- Cryo-bronchoscopy Breakthrough: A Rare Bronchial Mucoepidermoid Carcinoma
   Success Report
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### 7 ABSTRACT:

- 8 **Background:** Bronchial Mucoepidermoid Carcinoma (MEC) is an extremely rare
- 9 malignancy, accounting for only 0.1-0.2% of primary lung cancers and <1% of primary
- 10 bronchial tumors. It often presents with airway obstruction symptoms such as cough,
- 11 dyspnea, and wheezing, mimicking common respiratory conditions like pneumonia. Due to
- 12 its rarity, optimal management strategies remain unclear.
- 13 **Case presentation**: We report a rare case of a 32-year-old male with bronchial MEC who
- 14 presented with chronic cough, weight loss, and exertional breathlessness for two months.
- 15 Imaging revealed an endobronchial lesion obstructing the right mainstem bronchus.
- 16 Bronchoscopy with cryo-biopsy confirmed the diagnosis of MEC through histopathological
- and immunohistochemical analysis. Given the tumour's localized nature (pT1N0M0), a
- 18 minimally invasive approach was pursued. The patient underwent successful cryo-
- bronchoscopy, achieving complete airway recanalization without requiring traditional
- surgical interventions such as sleeve lobectomy. A three-month follow-up bronchoscopy
- showed no recurrence, with the patient remaining symptom-free.
- 22 **Conclusion:** This case highlights the potential of cryo-bronchoscopy as an effective and
- 23 minimally invasive therapeutic option for early-stage bronchial MEC, potentially avoiding
- the need for major surgery. Given the rarity of this condition, further studies are needed to
- establish optimal diagnostic and treatment protocols.

## 26 KEY WORDS: Mucoepidermoid carcinoma (MEC), Bronchoscopy, Cryotherapy,

27 Endobronchial tumor

# 28 Background:

- 29 Mucoepidermoid carcinoma (MEC) is a rare tumour of the lung that accounts for 0.1 to 0.2%
- 30 of all primary lung carcinomas, however, MEC of the salivary gland is relatively
- 31 common. [1] Pulmonary MEC is extremely uncommon with a bronchial localization making
- 32 it a rarity. Bronchial MEC usually presents as an intraluminal mass causing luminal
- 33 occlusion. It can arise from the bronchial glands of the main, lobar or segmental bronchus.
- 34 MECs are known to be classified as low or high grade, with the former being easily managed
- 35 by surgical resection alone. The precise nature of these neoplasms is not yet clear and little is
- 36 known about the pathogenesis of the disease. [2] Symptoms are usually due to airway
- 37 obstruction because of luminal occlusion such as cough, dyspnoea, wheezing, hemoptysis and
- 38 obstructive pneumonia. This article here aims to present a rare case of a bronchial MEC with
- a detailed pathological, immunohistochemical, and molecular analysis which was diagnosed
   and treated by cryo-bronchoscopy instead of traditional surgical methods or sleeve lobectomy
- 41 achieved using open or video-assisted technique.

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#### 43 Case presentation:

