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Surgical experience of primary salivary gland tumors of lung: a case series

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ABSTRACT

Introduction

Primary salivary gland type tumors of lung (PSGTTL) are rare intra-thoracic malignant neoplasm. Their description in literature is largely limited to a few case series/case reports. We herewith present our surgical experience of and review its clinical presentation, management options and survival outcomes.

Methods

This retrospective analysis of prospectively maintained computerized data-base of patients was conducted in a tertiary teaching oncology centre in North India. The case records of all the patients who underwent surgery for PSGTTL were reviewed. Details concerning the clinical presentation, preoperative therapy, operative procedure, histopathological examination, postoperative complications and outcome were retrieved from the case records.

Results

There were seven patients who underwent surgery for PSGTTL during the period from January 2012 to December 2014. Hemoptysis (n=6, 85.7%) and dyspnoea (n=6, 85.7%) were common presenting clinical features. Fiber-optic bronchoscopy revealed endobronchial growth in all patients – five patients had growth in left main bronchus while one each had growth in right main bronchus and right intermediate bronchus. Biopsy confirmed adenoid cystic carcinoma in 4 (57.1%) and muco-epidermoid carcinoma in 3 (42.9%) patients. All but one had R‘0’ resection – pneumonectomy in five and bilobectomy in one patient; one patient was found to be unresectable in view of dense adhesions between lung and heart. Median pathological tumor size

was 3.5 cm; none of the patient was found to have metastatic spread to lymph nodes. Overall, six patients are alive after a median follow up of 5 months (range 1-30).

Conclusion

Radical surgery to achieve R'0' resection is the main stay of treatment of PSGTTL to achieve prolonged survival.

Key words: Lung neoplasms; Salivary gland neoplasms; Bronchoscopy; Lung surgery; Pneumonectomy; Adenoid cystic carcinoma; Mucoepidermoid carcinoma

INTRODUCTION

Salivary type neoplasms are known to occur at multiple organ sites in view of basic structural homology among exocrine glands in these anatomic sites. [1] Primary salivary gland type tumors of the lung (PSGTTL) are rare neoplasms; they account for less than 1% of all lung tumors. [1] They are histologically not indifferent from their counterparts of salivary origin; they are thought to arise from the sub-mucosal glands of the trachea-bronchial tree. [2] Majority of them is either adenoid cystic or mucoepidermoid carcinoma; rare types are epithelial-myoepithelial carcinoma, acinic cell carcinoma, and mixed tumors. [1,3] PSGTTL are slow growing indolent tumors and surgery is the main stay of treatment; there is limited role of chemoradiotherapy in the management of PSGTTL. Clinical importance of PSGTTL lies in the fact that their complete surgical resection (R'0' resection) usually results in prolonged survival, unlike how the conventional pulmonary carcinomas behave. A greater awareness of PSGTTL is essential for accurate diagnosis and proper clinical management. We herewith present our experience of seven patients of PSGTTL and review its clinical presentation, management options and survival outcomes.

MATERIALS AND METHODS

Study design and settings

The study was a retrospective analysis of a prospectively maintained computerized data-base of patients who underwent oncological surgery at a tertiary teaching oncology centre in North India.

Study population

All the consecutive patients of intra-thoracic neoplasms who underwent oncological surgery for histopathologically confirmed PSGTTL between 1st of January 2012 to 31st December 2014. Details concerning the clinical presentation, management, histopathological diagnosis and

follow-up of these patients were retrieved from the prospectively-filled case-records, and were analyzed using SPSS version 16.

Literature review

A pubmed search using MESH words "Salivary Gland Neoplasms/pathology"[Majr] and "Lung Neoplasms"[Mesh] was conducted on 08th February, 2015. A review of the case studies of PSGTTL was done to assess clinical profile, management options and survival outcomes.

