

A Malignant Bronchial Oncocytoma - A Case Report -

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Abstract

Primary malignant bronchial oncocytoma is a very rare pulmonary neoplasm. A 59-year-old male with a presumed oncocytic carcinoid was referred to this hospital. An endobronchial polypoid bossolated mass within left main distal bronchus was detected on bronchoscopy and on computed tomographic scan. The left lung was resected, and final pathologic diagnosis of malignant bronchial oncocytoma was confirmed. This neoplasm is composed predominantly of oncocytes with numerous mitochondria and lack of neurosecretory granules in transmission electron microscopy. In respect of pathologico-clinical difference between the malignant oncocytoma and oncocytic carcinoid, the author reviewed previous literatures and report this very rare case.

Key words : Bronchial carcinoma, Oncocytoma, Transmission electron microscopy

INTRODUCTION

Oncocytes have an eosinophilic and granular cytoplasm and a round nucleus, and ultrastructurally and histochemically abundant mitochondria with oxidative enzyme activity. The first description of an oncocytoma, defined as a neoplasm composed predominantly or entirely of oncocytes, was made in 1932 by Jaffe,¹⁾ who described an oncocytoma of the salivary gland. Oncocytomas were subsequently reported in other organs such as the kidney, salivary gland, and thyroid.²⁾ In 1973 Fechner and Bentinck³⁾ reported the first case of a bronchial oncocytoma ultrastructurally confirmed. In the following twenty-four additional cases of oncocytic tumors of the lung with ultrastructural confirmation have been reported. Sixteen of the twenty-four tumors were reported in the

diagnosis of oncocytic carcinoid, but the remaining eight tumors were considered benign or malignant bronchial oncocytoma characterized by mitochondrial hyperplasia and lack of neuroendocrine differentiation. Only one of eight pulmonary oncocytomas, reported by Nielsen,⁴⁾ showed signs of malignancy, i.e., local invasion, or metastases. Here the author report a malignant bronchial oncocytoma with local invasion beyond the cartilage and cellular atypia, second case in the following of Nielsen's case report.

CASE REPORT

A 59-year-old male with a presumed bronchial oncocytic carcinoid was referred to this hospital. On admission to this hospital, the patient suffered from mild dyspnea on exertion, coughing, and sputum production. He has received therapy for diabetes mellitus for about 10 years. A chest CT scan showed a 1.2x0.8 cm-sized, homogenous enhancing nodular lesion within left main bronchus, and subsegmental atelectasis in lateral basal segment of lower lobe of left

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lung (Fig.1 A).

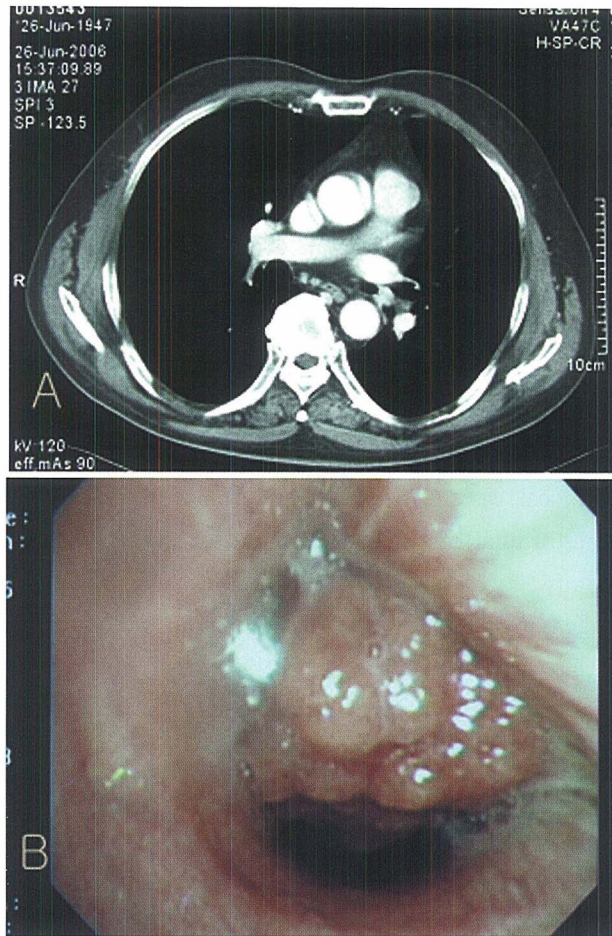


Fig. 1 A, Chest computed tomography scan (CT scan) showing a 1.2x0.8 cm-sized, homogenous enhancing nodular lesion within left main bronchus, and B, bronchoscopic examination revealing an endobronchial polypoid bosselated mass obstructing about a half of the bronchial lumen within left main distal bronchus