A 32-year-old male patient presented with complaints of dry cough, loss of appetite and 44 significant weight loss of about 15 kg in the past year, along with on and off hemoptysis and 45 exertional breathlessness for 2 months. A history of exposure to petro chemicals was noted, 46 47 with no history of smoking. On presentation, general examination revealed tachypnea (respiratory rate of 30/min), tachycardia (120 beats/min) and hypoxia with oxygen saturation 48 49 of 89% at room air. On physical examination there was reduced vocal fremitus and vocal resonance over right side of chest with decreased air entry on the right side on auscultation. 50 51 Routine blood tests were within normal limits. Chest radiograph showed homogenous opacity over right lower zone and silhouetting present (Figure 1). Subsequently a contrast enhanced 52 computed tomography (CECT) of chest was performed which showed soft tissue mass lesion 53 in the right main stem bronchus causing mild expansion of right main stem bronchus 54 (measuring  $\sim 19x17$  mm) and showing mild heterogeneous enhancement on post contrast 55 study (Figure-2). There was evidence of subsegmental collapse and consolidation of right 56 lower lobe involving postero-basal and medial basal segments with air bronchogram seen on 57 lung window (Figure-3). Bronchoscopy was performed, revealing a smooth, well-58 circumscribed endobronchial lesion originating from the right upper lobe orifice and 59 occluding 90% of the distal airway. [Figure-4] During the procedure multiple cryo-biopsy 60 fragments were taken for histopathological examination following which he underwent 61 complete recanalization of airway using 1.9 mm cryoprobe and haemostasis achieved. 62 Histopathology report showed a tumour arranged in the form of nest and glands. The nest 63 comprises of tumour cells that have hyperchromatic nuclei, inconspicuous nucleoli and 64 scanty cytoplasm. Mitoses were < 4/10 high power fields. (Figure-5) The tumour showed 65 infiltrative borders with majority of tumour cells being mucoid in nature suggestive of 66 bronchial mucoepidermoid carcinoma. Immunohistochemistry was positive for P40, 67 cytokeratin (CK5/6), monoclonal carcinoembryonic antigen (mCEA) and cytokeratin (CK7) 68 while being negative for thyroid transcription factor (TTF1). (FIG-6) Ki67 index was 8%. 69 The staging process was completed with a positron emission tomography (PET) scan which 70 showed no lymphatic or distant metastasis. The histopathological examination of the 71 72 specimen confirmed the preoperative diagnosis and stage (pT1N0M0), as well as the oncological radicality of the bronchoscopic procedure. No further therapies were employed, 73 given the stage of the disease. On 3 months follow-up a check bronchoscopy was performed 74 which showed no intraluminal mass or growth with resolution of symptoms and a disease free 75 state (Figure-7). 76

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### 78 Discussion and conclusion

79 The two most common types of primary salivary gland tumours are pulmonary

80 mucoepidermoid carcinoma (PMEC) and pulmonary adenoid cystic carcinoma (PACC).

Among all PACCs, 55% are seen in the trachea and main stem bronchus, while 85% of all

82 PMECs are seen in the peripheral lung. There has been no clear sex predilection or familial

83 predisposition [3]. These neoplasms mainly involve the lobular or segmental bronchi, often

84 causing complete or partial atelectasis, with subsequent obstructive irritation and

85 inflammation. This leads to the typical clinical manifestations like cough, wheezing,

- haemoptysis, fever, and pneumonia [4]. Grossly, the tumour size at diagnosis ranges from 0.5
- to 6 cm in diameter with an average size of  $\sim 2.2$  cm in the reported literature. They are soft,