RESULT

104 patients of lung cancer were operated during the period between January 2012 to December 2014. There were seven patients who underwent surgery for primary salivary gland type tumors of lung. Median age of the patients was 42.0 years (range 27-52); all patients were male. All of them admitted to be smokers. Hemoptysis (n=6, 85.7%) and dyspnoea (n=6, 85.7%) were common presenting clinical features, while chest pain and cough were present in 3 (42.8%) patients each. Four patients reported to have received anti-tubercular treatment for their symptoms. Fiber-optic bronchoscopy revealed endobronchial growth in all patients – five patients had growth in left main bronchus while one each had growth in right main bronchus and right intermediate bronchus. Biopsy confirmed adenoid cystic carcinoma in 4 (57.1%) and mucoepidermoid carcinoma in 3 (42.9%) patients. Two patients underwent rigid bronchoscopic debulking to relieve airway obstruction and to delineate the true extent of tumor. All but one had R‘0’ resection – pneumonectomy in five and bilobectomy in one patient; one patient was found to be unresectable in view of dense adhesions between lung and heart. He was given radical radiotherapy; he has been undergoing repeated bronchoscopic debulking of residual tumor. All the patients but one had uneventful postoperative recovery. One patient who had left carinal pneumonectomy developed pneumonia in postoperative period and succumbed to it. The other

patient who could not undergo R '0' resection has been having repeated bronchoscopic mechanical debulking; he is alive and symptom free after 17 months of follow up. Histopathological examination of the resected specimen in the operable patients confirmed the preoperative diagnosis. Figure 1 and 2 displays the microscopic pictures of MEC and ACC respectively. Median pathological tumor size was 3.5 cm (range 1.8 – 7 cm) and median number of harvested lymph nodes were 9 (range 4 – 18 cm); though none of the node in any patient was found to be metastatic. Overall, six patients are alive after a median follow up of 5 months (range 1-30). None of them were found to have salivary gland tumors at any other site in the follow-up evaluation.

A pubmed search using MESH words "Salivary Gland Neoplasms/pathology"[Majr] and "Lung Neoplasms"[Mesh] yielded 138 articles. Majority of the PSGTTL are either MEC or ACC; we focused our review on these histological types. Table 1 represents clinic-pathological characteristics of patients our series and previously published series; table 2 displays the treatment and survival outcomes of these patients.

DISCUSSION

Though different histological types of PSGTTL are known, MEC and ACC are the common types. In our series, they were almost equally distributed. Zhu et al [4], in their experience of 88 cases, found MEC in 78.4%, ACC in 13.6% and EMC in 7.9%; while Moline et al [2] reported ACC in 64.5% and MEC in 32.3% in their experience of 62 patients of PSGTTL. Kang et al [5], in their experience of 48 cases of PSGTTL, found MEC in 54.1%, ACC in 41.7% and EMC in 4.2% Other published series focused on a particular histological type.

Though PSGTTL usually involve a wide age range from 3 years to 78 years, they mainly affect people in their middle age. Median age of our patients was 42 years. Previously published case

series have also reported the similar age predilections. Kang et al [5] and Molina et al [2] showed median age of involvement in MEC was younger age group than ACC , while Zhu et al [4] did not find any difference. Though all of our patients were male, previously reported case series reveal a conflicting gender predilection for PSGTTL. Zhu et al [4], Molina et al [2], and Maziak et al [6] could not find any gender predilection for PSGTTL while Moran et al [7], Mondal et al [8] and Kang et al [5] reported male predilection.

All of our patients had endobronchial growth in central airways. However, literature is not uniform regarding the location of PSGTTL: central airway involvement varies from 6.2% to 100%. [2,4–8] Centrally located endobronchial tumors cause obstructive symptoms like cough, dyspnea, hemoptysis and peripheral lung collapse. In tuberculosis endemic country like ours, these symptoms may be attributed to tuberculosis and the patients may be prescribed anti-tuberculosis treatment erroneously. More than half of our patients had received anti-tuberculosis treatment before they came to our hospital. One of our patients had received taxol-platinum based chemotherapy in view of T4 lesion in another hospital where bronchoscopy biopsy was misdiagnosed as adenocarcinoma. Greater awareness of PSGTTL is required to diagnose these lesions as complete resection of these tumors, even locally advanced, result in good survival outcomes in contrast to epithelial pulmonary neoplasms.

Previous literature clearly suggests that complete surgical resection (R'0' resection) provides the best chance of long term survival. Though attempts must be made to preserve maximum lung parenchyma, location of the tumor would decide extent of resection to address the key concept of oncological safety (R'0' resection). As all of our patients had central airway involvement, 71.4% of our patients underwent pneumonectomy to achieve R'0' resection.

