

## Case Report

# Glomus tumor of uncertain malignant potential of the lung: a case report and review of literature

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**Abstract:** Glomus tumor is an uncommon tumor usually presenting in the dermis. Rarely, it occurred in visceral organs including stomach, liver and lung. The majority of glomus tumors were benign. Herein, we present a case of glomus tumor located in the left lobe of the lung in a 49 year-old Chinese male. An irregular mass measuring 3 cm was detected by imaging examination because of his suffering from cough, dyspnea and chest pain. Histologically, the tumor is composed predominantly of sheets of ovoid to round cells with clear border, pale cytoplasm and fine granular chromatin. The mitotic count was less than 5 per 50 HPF. The tumor focally invaded the surrounding normal bronchial and alveolar tissue. Immunohistochemical staining showed that the cells were diffusely positive for SMA, caldesmon, and vimentin. The Ki-67 proliferation index was approximately 20%. Based on morphologic features and the immunohistochemical profile, the tumor was consistent with glomus tumor of uncertain malignant potential.

**Keywords:** Glomus tumor, uncertain malignant potential, pulmonary neoplasm

## Introduction

Glomus tumors are relatively rare tumors deriving from smooth muscle cells of glomus body [1]. The majority of them occurred in the subungual region. Rarely, it occurred in visceral organs including stomach [2, 3], liver [4] and lung [5, 6]. So far, fewer than 40 cases of glomus tumors of the lung were reported in the English literatures [7]. Clinically, the majority of glomus tumors were benign [8]. Rarely, the tumor could show malignant behavior or uncertain malignant potential [5, 7, 9]. Herein, we present a case of glomus tumor of uncertain malignant potential located in the left lobe of the lung in a 49 year-old Chinese male. The tumor also displayed the marked infiltrative growth.

## Case report

### *Clinical history*

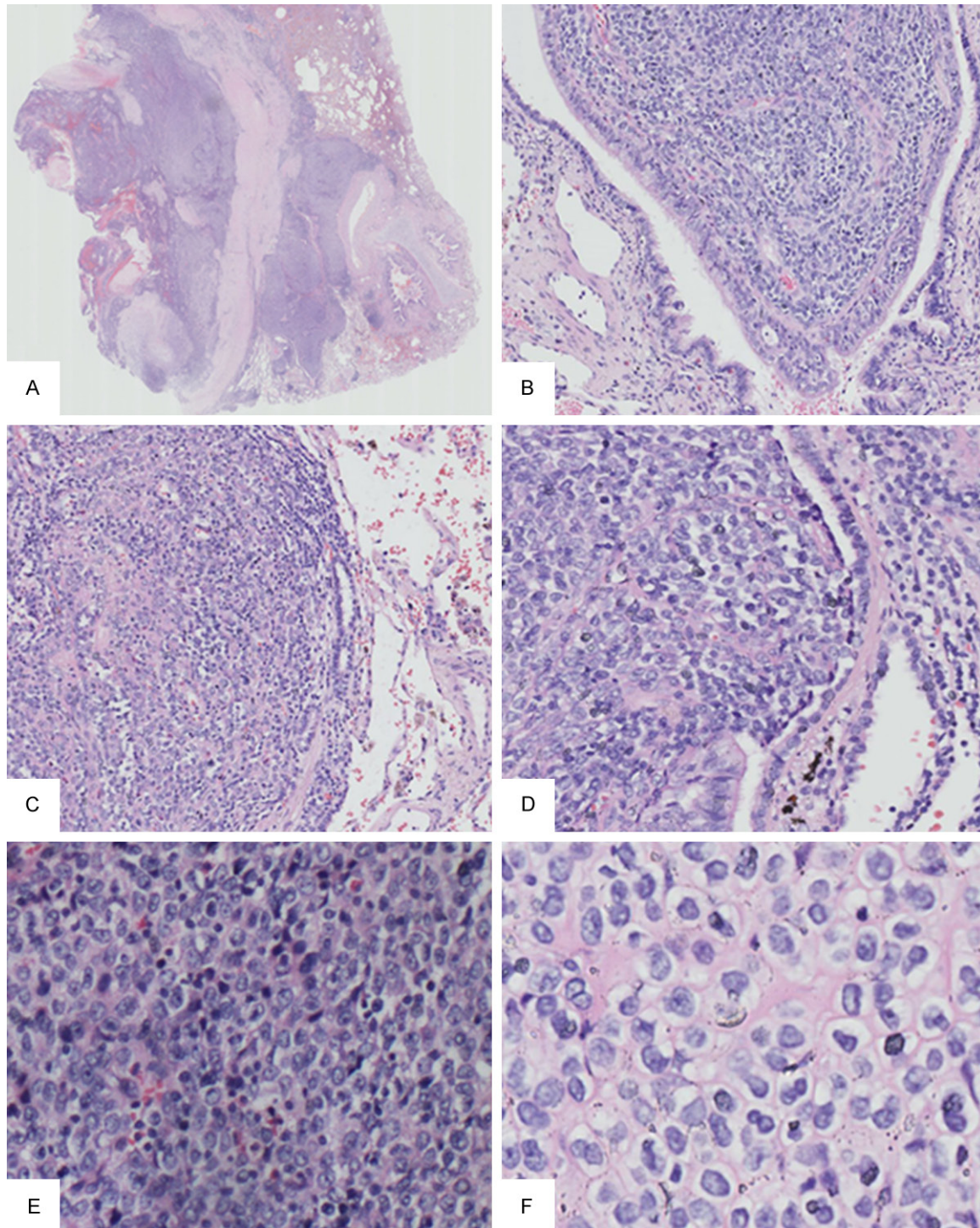
A 49-year-old male without a history of smoking was admitted to our hospital for complaining of cough, dyspnea and chest pain for a month.

