Primary Synovial Sarcoma of the Pharynx: A Series of Five Cases and Literature Review

Syeda Samia Fatima¹ · Nasir Ud Din¹ · Zubair Ahmad¹

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Abstract Synovial sarcoma comprises approximately 10 % of all soft tissue sarcomas. Although synovial sarcoma has been reported in practically every organ, the extremities are the commonest site of occurrence followed by the head and neck. Primary synovial sarcoma of the pharynx is rare and only case reports have been published. We report a series of five cases of primary synovial sarcoma involving the pharynx.

Keywords Synovial sarcoma · Pharynx · Biphasic · Monophasic · TLE 1

Introduction

Synovial sarcoma (SS) is a malignant neoplasm that arises from the primitive pluripotent mesenchymal cells near to or remote from the articular surfaces [1]. It is a relatively rare tumor, occurs mainly in adolescents and young adults, has a slight male predominance, and comprises approximately 10 % of all soft tissue sarcomas [2]. The extremities are the commonest site of occurrence followed by the head and neck region (5–10 % of all cases) [3, 4]. Most of these latter cases arise in the paravertebral connective tissue spaces and manifest as retropharyngeal and/or parapharyngeal masses. The first case of primary hypopharyngeal SS was reported by Jernstorm [5]. Since then there have been several independent case reports. However, there are very few case series of primary SS of the pharynx in

English literature. Here, we describe five cases of SS of the pharynx reported from our institution.

Cases

We searched our archives for cases of SS reported over a period of 10 years (2005–2014). A total of 347 cases were reported during this time. Of these, 22 were located in the head and neck region including 5 cases in the pharynx. Of these five patients, three were male and two were female. Age ranged from 14 to 29 years (mean 23 years). History of difficulty in swallowing and progressively increasing shortness of breath was present in two cases (Case 1 and Case 2 respectively). In three of the cases, the tumors were located in the hypopharynx (Cases 1, 4, and 5), while in two cases, tumors were located in the pharynx and pyriform fossa.

Histology

Out of the five cases, four were received for primary histopathological diagnosis while one case was referred to us for a second opinion (Case 3). The average size of the specimens was 5.3 cm in largest dimension. Two of the cases were grossly polypoidal and soft to firm in consistency (Fig. 1a, b), while the other three were received as multiple irregular tissue pieces. Representative sections were submitted, processed, and embedded in paraffin blocks. Routine Hematoxylin and Eosin (H and E) stain was performed. Histology of all five cases revealed a biphasic tumor with spindle and epithelial components. Surface stratified squamous epithelium was seen in two cases (Fig. 2a), while the remaining three cases showed

✉ Nasir Ud Din
nd176@yahoo.com; nasir.uddin@aku.edu

¹ Department of Pathology and Laboratory Medicine, Aga Khan University Hospital, Karachi, Pakistan

Fig. 1 **a** CT scan showing a polypoid tumor protruding into and partially occluding the pharyngeal lumen. **b** Gross image of the same patient exhibiting polypoid tumor with a grey white and fleshy cut surface

Fig. 2 **a** Biphasic synovial sarcoma covered by stratified squamous epithelium (H&E, $\times 10$ magnification). **b** Bands of stromal collagen in between biphasic components (H&E, $\times 20$ magnification). **c** Stromal

calcifications involving a dominant spindle cell area (H&E, $\times 10$ magnification). **d** Strong nuclear TLE 1 positivity in both epithelial and spindle cell areas ($\times 20$ magnification)

surface ulceration. The spindle cells were arranged in sheets and fascicles and demonstrated moderate nuclear pleomorphism. Interspersed among these spindle cells were glands and solid nests of epithelial cells. These cells were cuboidal to columnar with moderate nuclear pleomorphism (Fig. 2a, b). Focal myxoid change and stromal collagen bands were seen in three cases each. One case showed focal calcifications (Fig. 2c). Mitotic figures ranged from 1 to 5

mitoses/10 HPFs (mean 2.6 mitoses/10 HPFs). Immunohistochemical stains EMA, CKAE1/AE3, CK7, CK19, CK5/6, CD34, CD99, BCL2, and Vimentin were performed, the results of which are summarized in Table 1. A diagnosis of biphasic SS was rendered on all five cases. IHC stain TLE1 was performed retrospectively and demonstrated strong nuclear positivity in all five cases (Fig. 2d), further supporting the diagnosis. Follow up was