Role of regional lymphadenectomy is doubtful in all cases of PSGTTL in view of available literature. All the patients in our case series had regional lymphadenectomy; however, none of the nodes show metastatic deposits. Other studies have also shown low lymph nodes involvement (11.4 - 20%) in PSGTTL. [2,4–6] Molina et al [2] reported that ACC is more likely to have lymph node involvement than MEC. It seems that lymphadenectomy would perhaps be beneficial to patients with enlarged regional lymphnodes. Similarly, evidence form analysis of previously published data is also not robust to support role of adjuvant radiotherapy; however, patients with positive resection margin is a potential groups of patients where adjuvant radiotherapy needs to be considered. Zhu et al [4] also reported that adjuvant chemotherapy was prescribed in 8% of patients , though indication was not clear. High grade MEC may also be considered for adjuvant treatment as they are associated with high tumor invasiveness and lymph node involvement. [9] Molina et al [2] reported that grade was associated with tumor invasiveness; almost 50% of patients with high grade MEC in their series had invasion through the bronchial wall into adjacent lung parenchyma or soft tissue, in contrast to low grade tumors, in which a single patient had invasive disease. Though prospective studies are needed to optimize the treatment for PSGTTL; infrequent occurrence of these tumors makes it remote possibility. Multidisciplinary approach must be used to individualize the treatment for PSGTTL.

Bronchoscopic interventions may be used to relieve airway obstruction prior to definitive treatment; it also helps to assess the true extent of tumor which may be difficult to assess at times due to overhanging tumor. [10,11]

Distant Metastasis at presentation is rare in PSGTTL. None of our patient had distant metastasis at presentation. However, Molina et al [2] reported that almost one third of their patients had metastasis at presentation; it was more commonly observed in ACC than in MEC. Palliative

chemotherapy or radiotherapy may be used in this group of patients. Bronchoscopic debulking may be used to relieve airway obstruction. One of our patients who was surgically unresectable has been having repeated bronchoscopic mechanical debulking; he is alive and symptom free after 17 months of follow up.

PSGTTL are low-grade malignancy and have significantly better survival outcome. Though median follow up of our patients is small, six of seven patients are alive. Kang et al [5] reported a high 5-year survival of 97.6% and 10-year survival of 86.7%. Molina et al [2] also reported a significantly good 5-year survival of 65% and 10-year survival of 53%. Loco-regional recurrences are uncommon in PSGTTL following R'0' resection. None of our patients who had R'0' resection has developed loco-regional or distant metastasis. Previously published case series reported low loco-regional recurrence rate of less than 10%. [4–7]. Though distant failures are high but variable in PSGTTL; they vary from 4.1 to 44.7% in various series. [2,4–8]

In conclusion, radical surgery to achieve R'0' resection is the main stay of treatment of PSGTTL. Greater awareness of these tumors is necessary to avoid misdiagnosis and to prevent delaying of potential complete resection of PSGTTL.

Conflict of interest:

None to declare

Financial Interests:

None to declare

Ethical Approval

Permission of the institutional chief was obtained to review the patient data. As it was a retrospective study, patient's informed consent could not be obtained. However, strict compliance was adhered to ensure to maintain the confidentiality of personal information/images of the patients.

Research Registry

UIN - **researchregistry65**

Author contribution

All authors were involved in conception and design of study. All the authors were involved in the collection, analysis and interpretation of data. Pankaj Kumar Garg wrote the initial manuscript draft. All the authors were involved in the preparation of final manuscript. They have all read the final manuscript and approved it.

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FIGURE LEGENDS

Fig. 1 Mucoepidermoid carcinoma (A) (x200;H&E) Microscopic image shows fragment of bronchial cartilage (arrow) and a subepithelial tumor composed of squamoid and intermediate cells (B) (x400; H&E) High power magnification shows sheets of squamoid and intermediate cells(arrow) mixed with scant mucin-secreting cells. Significant mitotic activity, nuclear pleomorphism and necrosis were absent (C) (x400) Tumor cells are immunopositive for Cytokeratin (D) Proliferative index (Ki-67) is low(approximately 2%)

