Synovial Sarcoma: Laryngopharynx a Challenge

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Abstract Synovial sarcoma is a rare malignant tumor. It derives from a mesenchymal precursor stem cell that is unrelated to mature synovial tissue. Synovial sarcoma classically affects lower limbs between the ages of 15 and 40 years and the proportion of male-to-female patients is 3:2. It is very rare in the head and neck region especially in laryngopharynx. Till date, only six cases of synovial sarcoma involving laryngopharynx have been reported in the English literature. Painless mass, hoarseness, upper respiratory distress, and dysphagia characterize the original complaints in laryngopharyngeal synovial sarcoma. Because head and neck synovial sarcoma in clinical practice is so uncommon, early diagnosis is difficult and the treatment protocol is unclear. Therefore, every case report should include complete information on presentation and management. Also, long-term prognostic indices need to be evaluated. We hereby report a case of large laryngopharyngeal synovial sarcoma confirmed by histopathology and immunohistochemistry with review of literature.

Keywords Synovial sarcoma · Laryngopharynx · Immunohistochemistry

Introduction

The term ‘Synovial sarcoma’ was coined, early in the twentieth century as some thought that the microscopic similarity of some tumors to synovium and its propensity to

arise adjacent to joints indicated a synovial origin; however, the actual cells from which the tumour develops are unknown and not necessarily synovial.

Synovial sarcoma is rare. It accounts for 3–10 % of all soft tissue sarcomas [1]. It represents a mesenchymal malignancy of unknown histogenesis developing from pluripotential mesenchymal cell through abnormal differentiation into synovial neoplasms. It is clinically, morphologically and genetically a distinct sarcoma, characterized by the specific chromosomal translocation t(X;18)(p11;q11). They lack precise normal tissue counterpart and classified as malignant tumors of uncertain differentiation.

These sarcomas, most often occurs in the lower limbs of young adults. Synovial sarcoma classically affects patients between the ages of 15 and 40 years and the proportion of male-to-female patients is 3:2. The head and neck region is a relatively rare location. Jernstrom [2] published the first ever case of a synovial sarcoma of hypopharynx in 1954. We could find only six cases of synovial sarcoma arising from laryngopharynx in the English literature [3–6].

Case Report

K, young female attending our set up with the complaints of difficulty in breathing and swallowing, change in voice and a lump in the throat for the last 6–7 months. The complaints are of slow onset and progressively increasing. She was unable to lie supine as she will get respiratory distress and bouts of cough for the last 2 months. On examination, she was poorly built female. Ear, nose throat examination revealed a multilobulated mass in the oropharynx. It looked cystic/soft, non tender, glistening overlying surface (Fig. 1).

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Fig. 1 Multilobulated mass

Indirect laryngoscopic examination was not possible. MRI done shows a focal mass lesion with smooth sharply defined margins in the laryngopharynx compressing the aerodigestive tract. It was hyperintense on T2 and intermediate signal on T1W1. There was no infiltration to the surrounding structures. The laryngeal framework with true and false vocal cords and laryngeal muscles were normal (Fig. 2). Fine needle aspiration reported well cohesive spindle cells with regular delicate elongated nuclei and absence of malignant cells with opinion in favour of neurofibroma or leiomyoma. Subsequently, the patient developed respiratory distress. She was tracheostomised under LA. General anesthesia was administered through tracheostomy. Direct examination using Boyle's Davis mouth gag was done. There was a multi-lobulated, trabeculated, greyish soft/cystic smooth mass filling the oropharynx attached to the right side of the laryngopharynx. Since the FNAC report was that of neurofibroma/leiomyoma, we decided to remove the mass per orally. The mass was excised in one piece from its base or attachment. The mass measured 8.5 cm × 4.5 cm Fig. 3. There was minimum bleeding. The raw surface margins of laryngopharynx was marsupialised. There was no involvement of true and false vocal cords, epiglottis, tongue, arytenoids, aryepiglottic folds and post cricoid region except edema in the arytenoids and aryepiglottic folds. The tracheostomy was decannulated on 4th postoperative day and patient discharged on 5th postoperative day with the advice to report if there is any recurrence of the tumour. Histopathology revealed compact spindle cells in fascicles with scanty fibrinous stroma and prominent vesicular nuclei came out to be consistent with Spindle cell sarcoma with mitosis 4–5/10 HPF. The tumor cells were positive for CK, EMA, BCL-2, and Mic2 whereas they were negative for SMA, CD34, and S100. The histopathological and immunological diagnosis is biphasic synovial sarcoma (Fig. 4a–c).

Discussion

Synovial sarcoma represents a mesenchymal malignancy of unknown histogenesis developing from pluripotential mesenchymal cell through abnormal differentiation into synovial neoplasms [3].

It is clinically, morphologically and genetically a distinct sarcoma, characterized by the specific chromosomal translocation $t(X;18)(p11;q11)$. They lack precise normal tissue counterpart and classified as malignant tumours of uncertain differentiation (WHO 2002) [7]. A translocation involves the mechanical breakage and reconnection between different chromosomes.

A painless mass remains the most frequent presentation. In head and neck region, there is difficulty in swallowing and breathing and alteration of voice. Pain may be related to the involvement of nerves. Because the tumor grows slowly, symptoms may be present for a long time before the diagnosis is made. This may delay diagnosis. These tumors tend to be multi-nodular and can be cystic. When they grow slowly, they tend to have pushing margins and are circumscribed by a fibrous pseudo-capsule.