Table 1 Summary of pharyngeal Synovial sarcoma cases

Serial no.	Age/sex	History	Site	Size (cm)	Type	IHC	Follow up
Case 1	14/F	Difficulty in swallowing 1 year	Hypopharynx	5 × 4	Biphasic	CK Cam 5.2+, CK7+, CK19+, BCl 2+, TLE 1+, EMA & CD99 focal+, Desmin–, CK5/6–	NA
Case 2	20/M	Progressively increasing SOB 4 months	Pyriform Fossa	6 × 5	Biphasic	CKAE1/AE3+, CK19+, BCl2+, CD99+, Vimentin+, TLE 1+, CD34–	NA
Case 3	29/M	Not received	Pharynx	8 × 7	Biphasic	CKAE1/AE3+, EMA+, BCl2+, TLE 1+, CD99 focal+, Vimentin+, S100–, ASMA–	Received Chemo. DOD 3 years after dx
Case 4	24/F	Not received	Hypopharynx	5.5 × 4	Biphasic	CKAE1/AE3+, EMA+, CK19+, BCl2+, TLE 1+, CD99–, S100–, ASMA–, Desmin–	FOD 13 months after dx
Case 5	28/M	Not received	Hypopharynx	2 × 1.5	Biphasic	CKAE1/AE3+, EMA+, CK7+, CK19+, TLE 1+	FOD 10 months after dx

SOB shortness of breath, *dx* diagnosis, *NA* not available, *DOD* died of disease, *FOD* free of disease

available in three patients. One patient received chemotherapy following surgical excision. However, he died of the disease 3 years later. The other two patients are free of disease 13 and 10 months after surgery.

Discussion

Synovial sarcoma is a translocation associated malignant neoplasm mainly affecting young adults with a propensity to occur in extremities (particularly the knee) followed by the head and neck region, the latter accounting for 5–10 % of all cases [1, 3, 4]. Head and neck SS usually arise in the paravertebral connective tissue and present as retropharyngeal and/or parapharyngeal masses [3]. Males are affected twice as often as females [6]. SS typically show a t(x;18) translocation with fusion between SSX1 or SSX2 and SYT genes. FISH and RT-PCR have been employed for the rapid diagnosis of SS [1, 3].

Since the first case of primary hypopharyngeal SS reported by Jernstorm [5], several independent case reports have been published. However, there are very few case series of primary SS of the pharynx in English literature [1]. In spite of extensive review of the literature, we could not find case series focusing exclusively on pharyngeal SS. However, pharyngeal SS are included in a number of case series looking at head and neck SS in general. These series describe SS not only in the pharynx but also in other head and neck locations such as nose, paranasal sinuses, larynx, parapharyngeal space, etc. We have described five cases of SS of the pharynx reported in our department over a period of 10 years (2005–2014). The comparison of our cases with the

published case series [7–12] is shown in Table 2. As shown in this table, the average age, male to female ratio, and average tumor size in our series are similar to the findings in these studies. However, the number of monophasic SS is much higher in the studies by Roth et al. [7] and Crowson et al. [11].

Histologically there are two major categories of SS: biphasic and monophasic type. Biphasic SS has distinct epithelial and spindle cell components. Of the monophasic SS, the vast majority are the monophasic fibrous type which itself is the most common type of SS [3]. Monophasic epithelial type of SS has also been described but this tumor cannot be reliably recognized and distinguished from adenocarcinoma without cytogenetic or molecular tests. SS may also present as a poorly differentiated round cell sarcoma often arranged in pericytomatous pattern (poorly differentiated sarcoma). This is not a distinct subtype of SS; rather it represents a form of tumor progression that can occur in either monophasic or biphasic SS [3]. Histologically, no tumor in the body resembles biphasic SS. However, many tumors such as fibrosarcoma, malignant peripheral nerve sheath tumor (MPNST) and hemangiopericytoma can simulate monophasic SS [13]. Poorly differentiated SS can mimic Ewing's sarcoma. A panel of Immunohistochemical stains is thus necessary to avoid pitfalls in the diagnosis. Immunohistochemically, CD99, BCL-2, and Vimentin positivity is seen in the spindle cells. Cytokeratin expression is seen in 90 % of SS both in the epithelial and a few cells of the sarcomatous component. Expression of cytokeratin 7 and cytokeratin 19 along with epithelial membrane antigen (EMA) is also observed [14]. Transducer like enhancer of split 1 (TLE 1)