Laboratory findings including serum neuron specific enolase were normal. Bronchoscopic examination revealed an endobronchial polypoid bosselated mass with nearly normal mucosal color within left main distal bronchus. The polypoid mass obstructed about a half of the bronchial lumen (Fig.1 B). The bronchial mass was clinically diagnosed as submucosal carcinoid. He underwent left pneumonectomy and mediastinal lymph node dissection. The pneumonectomy specimen showed a well demarcated

bosselated and firm solid mass, measuring 1.5x1.5x1.3 cm in size, with pinkish yellow cut surface, nearly totally obstructing the bronchial lumen of the orifice of left lower lobe (Fig.2).



Fig. 2 The pneumonectomy specimen showing an partially ill-defined bosselated, solid pinkish yellow mass, nearly totally obstructing the bronchial lumen of the orifice of left lower lobe, and extending beyond the bronchial cartilage into the peribronchial fat tissue

The mass extended beyond the bronchial cartilage into the peribronchial fat tissue. Hemorrhage or necrosis was not evident in the mass. Mediastinal lymph nodes were enlarged without frank gross metastases. Histologically the mass was composed of oncocytes arranged in tubular pattern, trabecular pattern, nests or clusters, separated by thin fibrous bands. Some remaining submucosal glandular ducts were admixed. Some clusters of neoplastic cells had infiltrated the bronchial wall, with focal destruction of cartilage and intact covering bronchial epithelium. Lobules of neoplastic cells had extended through the bronchial cartilage into the peribronchial fat tissue (Fig.3 A). The neoplastic cells had relatively abundant eosinophilic granular cytoplasm. The nuclei of the neoplastic cells were uniformly round, and many of them were enlarged with prominent nucleolus (Fig.3 B). Mitoses were not identified. Immunohistochemical study showed that the neoplastic

oncocytes were diffusely and strongly reacted to antibodies against cytokeratin 7 along the cellular membrane and cytoplasm (Fig.3 C). The neoplastic cells did not react with antibodies to chromogranin A, synaptophysin, neuron specific enolase, which are neuroendocrine phenotypic markers, and showed no immunostaining with antibodies to CD10 and TTF-1. The Ki-67 labeled proliferating index was less than 1 % in the neoplastic oncocytes. The dissected nine mediastinal and peribronchial lymph nodes were free of carcinoma. Although the specimen was taken from formalin-fixed, ultrastructurally all of the neoplastic cells examined contained abundant dilated mitochondria those were tightly packed almost completely filling the entire cytoplasm, often with some broken cristae (Fig.3 D).

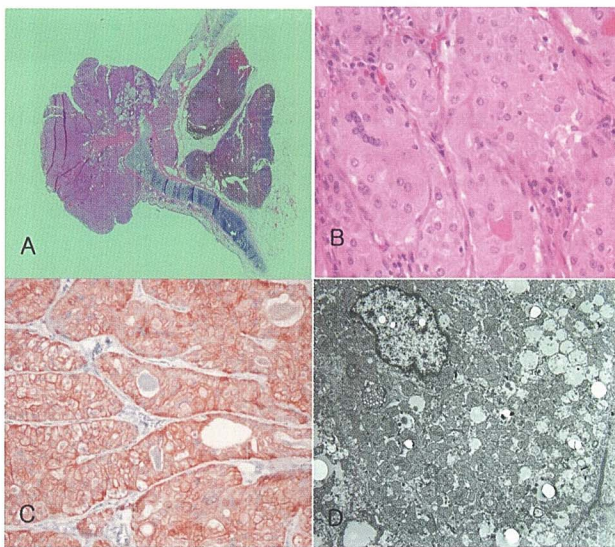


Fig. 3 A, Endobronchial polypoid mass infiltrated the bronchial wall, with focal destruction of cartilage, and extended through the bronchial cartilage into the peribronchial fat tissue (H-E stain, whole mount). B, The neoplastic cells have relatively abundant eosinophilic granular cytoplasm and uniformly round nuclei, often with prominent nucleolus, and a multinucleated giant cell (H-E stain, x400). C, Immunohistochemically the neoplastic oncocytes were diffusely and strongly reacted to antibodies against cytokeratin 7 along the cellular membrane and cytoplasm (x200). D, Transmission electron micrograph. The neoplastic oncocyte contained abundant dilated mitochondria often with some broken cristae, with membrane-bounded neurosecretory granules not identified (original magnification x8000).

