

# Primary Solitary Mastocytoma of the Lung: A Case Report

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## Case Report

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## Abstract

## Background

Extracutaneous mastocytoma is really rare. Although only four cases of extracutaneous mastocytoma in lung have been reported in the literature to date, the cellular composition of mast cell tumors has not yet been confirmed. Here we report a new case of primary solitary mastocytoma and try to discuss its cellular composition.

## Case report:

A 46-year-old woman, who has been having bronchial asthma for 3 years, had been found a nodules in the left lower lobe of lung by computed tomography (CT) scan because of chest pain, distress, and pain in the left thoracic region of the back for 10 days. Then the left inferior pulmonectomy and lymphadenectomy were performed. We confirmed the presence of mast cells in the resected tumor by immunohistology (i.e., strong CD117 and CD45 staining and positivity for tryptase) and toluidine blue staining. Additionally, our findings suggested that solitary mast cell tumors was consisted of mature mast cells and immature mast cells with features of epithelial cells. A diagnosis of solitary mastocytoma of the lung was suggested. By now, the patient's overall health was normal. No signs of recurrence was found. Symptoms of bronchial asthma were significantly alleviated as well.

## Conclusion

Solitary mastocytoma of the lung is rare, but operative and relative drug therapy can release symptoms effectively. Solitary mastocytoma may be consisted of mature mast cells and immature mast cells. But the reason why the tumor exhibited epithelial immunophenotype still needs further study.

## Background

Mastocytosis is a group of heterogeneous diseases characterized by abnormal proliferation of mast cells (MCs).<sup>[1-3]</sup> According to the consensus classification system of the World Health Organization (WHO), there are two major categories of mastocytosis: cutaneous mastocytosis and systemic mastocytosis. The former is characterized by the accumulation of mast cells limited to the skin, whereas the latter manifests as both systemic disorders and multifocal infiltration of the bone marrow or other extracutaneous organs.<sup>[1,4-6]</sup> Extracutaneous mastocytoma (ECM) is a variant of mastocytosis. Although it can be detected in the lungs, lung ECM is very rare.<sup>[7]</sup> To the best of our knowledge, only four cases of lung ECM have been reported to date, including the first case reported by Sherwin et al. in 1965.<sup>[8,9]</sup>

In this study, we discuss a new case of solitary mastocytoma of the lung and its immunohistochemical findings. Considering operative and relative drug therapy can release symptoms caused by mediators secreted by mast cells effectively, we expect our study will do some favor to diagnosis and treatment timely.

## Case Presentation

A 46-year-old woman had been experiencing chest pain, distress, and pain in the left thoracic region of the back for 10 days. The patient visited Laiyang Central Hospital on March 24, 2008. A computed tomography (CT) scan on the same day showed a lobular nodule in the size of 3.0 × 3.0 cm in the left lower lobe, exhibiting a spiculated pattern and uniform density. The patient denied having symptoms such as cough, expectoration, hemoptysis, fever, night sweat, hoarseness, and dysphagia and did not have a history of tuberculosis. However, the patient having bronchial asthma 3 years ago. No lesions were found on the skin, and complete blood counts demonstrated only the presence of acute inflammatory reaction. Liver and kidney function were normal. Except for right hepatic cysts measuring 1.2 × 1.1 cm, no obvious abnormalities were observed in ultrasound examination of the hepatobiliary tract, pancreas, or spleen.

According to these findings, left inferior pulmonectomy and lymphadenectomy were performed on March 30, 2008.

Specimens were fixed in 10% formalin and sliced. Tissue sections (4 μm thick) were stained with hematoxylin and eosin (H&E). A Roche autostainer, which uses the standard avidin/biotin/peroxidase complex technique, was applied for immunohistochemical studies. The primary antibodies included anti-CD117 (EP10), anti-CD45 (PD7/26 + 2B11), anti-thyroid transcription factor 1 (TTF-1; SPT24), anti-CAM5.2 (CAM5.2), anti-S-100 (4C4.9), anti-HMB45 (HMB45), anti-CD2 (UMAB6), anti-CD68 (KP1), anti-CD34 (UBEnD10), anti-actin (HHF35), and anti-Ki-67 and were purchased from Zhongshan (Beijing, China). Anti-mast cell tryptase (PB1058) was purchased from Boster (Beijing, China). Positive and negative controls were run simultaneously for all tested markers. All specimens were observed by two independent pathologists using an Olympus BX-43 microscope (Tokyo, Japan). Only clearly visible brown particles were categorized as positively stained.