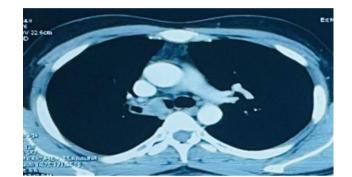
- 88 polypoid and pink-tan in colour, often with cystic changes and a glistening mucoid
- appearance [5]
- 90 MEC of the tracheobronchial tree is histologically similar to MEC of salivary glands and
- 91 these are categorised into low-, intermediate-, and high-grade tumours based on level of
- nuclear pleomorphism, necrosis, type of cell (mucous, intermediate, and epidermoid), and
- 93 degree of mitotic activity. Histologically, MEC is comprises a mixture of different cell types,
- 94 including mucin-secreting glandular cells, squamous cells, and intermediate cells.
- 95 Histological grade is an important prognostic indicator, with high-grade MECs demonstrating
- a greater risk for metastases, tumour recurrence, and death [6]. Low-grade tumours
- 97 predominantly contain cystic changes and solid areas typically comprising of small glands,
- tubules and cysts of mucin secreting and columnar epithelial cells with infrequent mitotic
- activity. High-grade MEC is very rare and demonstrate nuclear atypia with brisk mitoticactivity and a high nuclear to cytoplasmic ratio [4]. Low-grade tumors are slow-growing and
- are generally managed by surgery alone, whereas high-grade tumors have poor prognosis due
- 102 to greater chance of recurrence and metastasis, often requiring multimodal treatment [6].
- 103 Immunohistochemistry analysis for TTF-1 was positive in primary lung
- adenocarcinomas whereas cytokeratin (CK-7), Muc5Ac, p40, and p63 were positive in
- 105 MECs, all of which may provide a method for differentiating between the two carcinomas
- 106 [7]. While surgical resection remains the standard therapy for patients with pulmonary MEC,
- 107 different operative approaches have been used just like in our case [8]. Long-term cure has
- been achieved with complete resection in low grade MEC patients in most of the studies.
- 109 MEC can be treated with different surgical approaches including thoracotomy with
- 110 conventional lobectomy, sleeve lobectomy, and lobectomy, with bronchoplastic closure. The 111 goal of surgery is to obtain a complete resection with negative surgical margins [9]. Flexible
- bronchoscopy represents the main diagnostic tool for MECs, as it may allow direct
- visualization of the lesions and biopsies. The fibre-optic bronchoscopy view of a MEC tumor
- usually appear as pedunculated, polypoidal, smooth, exophytic mass with rich vascularity
- [10]. Bronchoscopic intervention has attracted extensive attention in the treatment of MEC
- patients over the past few years. Multiple bronchoscopic interventions including rigid
   bronchoscopy, argon plasma coagulation, CO<sub>2</sub> cryotherapy, and electric loop can be
- 118 conducted to remove the mass. For more serious cases, one-fifth of the patients need
- 119 bronchoscopic intervention as a bridge therapy before surgery because of respiratory distress.
- 120 Moreover, there were several case reports indicating the promising effect of interventional
- bronchoscopy for treatment of bronchial MEC [10]. In our case, we found that interventional
- bronchoscopy using cryo therapy could successfully eradicate the neoplasm and provide goodprognosis for the patient without significant trauma. We consider that, for low-grade MEC,
- since it is usually superficial and restricted to the bronchus, bronchoscopic intervention can
- completely eradicate the mass with few complications, preserve lung function and provide
- 126 good prognosis similar to that of surgery. For high-grade bronchial MEC, interventional
- bronchoscopic therapy could quickly relieve life-threatening obstruction as a bridge therapy
- prior to surgery. For bronchial MEC with distant metastasis, bronchoscopic intervention can
- 129 provide significant palliative relief of patients' respiratory distress and improve life quality.
- Bronchial Mucoepidermoid carcinoma (MEC) is extremely rare, comprising only 0.1–0.2%
- 131 of the primary lung malignancies and <1% of primary bronchial tumours. Our case presents a
- rare case of a bronchial MEC which was successfully managed by cryo-bronchoscopy instead
- 133 of surgical removal by traditional methods. Thus, proving cryobronchoscopy a breakthrough
- 134 success for treating bronchial MECs.

135	Abbreviations:
136	MEC: Mucoepidermoid carcinoma
137	<b>CECT:</b> contrast enhanced computed tomography.
138	CK5/6: cytokeratin 5/6,
139	mCEA: monoclonal carcinoembryonic antigen
140	<b>CK7:</b> cytokeratin 7
141	TTF: thyroid transcription factor
142	<b>PET</b> : positron emission tomography
143	PMEC: pulmonary mucoepidermoid carcinoma
144	PACC: pulmonary adenoid cystic carcinoma
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147	Declarations:
148	Ethics approval and consent to participate: Approval was obtained from the ethical
149	committee of Chandan Hospital.
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151 152	<b>Consent for publication</b> : Written and informed consent for publication of this case report and the corresponding images were taken from the patient.
153	report and an corresponding margers and anter from the partonal
154	Availability of data and materials: Not applicable
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156	Competing interests: We have declared that there are no competing interests.
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158	Funding: No funding.
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165	References:
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167 168 169	<ol> <li>H. K. Leonardi, Y. Jung-Legg, M. A. Legg, W. B. Neptune. Tracheobronchial mucoepidermoid carcinoma. Clinicopathological features and results of treatment. Journal of Thoracic and Cardiovascular Surgery. 1978:76; 431–8</li> </ol>