Fig. 2 Adenoid cystic carcinoma (A) (x200, H&E) Section shows a tumor arranged in glandular and cribriform pattern. (B) (x400, H&E) Tumor cells shows basaloid features with moderate pleomorphism, round to oval hyperchromaticnucleus. Characteristic balls of eosinophilic material(hyaline globules) are also seen (Arrow)

Table 1. Clinico-pathological characteristics of patients reported in our and previously published series

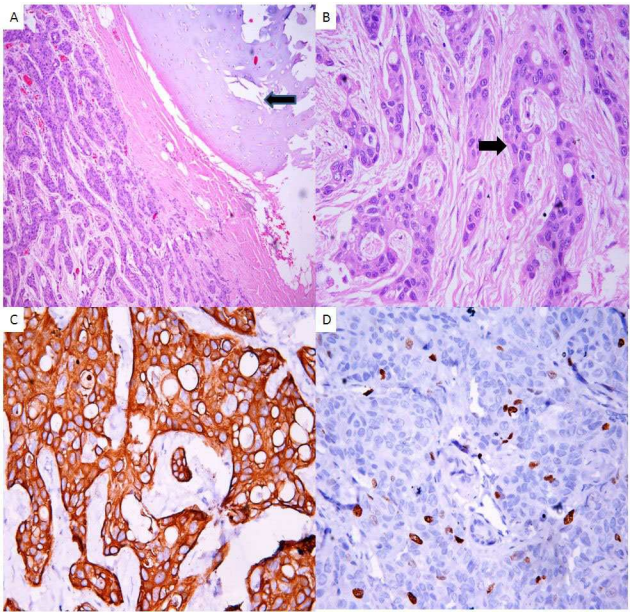
Authors	Duration of study	Number (n)	Age (in years) (Range)	Gender (male:female ratio)	symptom	Histological type	Tumor size	Central airway location
Molina et al (2)	1972-2002	62	Median 51 years Range (6-78)	34:26	Cough (70%), Dyspnoea (51.7%), Wheezing (38.3%), Obstructive pneumonia (30%), Haemoptysis (28.3%), Fever (16.7%)	ACC (64.5%), MEC (32.3%)	2.4	70.7%
Zhu et al (4)	2001-2013	88	Median 48 years Range (7-75)	47:41	Cough (48.9%), Hemoptysis (20.5%), Fever (15.9%), Dyspnoea (9.1%), Chest pain (5.7%)	MEC (78.4%), ACC (13.6%), EMC (7.9%)	2.5	15.9%
Maziak et al (6)	1963-1995	38	Mean (44.8 years), range (15-80 years)	18:20	Dyspnoea (72%), wheezing (39%), cough (23%), stridor (21%), hemoptysis (18%)	ACC	NA	100%
Mondal et al (8)	1996-2006	7	Range (48-65 years)	7:0	Cough, wheezing, dyspnoea, hemoptysis	ACC (100%)	Range (2.6-3.8 cm)	NA
Kang et al (5)	1995-2009	48	Mean age 41.5, Range 6-69 years	31:17	NA	MEC (54.1%), ACC (41.7%), EMC (4.2%)	mean 3.4 cm, range (0.5-12 cm)	37.5%
Moran et al (7)	NA	16	Mean age 54 years, Range 29-79 years	11:5	Cough, wheezing, dyspnoea, hemoptysis	ACC (100%)	Range 0.9-4.0 cm	6.2%
Present Series	2012-2014	7	42.0 (27-52)	7:0	Hemoptysis (85.7%), dyspnoea (85.7%)	ACC (57.1%), MEC (42.9%)	3.5	100%