Table 2 Reported series on Synovial sarcoma of head and neck

Author/study duration	Study duration	Total cases	No. of cases in pharynx/UAT	Average age (years)	M:F ratio	Average tumor size (cm)	Histologic type
Roth et al. [7] (1948–1969)	1948–1969	24	10 (all in hypopharynx)	25.2	8:2	6	10 monophasic 14 biphasic
Hazarika et al. [8] (1980–1993)	1980–1993	3	2 (1 each in oro & hypopharynx)	22	1:1	7.5	Both monophasic
Rangheard et al. [9] (1984–1997)	1984–1997	8	4 (all in hypopharynx)	30.5	3:1	4.2	2 monophasic 2 biphasic
Harb et al. [10] (1945–2004)	1945–2004	40	3 (1 each in oro, hypo & nasopharynx)	30.6	2.6:1	5	2 monophasic 1 biphasic
Crowson et al. [11] (1960–2012)	1960–2012	28	11 (UAT and neck) Exact sites not mentioned	35.3	1.2:1	Not given	22 monophasic 4 biphasic 2 indeterminate
Woshu et al. [12] (2013)	Not given	93	47 (UAT, exact site not given)	32.1	1.4:1	5	Not given
Fatima et al. (current study)	2005–2014	22	5 (3 in hypopharynx, 1 each in pyriform fossa and pharynx)	23	3:2	5.3	All 5 biphasic

UAT upper aerodigestive tract

is over expressed in SS. It is a sensitive and specific marker for SS and can be helpful in distinguishing SS from its histological mimics particularly if moderate or strong nuclear staining is observed. Although molecular confirmation remains the gold standard, immunohistochemical studies for TLE-1 along with a panel of other markers are valuable in reaching a correct diagnosis, especially when access to molecular testing is limited and/or when there are financial constraints [15].

All five cases in our series were biphasic on histological examination. Monophasic SS is considered to be the commonest histological type of SS [9]. The fact that all five of our cases were biphasic is interesting because monophasic SS usually outnumbers biphasic SS elsewhere in the body. However, single case reports describing SS of the pharynx provide mixed evidence with some showing biphasic and others showing monophasic histological pattern [1, 6, 16–19]. We suggest that there may be some as yet unreported association between SS of the pharynx and biphasic histological pattern. However, further studies with larger numbers of cases will be needed to prove this suggestion.

The tumor usually occurs as an asymptomatic mass until it attains sufficient size to cause pressure effects on neighboring structures. This process is usually more rapid in head and neck SS than those in the extremities [1]. Lockey et al. [20] reported that patients with head and neck SS were diagnosed an average 20 months earlier than those with tumors in the extremities. However, the better prognosis of head and neck SS is controversial. Pai et al. reported a higher survival in patients with neck disease than

in limb tumors [21]. In another study by Kartha and Bumpous, it was found that the 5-year survival rate of head and neck SS was 40 % as compared to 60 % 5-year survival in SS at all other sites [22].

The primary mode of treatment is wide surgical excision, which includes a normal appearing tissue cuff to ensure tumor negative margins. However, this cannot be accomplished in the head and neck due to the proximity of the tumor to vital structures. The results of multimodality treatment appear to be better than those seen with any single modality treatment or with any form of salvage therapy [1]. The role of radiation is confined to reducing the risk of local recurrence following resection. Radiation does not improve long term survival [1].

We have described five cases of primary biphasic SS of the pharynx. Consistent with the published literature, these comprised 1.4 % of all cases reported as SS from our department over a period of 10 years. Less than 90 cases of primary SS of the pharynx have been reported [1] and these have been individual case reports. This is the first case series of primary pharyngeal SS from our country.