A spherical, solid, fine texture nodule measuring 2.5 cm was found in the peripheral region of the left lower lobe of the lung. The nodule had clear boundaries with dark yellow to dark red cut surfaces. The remaining part of the left lower lobe was unremarkable (Fig. 1A). Furthermore, 10 lymphonodi were found.

The nodule was well circumscribed by a thin fibrous capsule and was composed of two types of cells. The first had a predominant lesion composition, polygonal mononuclear cell shape that was diffusely distributed in the nodules, and no clear boundaries between cells. These cells had clear or slightly eosinophilic cytoplasm and oval hypochromatic nuclei with coarse chromatin; small nucleoli were occasionally observed (Fig. 1B). The others were granular cells with deeply basophilic stained cytoplasm and relatively small hyperchromatic nuclei, which were scattered in the monocytoïd cells (Fig. 1C, D). The

proportion of granular cells among the total cell population was approximately 15–30% at different locations in the tumor. No mitosis or atypia was observed. However, necrosis was found, and abundant capillaries and arterioles were detected throughout the lesion. No lymph node metastasis was observed.

Toluidine blue staining showed many purple heterochromatic particles in the cytoplasm of mast cells and a 1:2 ratio of mast cells to monocytes (Fig. 2A). According to immunohistochemistry results, mast cells showed positive staining for CD117 (Fig. 2B) and CD45, whereas monocytoïd cells lacked immunoreactivity for these markers. Additionally, mast cells appeared positive for tryptase (strong positive staining in mast cells and weak positive staining in monocytoïd cells; Fig. 2C). The percentage of strongly positive cells among the total cell population ranged from 30–60% at different locations in the tumor. All cells were negative for cytokeratin 7 (CK7), S-100, HMB45, CD2, CD68, and actin; CD34 was only expressed in blood vessels, and CAM5.2, EMA,  $\beta$ -catenin (membrane localization), and vimentin were observed in all neoplastic cells (Fig. 2D-F). Finally, the proliferation index of Ki-67 was low (1–3%).

Considering the above findings and the diagnostic criteria of the WHO classification for mastocytosis,<sup>[8]</sup> a diagnosis of solitary mastocytoma of the lung was suggested.

As of July 8, 2019, the patient overall health was normal, and subsequent imaging showed no signs of recurrence. In addition, symptoms of bronchial asthma were significantly alleviated after operation.

## Discussion

ECM is a benign variant of mastocytosis. Although ECM is mainly detected in the lungs, lesions in the lungs are very rare.<sup>[1–3,7]</sup> According to the available literature, only four cases of ECM have been reported to date. The details of these cases and the current case are given in Table 1.<sup>[8–11]</sup>

