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CASE REPORT

Synovial Sarcoma: a Rare Tumor of Larynx

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Synovial sarcoma is a soft tissue sarcoma of unknown histogenesis and occurs predominantly in the lower extremities of young adults. The head and neck is a relative rare location. There are about 10 cases with laryngeal localization in the literature. We present a 24 year-old male with an endolaryngeal mass. Incisional biopsy and the hemilaryngectomy material revealed a biphasic synovial sarcoma. One year later a local recurrence occurred. Tumor excision and neck dissection were performed. Radiotherapy was added. Six months later lung metastases was discovered on thoracic CT. The patient received chemotherapy for 6 courses. The metastases responded well to chemotherapy and the patient is now alive without tumor on radiological and clinical examination after 3.5 years of follow-up. (Pathology Oncology Research Vol 9, No 4, 242–245)

Keywords: larynx, synovial sarcoma

Introduction

Synovial sarcoma is a mesenchymal malignancy of unknown histogenesis and occurs mostly in the extremities. About 9% of the cases were reported in the head and neck region.[19] Involvement of the larynx is very rare. The literature includes about 10 cases of synovial sarcoma of the larynx.[2-4,6,7,9-14] Most cases were treated either with surgery alone or combined with radiotherapy. Only two cases were reported to whom chemotherapy was administered.[3,12] A laryngeal synovial sarcoma treated with surgery, radiotherapy and chemotherapy was presented and the differential diagnosis was reviewed.

Case Report

A 24 years old male patient was admitted to the ENT Department of the University Hospital complaining of changing of his voice and dysphagia for several months. Under laryngoscopic examination, an endolaryngeal mass involving epiglottis was discovered. Magnetic resonance imaging revealed a tumor which filled up the entire supraglottic region (*Figure 1*). Under microlaryngoscopic procedure incisional biopsy was taken. The tumor was 1.5 cm in diameter and the histology was of a biphasic synovial sarcoma. Laryngectomy was planned but the patient came two months later; than a hemilaryngectomy was performed. The tumor was supraglottic in location and involved the left arytenoid and the aryepiglottic plica. The tumor measured 3x2.5x0.7 cm. The surgical margins contained no tumor. One year later a local recurrence occurred. The former operation was extended to total laryngectomy. A tumor 2.5 cm in diameter, a thyroid nodule and cervical lymph nodes were excised. The tumor was infiltrating the surrounding soft tissue and had the same histology. The thyroid nodule and the lymph nodes contained no tumor. The surgical margins were free of tumor. Following surgery, bilateral cervicofascial and left supraclavicular radiotherapy (each 45 Gy/25 fraction) was given. At 20 months of follow-up bilateral lung lesions and left pleural effusion developed. The patient underwent chemotherapy consisted of adriamycin (75 mg/m^2) and ifosfamide (2 g/m^2). To prevent hemorrhagic cystitis MESNA (1.5 g/m^2) was given. After 3 months regression was achieved. The patient received 6 cycles of chemotherapy at three weekly intervals. Ifosfamide was given for 3 days in every course. Radiological examination revealed no regional mass or metastatic nodules in lung at 3.5 years of follow-up.

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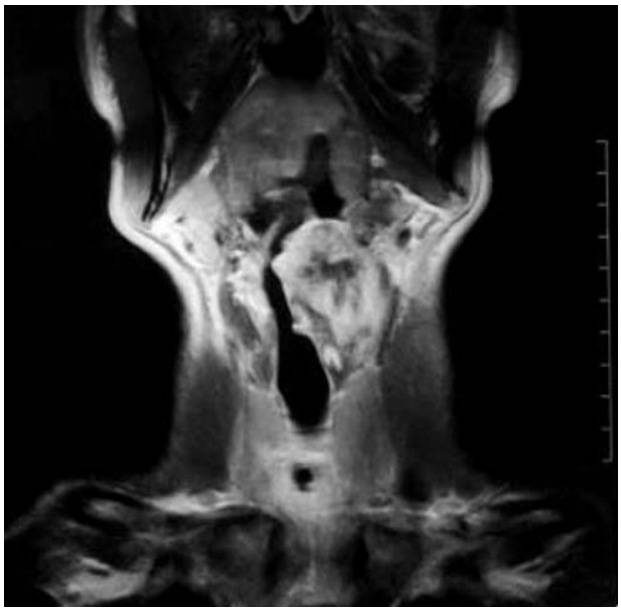

Figure 1. *Radiological appearance of the tumor*

Microscopical and immunohistochemical findings

The morphology was the same in all biopsy material. A biphasic tumor consisting of glandular structures and spindle cells was seen (*Figure 2*). Epithelial component was in the form of glands or clefts lined by cuboidal epithelial cells. In the lumina of the glands, PAS positive material was observed. The sarcomatous area was characterized by a cellular, spindle cell infiltration without any special pattern. Necrosis was 5%, calcification was absent, mitotic figures were counted as 7/10HPF.