Calcifications are present in more than 50 % of tumors and may be noted on radiography; this finding suggests the diagnosis [8]. Preoperatively, computed tomography and magnetic resonance imaging are the investigations of choice to determine the location and extent of the tumor. MRI demonstrates a characteristic non mucosal mass that is homogeneous on T1-weighted images and heterogeneous on T2-weighted images.

Histologically, synovial sarcomas are classified into monophasic epithelial, monophasic fibrous and biphasic and poorly differentiated variants. The classic features include spindle cells with interposed epithelial elements with delicate cleft-like glandular pattern highlighted by cytokeratin immunohistochemistry.

The biphasic type consists of epithelioid and spindle cells with predominantly spindle cells component. In this type, Mast cells, mitosis, areas of calcification and scanty collagen production are the diagnostic features. The epithelioid cells from pseudo-glandular cavities filled with mucin, which stain positive with Alcian blue, mucicarmine and periodic acid Schiff (PAS) stains. In spindle cell, mucin stains positive with Alcian blue.

Monophasic type consists of single cellular type i.e., epithelioid or spindle cells both staining positive for cytokeratin and epithelial membrane antigen (EMA). The difference between epithelioid and spindle cell component is done by vimentin, a mesenchymal marker. Vimentin stains positive with spindle cells and negative with epithelioid type.

Poorly differentiated synovial sarcoma grows rapidly with infiltrative margins, showing haemorrhage and necrosis. It is considered as a form of progression, with a more aggressive

Fig. 2 MRI scan neck showing focal mass

Fig. 3 Removed specimen

behavior and a higher percentage of metastases [9]. Poorly differentiated synovial sarcomas show one of three morphologic patterns: a large cell/epithelioid/rhabdoid pattern, a small cell pattern, and a high grade spindle cell pattern.

The diagnosis of synovial sarcoma is typically made based on histology and confirmed by immunohistochemistry which plays a major role and enables the epithelial differentiation. Both monophasic and biphasic synovial sarcomas are characterized cytogenetically by the

reciprocal translocation $t(X;18)(p11.2;q11.2)$ between chromosomes X and 18. The presence of this translocation confirms the diagnosis of synovial sarcoma. This translocation event between the SYT gene on chromosome 18 and one of 3 SSX genes (SSXI, SSX2, and SSX4) on chromosome X causes the presence of a SYT–SSX fusion gene. The resulting fusion protein brings together the transcriptional activating domain of SYT and the transcriptional repressor domains of SSX. SYT–SSX is thought to underlie synovial sarcoma pathogenesis through dysregulation of gene expression. There is some association between the SYT–SSX1 or SYT–SSX2 fusion type and both tumour morphology and 5-year survival.

The AJCC classifies all synovial sarcomas as high grade. Regional lymph node metastasis occur in fewer than 5 % of synovial sarcomas, whereas distant metastasis, most frequently to the lung, occur in 50 % of cases [8].

Like other soft tissue sarcomas, there is no universal grading system for reporting histopathology results. In Europe, the Trojani or French system is gaining in popularity while the NCI grading system is more common in the United States.

The French system, French Federation of Cancer Centers Sarcoma Group (FNCLCC), is the most often used for adult-type soft tissue sarcomas [10]. It is a score system in which the sum of D (differentiation; 'D3' by default in SS). M

Fig. 4 **a** Cleft like space with spindle cells surrounding it. **b** Low power-mucosa with tumour underneath. **c** Spindle cells beneath mucosal lining

(mitosis: below 10/10 HPF; between 10 and 19/10 HPF; more than 19/HPF) and N (necrosis: absent; <50 %; more than 50 %) gives the grade 1, 2 or 3. Even if in therapeutic protocols SS is considered among high-grade sarcomas by definition, the FNCLCC grade is reported as the most

predictive histological factor for metastasis in synovial sarcoma. Less than 10 mitoses/10 HPF, absence of necrosis, absence of poorly differentiated areas, pediatric age, size smaller than 5 cm, and eradicated localized tumors resulted in a better prognosis. In our case, mitosis was 4–5/10 HPF. The tumour cells are positive for CK, EMA, BCL-2, and Mic-2 and negative for SMA, CD34, and S100 (grade 1)

Primary surgical excision is the mainstay of treatment. Postoperative radiation therapy is reserved for residual or recurrent disease [11]. Postoperative radiotherapy is said to decrease the likelihood of local recurrence, but it has not improved long-term survival. Chemotherapy is to reduce the number of remaining microscopic cells. The role of chemotherapy is controversial and debatable. The future role of both radiotherapy and chemotherapy in the management of synovial sarcoma needs to be determined by a prospective study.

Adequate surgery includes both compartment resections (en bloc resection of the tumor and the entire compartment of origin, where tumor is entirely anatomically confined) and wide excisions (en bloc excisions through normal tissue, beyond the reactive zone but within the muscular compartment, removing the tumor with its pseudocapsule). In our case there is no recurrence of the tumour for the last 9 months.

Wright et al. [12] found that metastases tend to be blood borne in most cases, with 10–20 % of patients experiencing lymph node metastasis.

Conclusion

Synovial sarcoma of Laryngopharynx is uncommon, early diagnosis is difficult and the treatment protocol is unclear. Therefore, every case report must be published. It should include complete information on presentation and management. Also, long-term prognostic indices need to be evaluated. Immunohistochemistry and histopathology plays major role to diagnose these tumours. Adequate radical Surgical excision must be performed followed by radiotherapy if there is recurrence or residual disease.

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