Physical examination and routine laboratory studies were all within normal values. Chest computed tomography (CT) revealed that there was a irregular solid mass measuring 3.0 cm × 2.8 cm × 2.6 cm at the right lower lobe. In the current visit, the patient underwent wedge resection in our hospital.

### *Materials and methods*

The resected specimens were fixed with 10% neutral-buffered formalin and embedded in paraffin blocks. Tissue blocks were cut into 4-μm slides, deparaffinized in xylene, rehydrated with graded alcohols, and immunostained with the following antibodies: cytokeratin (CK), Vimentin, thyroid transcription factor 1 (TTF-1), epithelial membrane antigen (EMA), surfactant apoprotein A (SPA), CD45, CD34, synaptophysin, CD56, P63, CD99, S-100, HMB45, CD117, smooth muscle actin (SMA), caldesmon, desmin and Ki-67. Sections were stained with a streptavidin-peroxidase system (KIT-9720, Ultrasensitive TM S-P, MaiXin, China). The chromogen used was diaminobenzidine tetrahydro-

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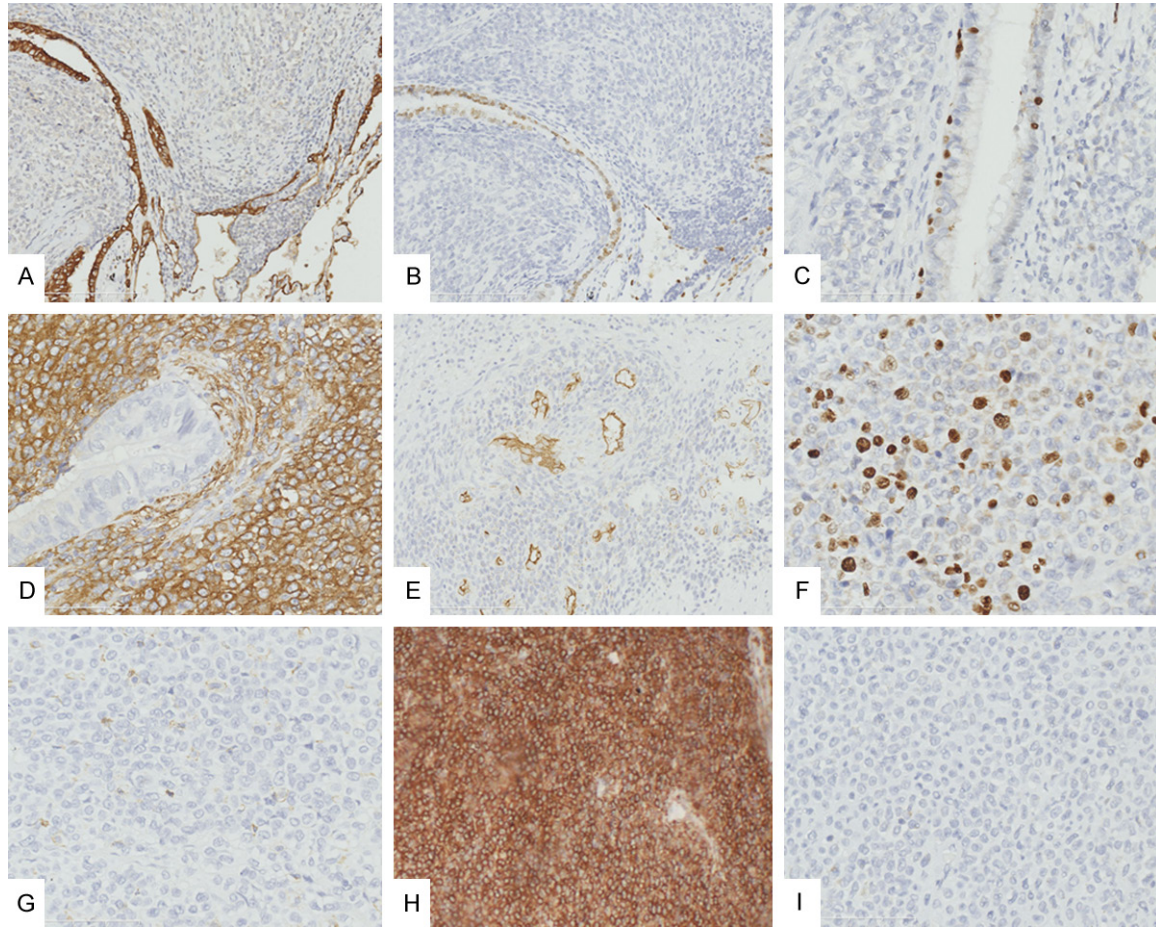


**Figure 1.** Morphological change of the tumor. A. The tumor was not well circumscribed with central hemorrhaging and peripheral infiltration into the normal lung tissue. B. In the periphery, a large bronchus was involved by the tumor. C. The tumor infiltrated into the normal alveolar tissue. D. The bronchus was involved, and the epithelial cells were also destroyed. E. The tumor comprised by sheets of round-oval cells. F. The basal lamina formed the chicken-wire pattern, and surrounded each cell.

chloride substrate (DAB kit, MaiXin, China), slightly counterstained with hematoxylin, dehy-

drated and mounted. For the negative controls, the primary antibody was replaced with PBS.

