

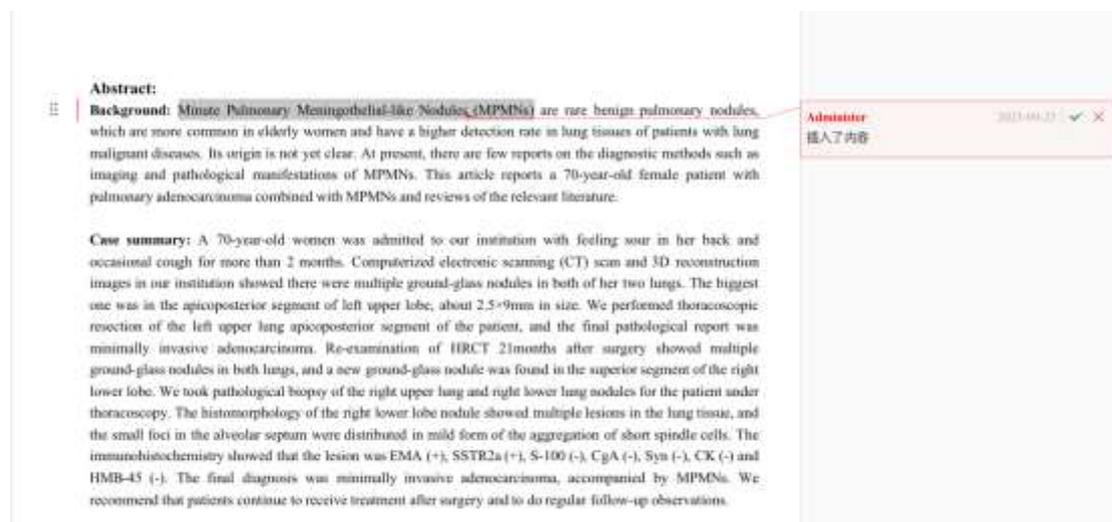
1. Abstract: The abbreviation "MPMNs" ought to be initially delineated with its full terminology before subsequent employment. This measure aligns with conventional scholarly practices for enhancing textual clarity and comprehension.

Reply 1: Thank you for your advice.

According to your request, I have added the full English name of the relevant abbreviations of "MPMNs" in the abstract. Thank you again for your review comments and work.

Abstract:

Background: Minute Pulmonary Meningothelial-like Nodules (MPMNs) are rare benign pulmonary nodules, which are more common in elderly women and have a higher detection rate in lung tissues of patients with lung malignant diseases.



2. Case Presentation: The refinement of the visual representation within Figures 3 and 4 is warranted to align with a more sophisticated visual demeanor. The strategic inclusion of directional indicators, such as arrows, is advisable to facilitate the identification of salient points of interest. Moreover, the elucidation of the immunohistochemistry figures necessitates a heightened precision in description, conducive to the advancement of scholarly rigor.

Reply 2: Thank you for your advice.

According to your request, we have added relevant detailed content descriptions and directional indicators such as arrows in Figure 3 and Figure 4. Thank you again for your work and suggestions.