References

- Kadapa NBP, Reddy LS, Kumuda RS, Reddy MVV, Rao LMCS. Synovial sarcoma oropharynx—a case report and review of literature. *Indian J Surg Oncol*. 2014;5:75–7.
- Daveau C, Buiret G, Poupart M, Barnoud R, Pignat JC. Synovial sarcoma of the lateral pharyngeal wall. *Eur Ann Otorhinolaryngol Head Neck Dis*. 2012;129:327–30.

3. Weiss SW, Goldblum JR. Enzinger and Weiss's soft tissue tumors. 6th ed. Philadelphia: Mosby Elsevier; 2013.
4. Carrillo R, Rodriguez-Peralto JL, Batsakis JG. Synovial sarcoma of the head and neck. *Ann Otol Rhinol Laryngol*. 1992;101:367–70.
5. Jernstrom P. Synovial sarcoma of the pharynx: report of a case. *Am J Clin Pathol*. 1954;24:957–61.
6. Jamshed A, Loya A, Tirmizi AH, Hussain R. Synovial sarcoma of the hypopharynx. *Int J Head Neck Surg*. 2013;4:86–8.
7. Roth JA, Enzinger FM, Tannenbaum M. Synovial sarcoma of the neck: a follow up study of 24 cases. *Cancer*. 1975;35:1243–53.
8. Hazarika P, Shah P, Pujary K. Synovial sarcoma of the head and neck-a report of three cases. *Indian J Otolaryngol Head Neck Surg*. 1999;51:36–41.
9. Rangheard AS, Vanel D, Viala J, et al. Synovial sarcoma of the head and neck: CT and MR imaging findings in eight patients. *Am J Neuroradiol*. 2001;22:851–7.
10. Harb WJ, Luna AM, Patel SR, et al. Survival in patients with synovial sarcoma of the head and neck: association with tumor location, size, and extension. *Head Neck*. 2007;29:731–40.
11. Crowson MG, Lalich I, Keeney MG, Garcia JJ, Price DL. Clinicopathologic factors and adjuvant treatment effects on survival in adult head and neck synovial cell sarcoma. *Head Neck*. 2015;37:375–80.
12. Wushou A, Miao XC. Tumor size predicts prognosis of head and neck synovial cell sarcoma. *Oncol Lett*. 2015;9:381–6.
13. Sharif MA, Mushtaq S, Mamoon N, Khan MT, Asghar Z. Synovial sarcoma of the oral cavity. *JCPSP*. 2008;18:713–5.
14. Mills SE. Sternberg's diagnostic surgical pathology. 5th ed. Philadelphia: Lippincot Williams and Wilkins; 2010.
15. Foo WC, Cruise MW, Wick MR, Hornick JL. Immunohistochemical staining for TLE1 distinguishes synovial sarcoma from histologic mimics. *Am J Clin Pathol*. 2011;135:839–44.
16. Palmer BV, Levene A, Shaw HJ. Synovial sarcoma of the pharynx and esophagus. *J Laryngol Otol*. 1983;97:1173–6.
17. Nakahira M, Sugawara M, Morita K. Monophasic synovial sarcoma of the nasopharynx. *Auris Nasus Larynx*. 2013;40:413–6.
18. Betal D, Babu R, Mehmet V. Monophasic synovial sarcoma of the pharynx: a case report. *Int Semin Surg Oncol*. 2009;6:9.
19. Daveau C, Buiret G, Poupart M, Barnoud R, Pignot J-C. Synovial sarcoma of the lateral pharyngeal wall. *Eur Ann Otorhinolaryngol Head Neck Dis*. 2012;129:327–30.
20. Lockey MW. Rare tumors of the ear, nose and throat: synovial sarcoma of the head and neck. *South Med J*. 1976;69:316–20.
21. Pai S, Chinoy RF, Pradhan SA, D'Cruz AK, Kane SV, Yadav JN. Head and neck synovial sarcomas. *J Surg Oncol*. 1993;54:82–6.
22. Kartha SS, Bumpous JM. Synovial sarcoma: diagnosis, treatment, and outcomes. *Laryngoscope*. 2002;112:1979–82.