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**Figure 2.** Immunohistochemical staining of the tumor. A. The tumor cells were negative for CK, whereas the destroyed and the remaining epithelia cells were positive for CK. B. TTF-1 staining highlighted the involved normal pneumocytes. C. The basal cells of the normal bronchus showed reactivity for P63. D. The tumor cells were diffusely and strongly positive for SMA. E. CD34 staining demonstrated the dilated vessels surrounded by the tumor cells. F. Ki-67 index was approximately 15%. G. The tumors cells were negative for CD45. H. The cells were also diffusely positive for caldesmon. I. CD99 was not expressed in the tumor cells.

### Results

#### Gross features

Grossly, there was approximately  $3.0 \times 2.7 \times 2.3$  cm irregular grey-white nodule with central hemorrhaging in the resected lung tissue. The nodule was not well circumscribed, and seemed to infiltrate the surrounding normal tissue.

#### Histologic features

Histologically, the tumor was composed predominantly of sheets of round-ovoid cells with branched or dilated vessels, which was surrounded by the cells. Moreover, every cell was surrounded by the fine basal lamina, leading to the clear border of the cells. The cells had clear

cytoplasm and round nuclei with inconspicuous or small nucleoli. The majority of the cells showed mild atypia with mitoses less than 5 per 50 HPF. In the central of the tumor, hemorrhaging was present. In contrast, in the peripheral area, the tumor infiltrated and destroyed the normal bronchial and alveolar tissue, although there was a fibrous capsule around the tumor in focal area. Focally, the residual or entrapped bronchial or alveolar epithelia could be identified in the tumor (**Figure 1**).