171 172		World J. Surg. Oncol. 2014:8;12:33.
173 174 175	3.	Kumar V, Soni P, Garg M, Goyal A, Meghal T, Kamholz S, Chandra AB. A Comparative Study of Primary Adenoid Cystic and Mucoepidermoid Carcinoma of Lung. Front Oncol. 2018:15;8:153.
176		
177 178 179	4.	Travis WD, Brambilla E, Burke AP, Marx A, Nicholson AG. Introduction to the 2015 World Health Organization Classification of Tumors of the Lung, Pleura, Thymus, and Heart. J Thorac Oncol. 2015; 10:1240-2.
180		
181 182 183	5.	CH. Chin, CC. Huang, MC. Lin, TY. Chao, SF. Liu. Prognostic factors of tracheobronchial mucoepidermoid carcinoma—15 Years experience. Respirology. 2008;13:275–80.
184		
185 186 187 188 189	6.	Huo Z, Wu H, Li J, Li S, Wu S, Liu Y, Luo Y, Cao J, Zeng X, Liang Z. Primary Pulmonary Mucoepidermoid Carcinoma: Histopathological and Moleculargenetic Studies of 26 Cases. PLoS One. 2015;10(11):e0143169.
190 191 192	7.	P. Vadasz and M. Egervary. Mucoepidermoid bronchial tumors: a review of 34 operated cases. European Journal of Cardio-thoracic Surgery. 2000;17:566–9.
	0	F. El Mezni, I. Ben Salha, O. Ismaïl et al.Mucoepidermoid carcinoma of the lung: a series of
193 194	0.	10 cases. Revue de Pneumologie Clinique. 2005; 61:78–82.
195 196 197 198	9.	Chin M, Gupta A, Gomes MM, Maziak D, Mulpuru S, Dyspnea, focal wheeze, and a slow growing endobronchial tumor. Respir Med Case Rep. 2021;32:101360.
199 200 201 202	10.	Zheng X, Herth FJF, Sun J. Initial Experience with Hybrid Argon Plasma Coagulation as a Novel Local Treatment Method for Tracheobronchial Mucoepidermoid Carcinoma. Respiration. 2019;98:461-6.
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**FIGURE 1**- Chest radiograph showing homogenous opacity over right lower zone and silhouetting present



**FIGURE 2-** CECT Thorax shows soft tissue mass lesion in the right main bronchus causing expansion of right main bronchus



**FIGURE 3-** CECT Thorax shows sub segmental collapse / consolidation of right lower lobe involving posterior and medial basal segments with air bronchogram.



**FIGURE 4** – Bronchoscopy reveals a well circumscribed endobronchial lesion at the level of carina which is originating from the right upper lobe orifice and occluding 90% of the right main stem bronchus.

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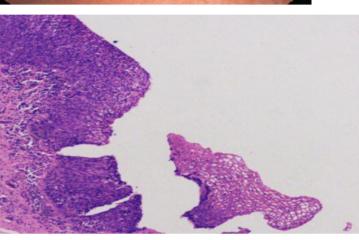
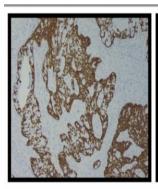


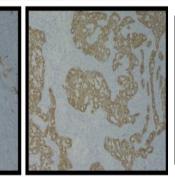
FIGURE 5- Histology shows a tumor arranged in the form of nest and glands. The nests comprise of tumor cells with hyperchromatic nuclei, inconspicuous nucleoli and scanty cytoplasm. Mitoses are < 4/10 high power fields.

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CK5/6 (EP24/EP67)

MCEA (2-7(MONO))



**FIGURE 5** - Immunohistochemistry, positive for P40, CK5/6, mCEA and CK7 while being negative for TTF1. Ki67 index was 8%.

CK7 (EP16)

**FIGURE -6**- Post bronchoscopy image at the level of carina after 3 months showing no intraluminal growth or mass.





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