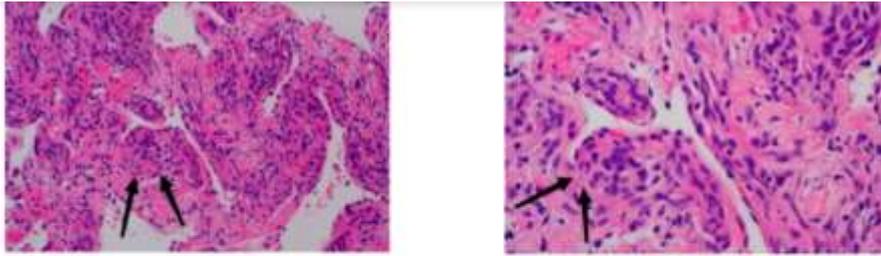
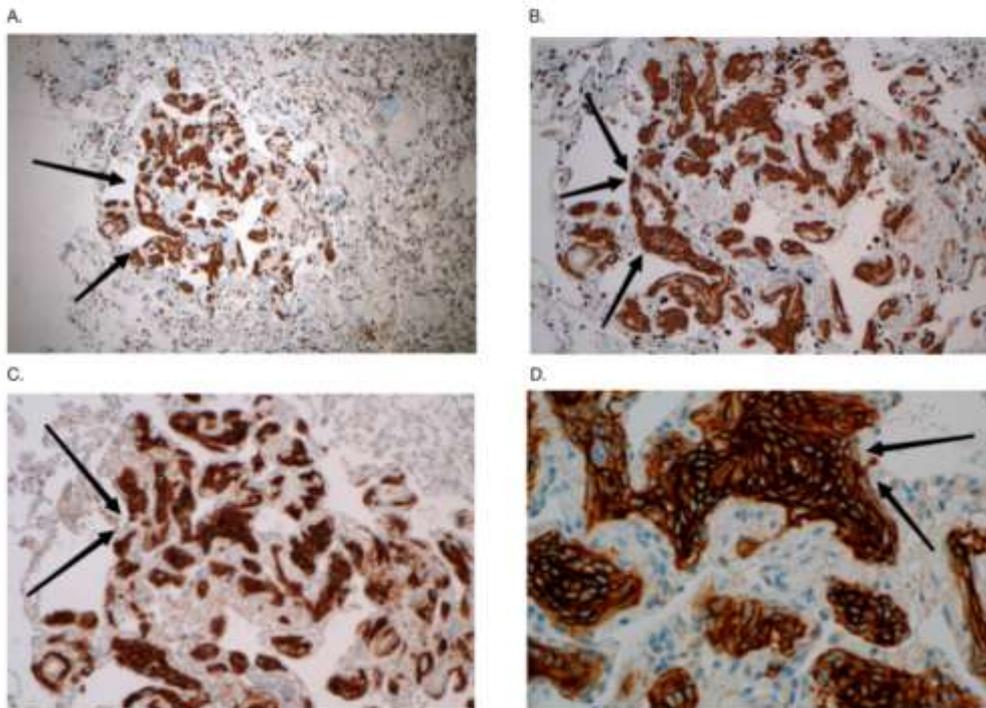


Figure 3: Histomorphological manifestation of right lower lobe nodule was the small foci in the alveolar septum were distributed in mild form of the aggregation of short spindle cells.

3



3. Conclusion Section: Regrettably, the omission of a conclusive segment diminishes the comprehensive closure that is quintessential to scholarly manuscripts. Integration of a structured conclusion would not only fortify the textual coherence but also provide a fitting summation of the insights garnered.

Reply 3: Thank you for your advice.

Conclusion

Through a comprehensive pathological diagnosis and immunohistochemical analysis of one case of Microscopic Pulmonary Meningothelomatous Nodules (MPMNs), we delved into the characteristics of this rare condition. The results demonstrated a certain diversity in immunohistochemical markers for MPMNs, with CK7, TTF-1, and EMA playing crucial roles in pathological diagnosis. Literature review further supported our findings. In conclusion, the diagnosis and differential diagnosis of MPMNs remain challenging and require the integration of various clinical and immunohistochemical information to ensure accurate diagnosis and selection of treatment strategies. This study provides valuable insights and references for the clinical management of MPMNs.

Final Diagnosis

The pathological diagnosis was Micro-invasive Adenocarcinoma with Minute Pulmonary Meningothelial-like Nodules

Treatment

We recommend that patients continue to receive treatment after surgery and to do regular follow-up observations.

Conclusion

Through a comprehensive pathological diagnosis and immunohistochemical analysis of one case of Microscopic Pulmonary Meningothelomatous Nodules (MPMNs), we delved into the characteristics of this rare condition. The results demonstrated a certain diversity in immunohistochemical markers for MPMNs, with CK7, TTF-1, and EMA playing crucial roles in pathological diagnosis. Literature review further supported our findings. In conclusion, the diagnosis and differential diagnosis of MPMNs remain challenging and require the integration of various clinical and immunohistochemical information to ensure accurate diagnosis and selection of treatment strategies. This study provides valuable insights and references for the clinical management of MPMNs.

Discussion

MPMNs, first describe by Kom et al.[9] in 1960, who considered they might be kinds of endocrine tumor called Minute Pulmonary Chemodectoma based on its cytologic characteristics, arrangement of cells and special relationship to vessels, have been considered to be benign lung lesions[1, 10]. Many subsequent studies have shown that it lacked the immunohistochemical and ultrastructural characteristics of endocrine cells, and did not contain endocrine particles[5, 10-12]. Therefore, Gefley et al.[10] renamed it as "Minute Pulmonary

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4. Immunohistochemistry: The visual depictions presented evince a commendable level of quality, underscoring the visual impact of the immunohistochemistry outcomes. However, it is incumbent upon the authors to furnish a comprehensive account of the immunohistochemistry protocols employed, a detail that has regrettably been omitted. Addressing this lacuna is paramount for assuring the reproducibility and methodological transparency of the conducted research.