Immunohistochemistry was performed using streptavidin-biotin-peroxidase system Primary antibodies used were: cytokeratin (Pan-Ab-1, Novacastra, antigen retrieval, 1/50, 60 min.); EMA (Neomarker; 1/50, 30 min); vimentin (Novacastra; antigen retrieval;1/800, 60 min), S-100 (Neomarker; antigen retrieval, 1/100, 60min); Ki-67 (Novacastra, antigen retrieval, 1/100, 60 min), p53 (Novacastra, antigen retrieval, 1/40, 60 min).

The epithelial component was positive for pancytokeratin (*Figure 3*) and EMA. Scattered spindle cells were also stained by cytokeratin antibody. Spindle cells were diffusely immunreactive to vimentin antibody. S-100 protein was negative. Ki-67(MIB-1) proliferation index was 30%. Twenty five percent of the nuclei were immunoreactive to anti-p53 antibody.

Discussion

Synovial sarcoma accounts for 5-10% of all soft tissue sarcomas.[3,16,19] More than 80% of cases occur in the extremities. Head and neck is a rare (3-9%), but well known location of synovial sarcoma.[2,3,19] About ten cases of primary laryngeal synovial sarcoma were reported (*Table 1*). We present a 24 years old male patient with a supraglottic tumor, measuring 4.5 cm and involving the aryepiglottic plica as in the most of the reported cases. The patients age is typical for synovial sarcoma, which is a tumor of young adults.

Primary tumors of larynx are predominantly squamous cell carcinoma.[2] Other unusual tumors in this location are fibrosarcoma, chondrosarcoma, osteosarcoma and rhabdomyosarcoma.[4,5] Carcinosarcoma of larynx is a composite tumor consisting of carcinomatous and sarcomatous areas; which was described by some authors in other names.

The term carcinosarcoma is applied when heterologous elements such as bone, cartilage or muscle are encountered in a tumor, that elsewhere shows one of the more convential patterns of carcinoma. In carcinosarcoma the patient is often in his late middle age with a long history of tobacco use. The tumor is polypoid and often ulcerated. The carci-

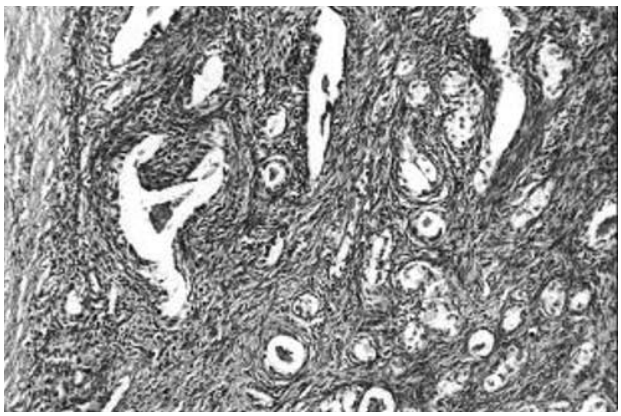

Figure 2. *Biphasic pattern consisting of glandular structures and spindle cell component (HEx310)*

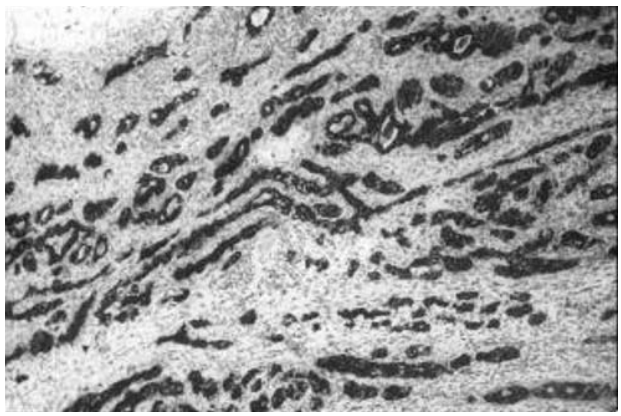

Figure 3. *Pancytokeratin positivity in the glandular component (immunoperoxidase x 125)*

nomatous element is usually a squamous cell carcinoma. Although the morphogenesis of carcinosarcoma remains controversial, it is suggested that the sarcomatous part seems to be a transformation of the epithelial component. Immunohistochemistry and electron microscopy support the view that carcinosarcoma is basically an epithelial tumour that shows varying degrees of mesenchymal differentiation.[1,3,8,18] In contrast, synovial sarcoma occurs predominantly in young adults. The mucosa coating the neoplasm is usually intact. Squamous metaplasia is very rare. Microscopic examination of the tumor in the presented case revealed a biphasic tumor beneath an intact epithelium. The mesenchymal component consisted of spindle cells. Osteosarcomatous, chondrosarcomatous or rhabdomyosarcomatous differentiation were not observed.