#### Immunohistochemical staining

Immunohistochemical staining showed that the cells were diffusely positive for SMA, vimentin and caldesmon, negative for TTF-1, EMA, CK, CD34, CD45, CD99, SPA, P63, synaptophysin,

CD56, S-100, HMB45, CD117 and desmin. The entrapped epithelial cells showed positivity for TTF-1, EMA, CK, SPA or P63. CD34 staining highlighted the dilated vessels presenting in the tumor. Ki-67 index was approximately 20% (**Figure 2**). According to the morphological and immunohistochemical findings, the tumor was diagnosed as glomus tumor of uncertain malignant potential.

### Discussion

As a tumor originated from smooth muscle cells of glomus body, glomus tumor presenting in the deep location was extremely rare. So far, fewer than 40 cases of pulmonary glomus tumors were reported in the English literature [7, 8]. According to WHO classification of tumors of soft tissue and bone described in 2013, glomus tumors clinically can be classified into benign, malignant and uncertain malignant potential [10]. If the tumor showed marked atypia or atypical mitotic figures, the diagnosis should be malignant glomus tumor. The tumors lacking criteria for malignant glomus tumor but having atypical features, or large size (>2 cm) and deep location should be diagnosed as glomus tumor of uncertain malignant potential.

Histologically, the tumor typically comprised by small and round cells surrounding dilated vessels. The cells usually have clear border, as each cell was surrounded by a basal lamina. In our case, the cells showed mild atypia and the mitotic figures were also no more than 5 per 50 HPF, however, the tumor had a size of more than 2 cm. Consequently the tumor was diagnosed as glomus tumor of uncertain malignant potential. In addition, the present case showed marked infiltration into the normal bronchial and alveolar tissue, the bronchial epithelia and pneumocytes were also destroyed. According to Folpe et al., although infiltrative growth was not associated with metastasis [11], we still think that the infiltrative growth might indicate the malignant potential of this tumor.

Immunohistochemically, the neoplastic cells typically showed reactivity for vimentin, SMA, and caldesmon. The staining for desmin and CD34 is variable [12, 13]. Immunostaining for type IV collagen, a marker for basal lamina, could outline the cells surrounded by the lamina [12, 13]. The current case was diffusely positive for SMA and caldesmon, and negative

for desmin and CD34. We did not stain for type IV collagen, as the lamina was well identified under microscope.

The differential diagnosis of the tumor includes a variety of tumors, such as carcinoid tumor, pulmonary sclerosing pneumocytoma, solitary fibrous tumor, leiomyoma, lymphoma, and peripheral primitive neuroectodermal tumor. Pulmonary glomus tumor was often histologically diagnosed as carcinoid tumor, because of the uniformity of the tumor cells and relatively high incidence of carcinoid tumor in lung. However, the negative expression of CK, and neuroendocrine markers such as chromogranin A and synaptophysin could exclude carcinoid tumor [14]. Pulmonary sclerosing pneumocytoma was characterized by two cell types, namely surface cuboidal cells and polygonal cells located in the stroma of the papillary structures. In the current case, the entrapped the epithelia cells resembled the cuboid cells, and the tumor cells resembled the polygonal cells in pulmonary sclerosing pneumocytoma. However, glomus tumor lacked the variable patterns in pulmonary sclerosing pneumocytoma. The polygonal cells in pulmonary sclerosing pneumocytoma showed positivity for TTF-1, which was also helpful for differential diagnosis [15]. Typical solitary fibrous tumor was composed of spindle to ovoid cells with characteristic stag-horn vessels. Solitary fibrous tumor was diffusely positive for CD34, which could aid in excluding this tumor [16]. Leiomyoma was characterized by intersecting fascicles of spindle cells with eosinophilic cytoplasm and blunt-ended nuclei, rather than uniform round cells. In addition, Immunohistochemically negative for CD45 and CD99 was useful for excluding lymphoma, and peripheral primitive neuroectodermal tumor.