Reply 4: Thank you for your advice.

According to your request, we have supplemented the contents of the related program of immunohistochemistry, etc. Thank you again for your suggestion.

The immunohistochemistry experimental protocol for this project comprises the following key steps: sample fixation, dehydration, paraffin embedding, sectioning, antibody staining, and result analysis. Firstly, tissue samples are subjected to fixation, followed by dehydration and paraffin embedding to prepare paraffin sections. Subsequently, specific

antibodies such as CK7, TTF-1, and EMA are used for staining, followed by microscopic observation and image recording. Finally, result analysis and pathological diagnosis are conducted based on the staining outcomes. Immunohistochemistry experiments are a crucial step in the study, utilized to identify immune markers, thereby supporting accurate disease diagnosis and classification.

Pathological examination

The histological findings of the right upper lobe nodule showed that cancer cells grew in a monolayer, with large nuclei, rich cytoplasm, mitotic figures were not easy to see, focal septal widening, interstitial fiber and fibroblast proliferation, dense proliferation or clustered proliferation of tumor cells, nucleoli was visible.

The immunohistochemistry experimental protocol for this project comprises the following key steps: sample fixation, dehydration, paraffin embedding, sectioning, antibody staining, and result analysis. Firstly, tissue samples are subjected to fixation, followed by dehydration and paraffin embedding to prepare paraffin sections. Subsequently, specific antibodies such as CK7, TTF-1, and EMA are used for staining, followed by microscopic observation and image recording. Finally, result analysis and pathological diagnosis are conducted based on the staining outcomes. Immunohistochemistry experiments are a crucial step in the study, utilized to identify immune markers, thereby supporting accurate disease diagnosis and classification.

The pathological manifestation of the right lower lobe nodule was no obvious nodule was visible to the naked eye. Histomorphology showed multiple lesions in the lung tissue, with diameter of 0.5-1.8mm, and the small foci in the alveolar septum were distributed in mild form of the aggregation of short spindle cells (Figure 3). And the Immunohistochemistry showed that the lesion was positive for Epithelial membrane antigen (EMA) and Somatostatin receptor 2a (SSTR2a) (Figure 4), and negative for S-100, Chromogranin A (CgA), Synaptophysin (Syn), Cytokeratin (CK) and HMB-45.



5. Biomarker Selection Rationale: The criteria underpinning the authors' selection of specific biomarkers necessitates elucidation in accordance with the scholarly requisites. Delving into the rationale governing the biomarker selection process would engender a deeper comprehension of the scientific underpinnings that steer the study's investigative trajectory.

Reply 5: Thank you for your advice.

We have based on your suggestion and request in the discussion section of the basic distance principle of biomarker selection for complementary immunohistochemistry experiments, etc, and thank you again for your suggestion.

The immunohistochemistry markers selected for this project include CK7, TTF-1, and EMA, which play crucial roles in pathological diagnosis. CK7 is a cytokeratin commonly expressed in epithelial cells, particularly in tissues like the lung, stomach, and biliary tract, making it highly useful for determining the epithelial origin of tumor cells. TTF-1 (Thyroid Transcription Factor-1) is a nuclear transcription factor, highly expressed in normal lung tissue, and frequently found in lung adenocarcinomas, aiding in distinguishing lung cancer from other malignancies. EMA (Epithelial Membrane Antigen) is a membrane-bound antigen specific to epithelial cells, providing valuable assistance in

confirming epithelial lesions. The selection of these immunohistochemistry markers is based on their specific expression in lung and epithelial cells, aiding in the identification and classification of microscopic pulmonary meningotheliomatous nodules (MPMNs). Immunohistochemistry experiments rely on the specificity of these markers, assisting in determining pathological types, guiding treatment strategy selection, and providing critical insights into disease progression and prognosis. Therefore, immunohistochemistry plays an indispensable role in MPMN pathological diagnosis, enhancing diagnostic accuracy and precision in clinical management.

certain degree of fibrosis [15].

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The diagnosis of MPMNs needs to be confirmed by immunohistochemistry. Table 1 shows the literature review of MPMNs immunohistochemistry[4-8, 10, 13, 18-21]. We can see that almost all MPMNs immunohistochemically showed positive responses to Vimentin, EMA, SSTR-2a, and CD56, and more than half of MPMNs were positive to PR, while negative for S-100, CK, Actin, HMB-45, Syn and Cga. For NSE, the study

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