Biphasic synovial sarcoma causes few problems in diagnosis but synovial sarcoma can display different patterns. The monophasic fibrous type can be misdiagnosed as a spindle cell sarcoma or a hemangiopericytoma.[1,3,19] The pure epithelial subtype can be confused with a carcinoma.[1-3,19] The poorly differentiated subtype has morphological similarities to small round cell tumors. CD99 antigen

Table 1. **Endolaryngeal synovial sarcomas: reported cases**

Reference	*Age/sex*	*Location*	*Therapy*	*Follow-up*
Miller	23/F	interarytenoid and left arytenoid	excision; supraglottic laryngectomy and total laryngectomy	NED after 12 years
Gatti	*same case as above reported by Miller*			
Geahchan	24/M	left arytenoid and left epiglottic fold	partial pharyngectomy, total laryngectomy	recurrence 4 years after surgery; lung metastasis after 6 years
Quinn	76/M	right subglottic area	hemilaryngectomy	NED after 3 years
Kitsmaniuk	15/M	left arytenoid; pyriform sinus, epiglottis, true and false cords	extended total laryngectomy	NED after 8 months
Kleinasser	58/F	subglottic area	partial resection	recurrence after 7 years
Pruszczynski	28/F	left aryepiglottic fold and false vocal cord	local excision, RT (66Gy)	NED after 3 years
Ferlito	28/M	right aryepiglottic fold, epiglottis	Preop. RT(25Gy), supraglottic laryngectomy, right neck dissection, postop. RT(50 Gy)	NED after 16 years
Danninger	53/M	right aryepiglottic fold	laryngectomy, neck dissection RT(64Gy)	NED after 16 months
Morland	14M	left arytenoid	excision, laryngectomy following recurrence, CT and RT(60Gy)	recurrence after 3 years NED after 10 months
Dei Tos	27M	right aryepiglottic fold	excision, hemilaryngectomy following recurrence, CT and RT(62Gy)	recurrence after 3 months NED after 9 months
Present case	24/M	left aryepiglottic fold, epiglottis and left arytenoid	excision, hemilaryngectomy, total laryngectomy, neck dissection, RT(45Gy) and CT	Recurrence after 1 year Lung metastasis after 20 months Alive and NED at 3.5 years

RT: Radiotherapy CT: Chemotherapy

is positive in 95% of Ewing's sarcoma/PNET family tumors; a synovial sarcoma can also be immunoreactive to anti-CD99 antibody.[3] Extensive sampling of the tumor and immunohistochemistry are helpful in the differential diagnosis. Cytogenetic analysis is also important in the differential diagnosis, because of the typical (x;18) translocation of synovial sarcoma.

Various prognostic factors have been accepted in synovial sarcoma including age, location, size of the tumor, necrosis, high mitotic index.[16,19] New studies have indicated several other possible prognostic parameters. A Ki-67 index of 10% or more was considered highly proliferative.[17] Our case showed a Ki-67 index of 30%. The significance of p53 immunostaining is not clear , but in a study of 34 synovial sarcoma cases it was suggested that the overall survival was significantly reduced in patients having synovial sarcoma with p53 alterations (cut off value: 10%).[15] We found that 25% of nuclei were immunreactive to p53 antibody. Our patient was therefore in a poor prognostic group concerning his age, tumor size, Ki-67 index and p53 positivity.

Surgery is the main therapy for synovial sarcoma and is often supplemented with radiotherapy.[2,16,19] Local recurrences of up to 80% have been recorded after inadequate surgery without radiotherapy.[16] Lymph node dissection is not necessary in most cases.[2,3] Because of a local recurrence and a palpable mass in the neck region of the presented case, neck dissection was performed, but the lymph nodes showed no infiltration. The cases shown in *Table 1* were all treated with surgery. In some of them radiotherapy was added. Only two cases underwent chemotherapy to whom ifosfamide was given in high doses.[3,12] In our case a chemotherapy consisting of ifosfamide and adriamycin were applied. The therapy was effective and the metastatic nodules disappeared.

We add a new case of laryngeal synovial sarcoma to the literature. Ifosfamide seems to be effective even in the metastatic disease. Because of the limited number of the laryngeal cases, every new case will bring some new information about the therapy.

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