### Conclusion

In conclusion, we presented a case of glomus tumor glomus tumor of uncertain malignant potential of the lung, which was extremely rare. It was necessary for careful histological observation and using enough immunohistochemical markers to confirm the diagnosis.

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## Disclosure of conflict of interest

None.

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## References

- [1] Tsuneyoshi M and Enjoji M. Glomus tumor: a clinicopathologic and electron microscopic study. *Cancer* 1982; 50: 1601-1607.
- [2] Fang HQ, Yang J, Zhang FF, Cui Y and Han AJ. Clinicopathological features of gastric glomus tumor. *World J Gastroenterol* 2010; 16: 4616-4620.
- [3] Wang ZB, Yuan J and Shi HY. Features of gastric glomus tumor: a clinicopathologic, immunohistochemical and molecular retrospective study. *Int J Clin Exp Pathol* 2014; 15: 1438-1448.
- [4] Hirose K, Matsui T, Nagano H, Eguchi H, Marubashi S, Wada H and Morii E. Atypical glomus tumor arising in the liver: a case report. *Diagn Pathol* 2015; 10: 112.
- [5] Wang S, Ding C and Tu J. Malignant glomus tumor of the lung with multiple metastases: a rare case report. *World J Surg Oncol* 2015; 7: 13: 22.
- [6] Nakajima Y, Koizumi K, Haraguchi S, Kawamoto M, Kubokura H, Okada D, Yoshino N, Kinoshita H, Takeuchi S, Fukuda Y and Shimizu K. Locally infiltrative glomus tumor of the bronchus: a case report. *Ann Thorac Cardiovasc Surg* 2010; 16: 113-117.
- [7] Dong LL, Chen EG, Sheikh IS, Jiang ZN, Huang AH and Ying KJ. Malignant glomus tumor of the lung with multiorgan metastases: case report and literature review. *Onco Targets Ther* 2015; 28: 1909-1914.
- [8] Ariizumi Y, Koizumi H, Hoshikawa M, Shinmyo T, Ando K, Mochizuki A, Tateishi A, Doi M, Funatsu M, Maeda I and Takagi M. A primary pulmonary glomus tumor: a case report and review of the literature. *Case Rep Pathol* 2012; 2012: 782304.
- [9] Zhu YZ, Li WP, Wang ZY, Yang HF, He QL, Zhu HG and Zheng GJ. Glomus tumor of uncertain malignant potential arising in the bronchus. *Cardiothorac Surg* 2013; 8: 146.
- [10] Fletcher CD. WHO classification of tumours of soft tissue and bone. Glomus tumors. In: Fletcher CD, editor. Lyon: IARC; 2013. pp. 116-117.
- [11] Folpe AL, Fanburg-Smith JC, Miettinen M and Weiss SW. Atypical and malignant glomus tumors: analysis of 52 cases, with a proposal for the reclassification of glomus tumors. *Am J Surg Pathol* 2001; 25: 1-12.
- [12] Mravic M, LaChaud G, Nguyen A, Scott MA, Dry SM and James AW. Clinical and histopathological diagnosis of glomus tumor: an institutional experience of 138 cases. *Int J Surg Pathol* 2015; 23: 181-8.
- [13] Wang ZB, Yuan J and Shi HY. Features of gastric glomus tumor: a clinicopathologic, immunohistochemical and molecular retrospective study. *Int J Clin Exp Pathol* 2014; 7: 1438-48.
- [14] Yilmaz A, Bayramgurler B, Aksoy F, Tuncer LY, Selvi A and Uzman O. Pulmonary glomus tumour: a case initially diagnosed as carcinoid tumour. *Respirology* 2002; 7: 369-71.
- [15] Lin XY, Wang Y, Fan CF, Liu Y, Yu JH, Dai SD, Wang L and Wang EH. Pulmonary sclerosing hemangioma presenting with dense spindle stroma cells: a potential diagnostic pitfall. *Diagn Pathol* 2012; 7: 174.
- [16] Chen Y, Wang F and Han A. Fat-forming solitary fibrous tumor of the kidney: a case report and literature review. *Int J Clin Exp Pathol* 2015; 8: 8632-8635.