Table 1  
Information about solitary mastocytoma of the lung reported

Author	Age(yr) and sex	Symptom	Site	Size (cm)	Histological findings	Specific stain (MC)	immunostaining	Therapy	Follow-up (months)	oth
Sherwin et al. <sup>8</sup> -1965	57, F	asymptomatic	Right upper lobe	2.5 × 2.0 × 2.0	proliferation of mast cells and histiocytes	Dominici's and Luna's stain, PAS stain (+)	-	Right upper lobectomy	-	a few
charrette et al. <sup>10</sup> -1966	68, F	asymptomatic	Right upper lobe	2 (Dia.)	proliferation of mast cells and epithelioid cells	Dominici stain(+)	-	Right upper lobectomy	-	-
Kudo et al. <sup>11</sup> -1988	53, M	asymptomatic	Left upper lobe	1.6 × 1.5 × 1.0	proliferation of mast cells and clear cells	alcian blue, toluidine blue and Giemsa stains(+)	MC: EMA, alpha 1-antitrypsin (+); Clear cells: EMA(+)	partial Resection, right upper lobe	2	vas inva elas
Ayadi et al. <sup>9</sup> -2012	51, F	chest pain cough dyspnea	Right lower and medium lobes	14 × 13 × 11	proliferation of mast cells and undifferentiated cells	toluidine blue(+)	MC: tryptase, CD117, CD68, CD14, CD45 (LCA), CD33(+); undifferentiated cells: EMA, cytokeratin (CK) (+)	upper and medium right lobectomy	4	loc agg (bu the seg bro and are hae
current case -2017	46, F	chest distress and pain, asthma	Left lower lobes	2.5 (Dia.)	proliferation of mast cells and monocytoïd cells	toluidine blue(+)	MC: CD117, CD45 (LCA); Monocytoïd cells: TTF-1(+); Both: tryptase, CAM5.2, EMA, $\beta$ -catenin, Vim(+)	Left lower lobectomy	129	-

In our case, numerous purple metachromatic granules of granular cells were visualized by toluidine blue staining, and these cells also showed immunoreactivity for CD117 and tryptase (strongly positive in mast cells and weakly positive in monocytoïd cells). Thus, the granular cells showed characteristics consistent with mast cells. Additionally, increased staining of cells was observed when using H&E, toluidine blue, and tryptase staining. Mariana et al.<sup>[12]</sup> showed that tryptase staining was more sensitive than toluidine blue staining; for example, poorly granulated mast cells could not be stained and identified with toluidine blue. Therefore, tryptase staining was recommended, our results also supported these opinions. Based on the weak positive

staining of tryptase in monocytoïd cells, we speculated that monocytes may be mast cells with few components. In our study, all neoplastic cells expressed CAM5.2, EMA, and  $\beta$ -catenin (cell membrane localization), and monocytoïd cells also expressed TTF-1. We hypothesized that solitary mast cell tumors may be composed of mature and immature mast cells with features of epithelial cells. However, further research is necessary to confirm this hypothesis and explore the reason why tumor cells exhibited epithelial immunophenotype.

The conservative growth pattern and relatively low proportion of Ki-67 staining indicated the benign nature of the tumor in our case. This helped us to rule out mast cell sarcoma. In addition, according to a study by Valent et al.<sup>[7]</sup> and the WHO criteria for systemic mastocytosis and ECM,<sup>[7,13]</sup> lack of CD2 expression and no remarkable findings in the skin or other systems provided us with clues and allowed us to exclude SM. Additionally, there were some morphological and immunohistochemical similarities of the current case with sclerosing pneumocytoma owing to the absence of papillary histology, sclerotic patterns, hemorrhage, glandular structure, and CK7 staining, excluding the existence of glandular epithelium. Thus, we reached a diagnosis of isolated mast cell tumors of the lung.

The patient in our case had asthma symptoms. We assumed that these symptoms may be caused by mediators of histamine, prostaglandin D2, cysteinyl leukotriene receptor, and platelet-activating factor released from mast cells.<sup>[7]</sup> The alleviation of symptoms after lobectomy may support this view.

## Conclusion

In this report, we described a new case of solitary mastocytoma. This tumor may cause some symptoms by the mediators it released, and pneumonectomy can be an effective treatment method. Based on the significant immunohistochemical and special staining characteristics, we proposed that solitary mastocytoma may be made up of mature mast cells and immature mast cells with features of epithelial cells. However, considered by the rare number of cases and the lack of some equipment such as electron microscope, there may be some limitation in our conclusion, and the real cell components of solitary mastocytoma are not clear yet. Further studies are needed to fill this knowledge gap in the future. We hope our study can do some favor to diagnosis and treatment timely.

## Abbreviations

MCs = mast cells, WHO = the World Health Organization, ECM = Extracutaneous mastocytoma, CT = computed tomography

## Declarations

Ethics approval and consent to participate: The Ethics Committee of Qilu Hospital of Shandong University (Qingdao) (Grant No.KYLL-2019006) approved this study.

