcoma with a high rate of death and short survival time. A large number of patients, 50% in some series, also had metastasis, and a significant number (20%) had local recurrences.[10] Older patient age, retroperitoneum location, and larger tumor size are unfavorable prognostic factors. Approximately 66% of retroperitoneal angiosarcomas recur locally in the tumor bed and can recur diffusely throughout the peritoneal cavity.

In conclusion, when AS occurs in the SMG and presents with a neck mass, with variable imaging and cytological features, make pre-operative diagnosis difficult. The presence of a radiographic enhanced head and neck tumor with peripheral structure extension and destruction suggests a hypervascular and aggressive neoplasm, AS should be considered. Spectrum of vascular tumors are variable, and excision biopsy should be performed to establish the diagnosis. The final diagnosis must be made according to histological examination, immunocytochemical studies and clinical behaviors.

DISCLOSURE

The authors declare that this study has no con?ict of interest.

REFERENCES

1. Aust MR, Olsen KD, Lewis JE, Nascimento AG,

Meland NB, Foote RL, Suman VJ. Angiosarcomas of the head and neck: clinical and pathologic characteristics. Ann Otol Rhinol Laryngol. Nov 1997;106:943-951.
2. Fanburg-Smith JC, Furlong MA, Childers EL. Oral and salivary gland angiosarcoma: a clinicopathologic study of 29 cases. Mod Pathol. Mar 2003;16:263-271.
3. Fayette J, Martin E, Piperno-Neumann S, Le Cesne A, Robert C, Bonvalot S, Ranchère D, Pouillart P, Coindre JM, Blay JY. Angiosarcomas, a heterogeneous group of sarcomas with specific behavior depending on primary site: a retrospective study of 161 cases. Ann Oncol. Dec 2007;18:2030-2036.
4. Karube R, Sasaki H, Shinozuka K, Fujisawa Y, Yanagawa T, Yamagata K, Onizawa K, Otsuka F, Bukawa H. Angiosarcoma of the scalp diagnosed by the presence of neck inflammation: a case report. Int J Oral Sci 2012 Sep;4:166-169, doi: 10.1038/ijos.2012.36.
5. Coldwell DM, Baron RL, Charnsangavej C. Angiosarcoma. Diagnosis and clinical course. Acta Radiol Nov-Dec 1989;30:627-631.
6. Bernathova M, Jaschke W, Pechlahner C, Zelger B, Bodner G. Primary angiosarcoma of the breast associated Kasabach-Merritt syndrome during pregnancy. Breast. Apr 2006;15:255-258.
7. Costa MJ, Campman SC, Davis RL, Howell LP. Fine-needle aspiration cytology of sarcoma: retrospective review of diagnostic utility and specificity. Diagn Cytopathol. Jul 1996;15:23-32.
8. Liu K, Layfield LJ. Cytomorphologic features of angiosarcoma on fine needle aspiration biopsy. Acta Cytol. May-Jun 1999;43:407-415.
9. Weiss SW, Enzinger FM. Epithelioid hemangioendothelioma: a vascular tumor often mistaken for a carcinoma. Cancer. Sep 1 1982;50:970-981.
10. Meis-Kindblom JM, Kindblom LG. Angiosarcoma of soft tissue: a study of 80 cases. Am J Surg Pathol. Jun 1998;22:683-697.