DISCUSSION

Primary oncocytic neoplasms are very rare in the lung. Oncocytes are generally detected in older adults, and occur in many organs including the salivary gland, larynx, trachea, esophagus, thyroid and parathyroid. Therefore oncocytomas occur largely in salivary gland, kidney, thyroid, adrenal, and parathyroid.^{2,5)} Oncocytic neoplasm, such as oncocytoma or oncocytic carcinoid occurred in the lung, was first reported in 1937 by Hamperl, but Fechner and Bentinck³⁾ reported the first case of a bronchial oncocytoma ultrastructurally confirmed with exuberant mitochondria in the cytoplasm. After that, twenty-four additional cases of oncocytic tumors of the lung with ultrastructural confirmation have been reported. Eight of the twenty-four tumors were considered benign or malignant bronchial oncocytoma. Malignant oncocytoma is diagnosed with the following criteria,^{4,6)} first, the neoplasm consists of large, brightly stained oncocytic cells with an eosinophilic and granular cytoplasm and an atypical nucleus, second, ultrastructurally and histochemically, the tumor cells are like non-neoplastic oncocytes with abundant mitochondria and oxidative enzyme activity, and third, the neoplasm shows signs of malignancy, such as local invasion, metastases, or invasion of blood or lymph vessels. Only one of eight pulmonary oncocytomas showed local invasion and metastasis to parabranchial lymph node. Malignant oncocytoma constitutes only 5% of all oncocytomas.⁷⁾ The present case also showed local invasion through the bronchial cartilage to peribronchial fat tissue and numerous neoplastic cells with an atypical nucleus.

Oncocytic neoplasms in the lung include oncocytoma and oncocytic carcinoid. Sun et. al⁸⁾ named oncocytic neoplasms in the salivary gland "intracellular neoplasm of mitochondria" or "mitochondrioma", but Spencer⁹⁾ asserted that numerous oncocytoma had neurosecretory granules characterizing carcinoid, so they were properly named oncocytic carcinoid. According to Walter et. al¹⁰⁾ and Sklar et. al,¹¹⁾ oncocytes and carcinoid cells represented the

extremes of a morphologic spectrum, and both cell types were demonstrated in the same tumor. But Fechner et al.³⁾ and other authors stressed the importance of classifying bronchial oncocytic tumors as carcinoid or adenoma, since they believed the latter to be entirely benign. The author support the opinion of naming the oncocytic neoplasm without neuroendocrine differentiation oncocytoma. Carcinoid tumor is defined as tumors characterized by growth patterns of neuroendocrine morphology and neuroendocrine differentiation, such as presence of neuroendocrine markers immunohistochemically and/or of neurosecretory granules ultrastructurally. The bronchial oncocytic neoplasms containing abundant dilated mitochondria those were tightly packed and almost completely filling the entire cytoplasm ultrastructurally without neurosecretory granules and immunohistochemically without neuroendocrine markers are not an oncocytic variant of carcinoid.

The reports of oncocytic tumors of the bronchus published to date have all described noninvasive tumors with no metastatic deposits, except for Nielsen's report.⁴⁾ The Nielsen's report demonstrated the bronchial oncocytoma with bland cytology of neoplastic oncocytes and infiltrative growth and a regional metastatic deposit. In malignant oncocytoma arising in head and neck, it appears that the most important prognostic indicator is the presence of absence of distant, rather than local lymph node, metastases. Bronchial typical carcinoid tumors even with lymph node metastasis carry an excellent prognosis, if all tumor-bearing tissue is resected. Nielsen proposed that this result was also expected for the oncocytic bronchial variant, although to date no cases with adequate follow-up data have been published. He stated that the bronchial oncocytic adenoma in his report showed infiltrative growth and a metastatic deposit and this supported the observations of Walter et. al.¹⁰⁾ and Sklar et. al.,¹¹⁾ with regard to the malignant potential of all bronchial adenoma.

Another problematic differential diagnosis was metastatic eosinophilic variant of chromophobe cell renal

carcinoma (EVCCRC). Although EVCCRCs have abundant eosinophilic cytoplasm ultrastructurally with numerous mitochondria, they also reveal presence of numerous cytoplasmic microvesicles, unlike oncocytoma which show numerous mitochondria occupying more than 60% of total area of the cytoplasm and often lipid droplets instead of microvesicles.¹²⁾

In conclusion the author report an extremely rare case of malignant bronchial oncocytoma with local invasion beyond the cartilage and cellular atypia. This case is second case in the following of Nielsen's case report. The prognosis of malignant bronchial oncocytoma could be expected if more cases with adequate follow-up data are published.

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