Consent for publication: The written informed consent was obtained from the patient.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests

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Authors' contributions: HW and YX performed the histological examination. HW was a major contributor in writing the manuscript. HFJ analyzed and interpreted the Histological and immunohistochemical results of the tumor and made the diagnosis. All authors read and approved the final manuscript.

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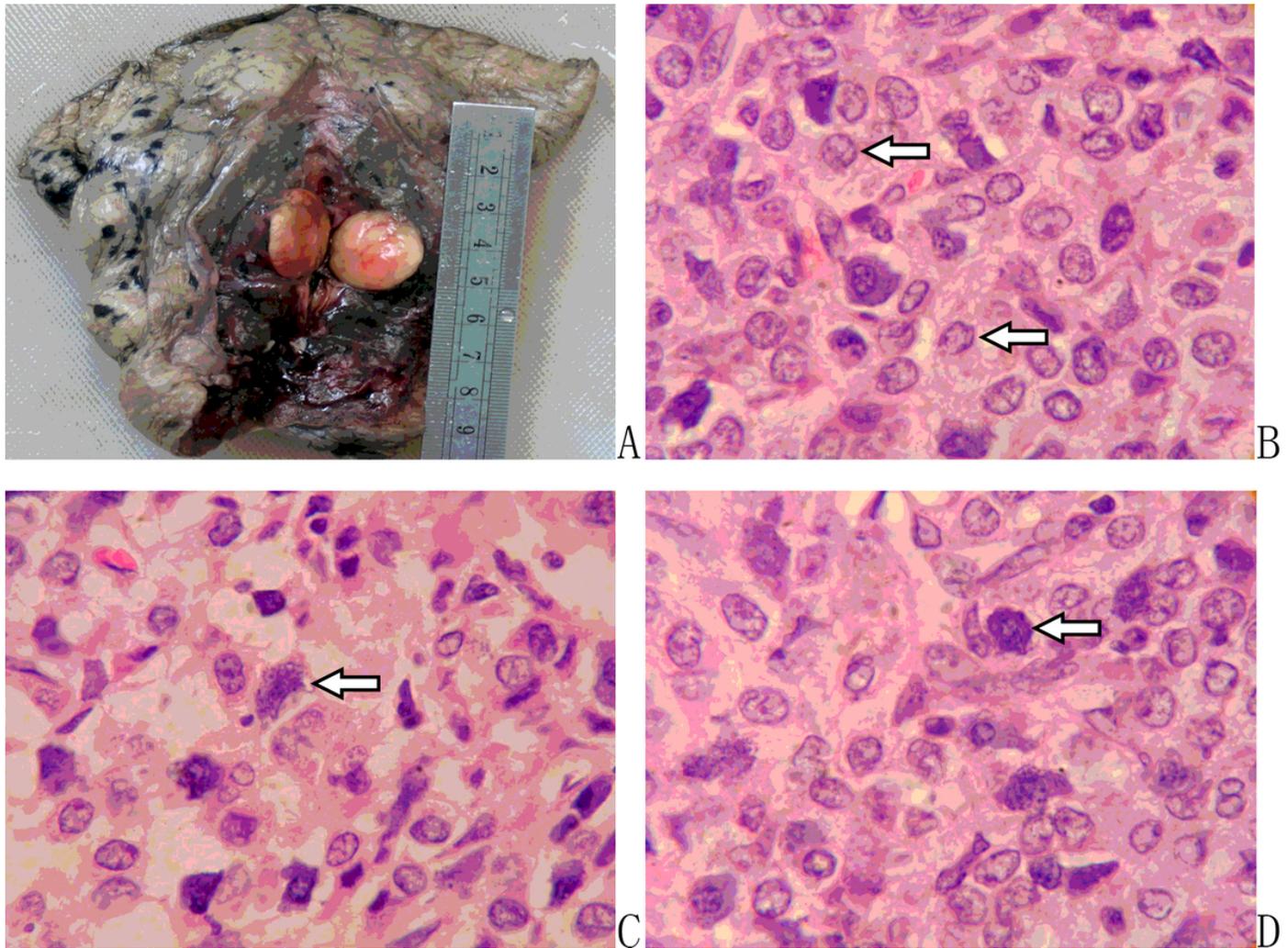
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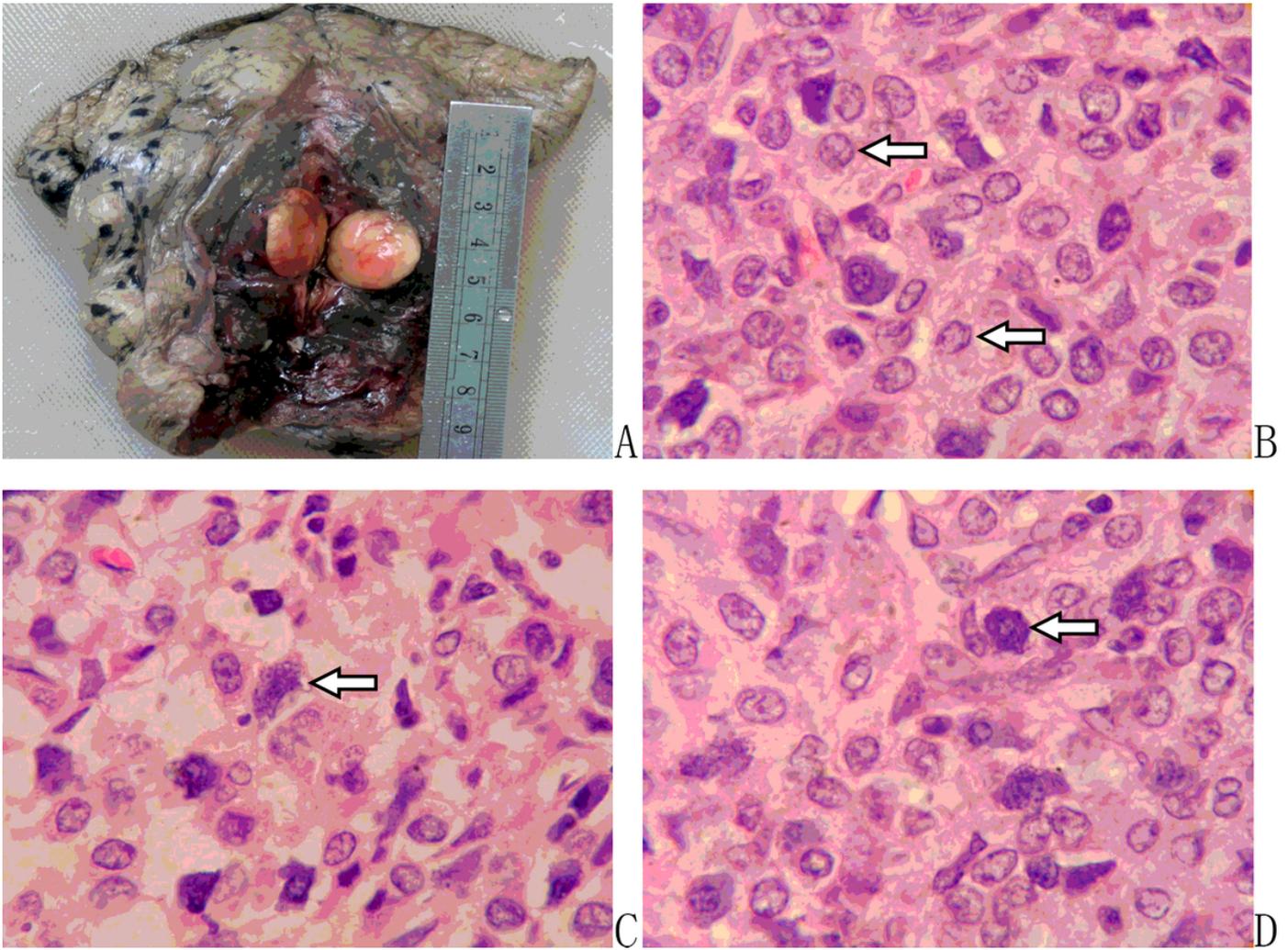
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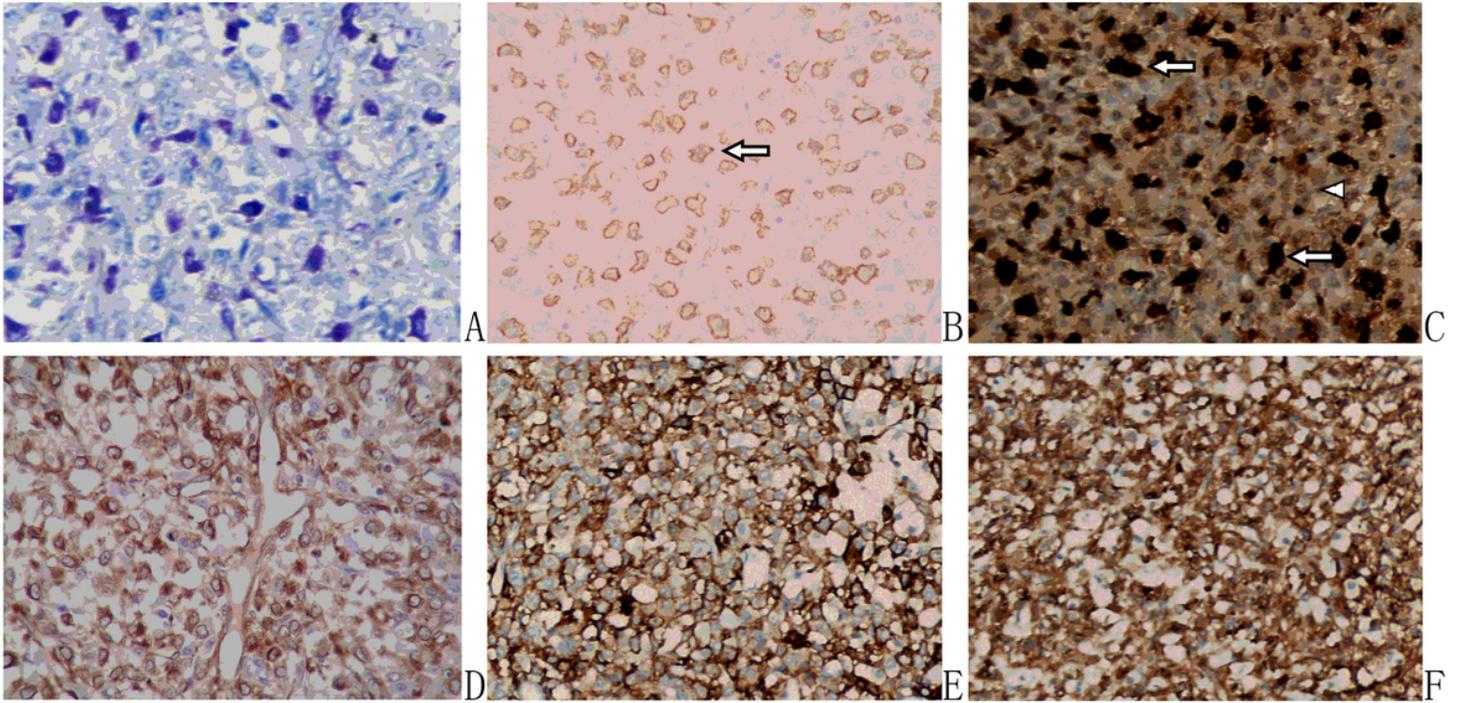
## Figures