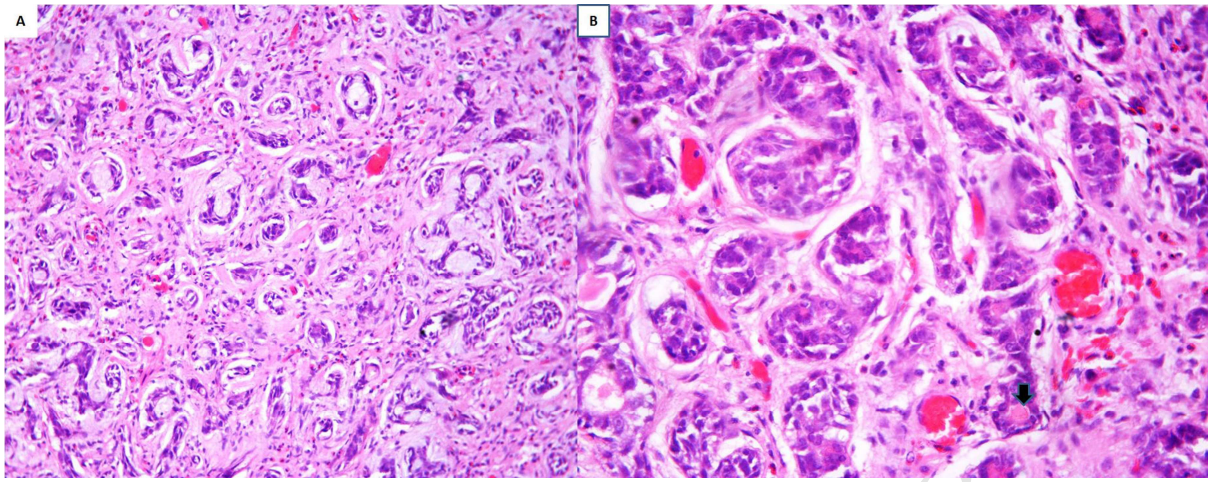
ACC - Adenoidcystic cancer, MEC - Mucoepidermoid cancer, NA - Not available

Table 2 Treatment and survival outcomes of patients reported in our and previous published series

Authors	Management	Common surgical procedure	lymph nodes involvement	Median Follow up	Recurrences	Survival
Molina et al (2)	Surgery in 71.3%, Adjuvant RT in 23.7%,	Lobectomy (44.2%), Tracheal resection (25.6%), pneumonectomy (18.6%), sleeve resection (9.3%)	20%	NA	Local NA, Distant 30.4%	3-year OS= 80%, 5-year survival = 65%, 10-year survival = 53%
Zhu et al (4)	Surgery in 95.4%, adjuvant RT in 11.4%, Adjuvant CT in 8%.	Lobectomy (55.7%), Sleeve lobectomy (18.2%)	11.4%	49 (3-134)	Local 4.5% Distant 12.5%	3-year OS= 91.3%, 5-year survival = 86%, 10-year survival = 80.6%
Maziak et al (6)	Surgery + adjuvant RT in 42.1%, neoadjuvant RT + surgery in 23.6%, Surgery alone in 18.4%, RT alone in 15.7%	Tracheal resection (93.7%) including carinal resection ± lung resection in 40%	13.1%	NA	Local 7.8%, Distant 44.7%	Mean survival 85 months , Range (5 days - 29 years)
Mondal et al (8)	Surgery alone in 85.7%, Surgery + RT in 14.3%	Pneumonectomy (71.4%), Lobectomy 28.6%)	NA	Range (5-9 years)	28.6%	NA
Kang et al (5)	Surgery primary modality in 48 (97.9%), Neoadjuvant treatment in 12.5% (n=6, CT in 5, Chemoradiotherapy in 1), Adjuvant treatment in (n=19, RT in 12 and CT in 7)	Sleeve bilobectomy (31.2%), Sleeve lobectomy (27.1%),Tracheal resection (16.7%), Pneumonectomy (14.6%), Carinal sleeve resection (10.4%)	19%	Median (59.8 months (range 0.7-155 months)	Distant 4.1%	5 year OS = 97.6%, 10 year OS 86.7%.
Moran et al (7)	Surgery alone in 81.2%, Surgery + CT in 12.5%, CT alone in 6.3%	Lobectomy (53.3%), Pneumonectomy (46.7%)	NA	2 months to 10 years	local 7.6%, Distant 7.6%	NA
Present Series	Surgery alone 100%.	Pneumonectomy (71.4%), Lobectomy (14.2%)	0	5 (1-30)	None	85.7% alive

CT - Chemotherapy, RT-Radiotherapy, NA - Not available





1. Primary salivary gland type tumors of the lung are rare neoplasms.
2. Mucoepidermoid and adenoidcystic cancer are common histological subtypes.
3. Surgery is the mainstay of treatment.
4. Regional node metastasis is rare.
5. Complete surgical resection results in excellent overall survival.