**Figure 1**  
The macroscopic character and histological character A spherical, solid, fine texture nodule was located in the peripheral region of the left lower lobe of the lung. The cut surface was white to dark red(Fig.1.A).Predominant cells of tumor distributed in a diffused manner and without clear limit between each other. They had clear or slightly eosinophilic cytoplasm (arrow) (Fig.1.B,HE,X400).Granular cells were filled with granules, deeply basophilic stained cytoplasm and a relatively small hyperchromatic nuclei(arrow).(Fig.1.C-D,HE, X400).

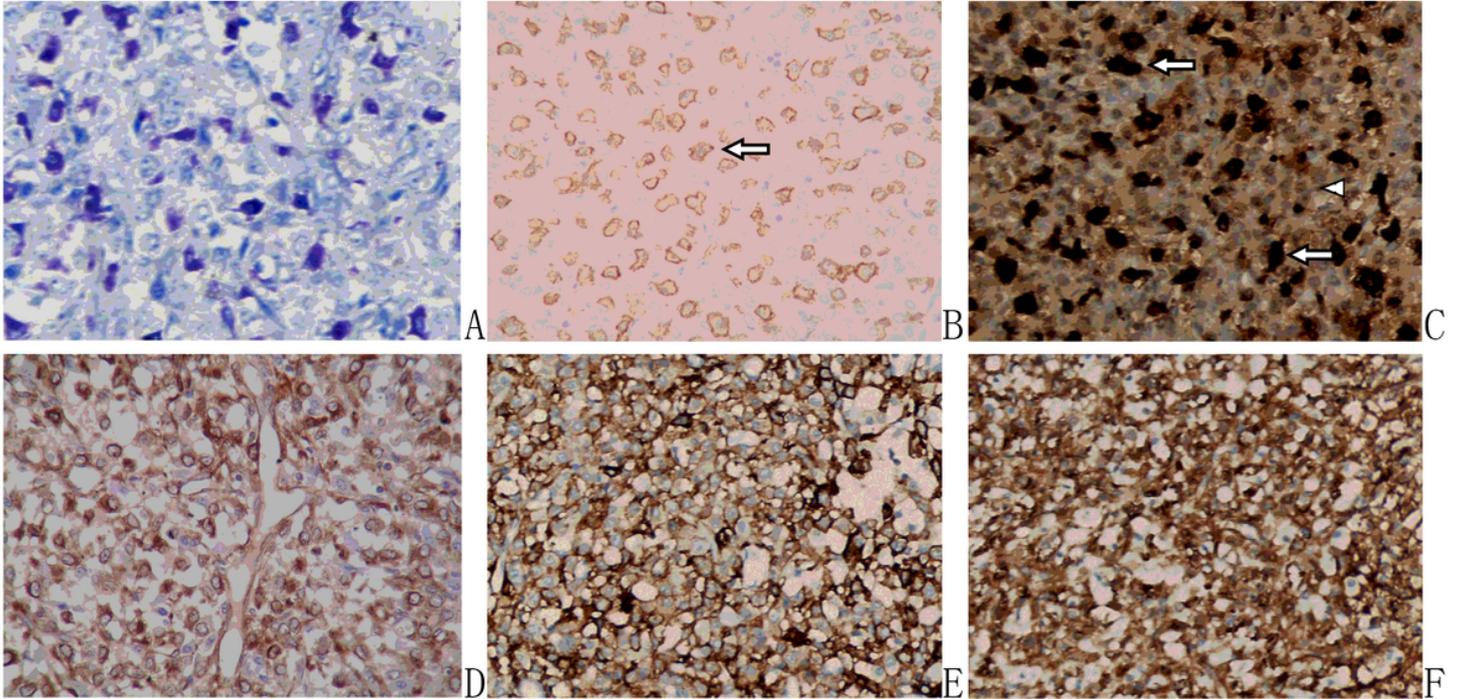


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**Figure 2**

Immunophenotypes and specific stain Toluidine blue stain manifested numerous purple metachromatic granules which shows the cytoplasm of mast cells.( Fig.2.A,Toluidine blue stain, X200).Immunohistochemical reactivity of mast cells with CD117, and showed positive staining (arrow)(Fig.2.B,X200), Immunohistochemical reactivity of tryptase, and showed strong positive staining for the mast cells(arrow) and weak positive staining for the monocytoid cells(arrow head) .(Fig.2.C,X200).Immunohistochemical reactivity with CAM5.2(Fig.2.D,X200), EMA(Fig.2.E,X200), β-catenin(Fig.2.F,X200).



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