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Review Article

A Rare Case Diagnosed by Lung Cryobiopsy: Diffuse Pulmonary Meningotheliomatosis

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Abstract

The article describes a clinical case of a rare pathology - "diffuse pulmonary meningotheliomatosis". A review of the literature, possible mechanisms of development, diagnostic features, and observations are presented.

Keywords: *Minute Pulmonary Meningothelial-Like Nodules (MPMN); Diffuse Pulmonary Meningotheliomatosis (DPM)*

Pulmonary small meningothelial nodules (minute pulmonary meningothelial-like nodules (MPMN)) are predominantly benign, asymptomatic lesions of unclear clinical significance. Diffuse pulmonary meningotheliomatosis (DPM), visualized as multiple bilateral miliary nodules, is a relatively rare finding and is often diagnosed in association with neoplasia, as well as with chronic lung and vascular diseases [1].

We present a clinical case of a patient who came to us with complaints of intermittent cough and changes in the lungs on chest computed tomography (CT).

Patient, 56-year-old female with a BMI of 38 kg/m^2 during a viral infection (SARS-CoV-2), in addition to "Ground-glass opacity" (GGO) lesions, multiple small foci in both lungs were detected on chest CT (Figure 1).

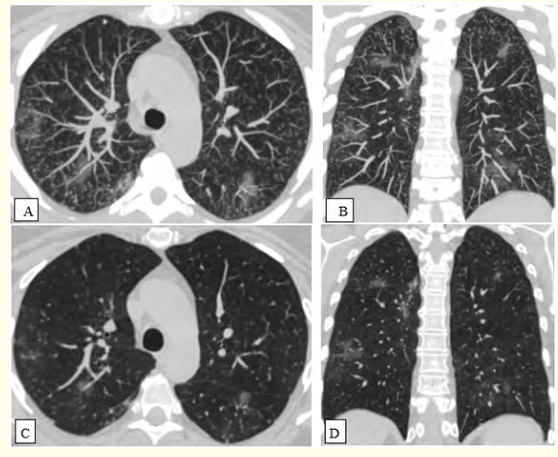

Figure 1: *CT image of multiple bilateral areas of "ground glass opacity" and small foci of both lungs: A- Axial plane, MIP mode; B- Frontal plane, MIP mode; C- Axial plane, MPR mode; D- Frontal plane, MPR mode. Note: MIP (Maximum Intensity Projection) is the maximum intensity mode of the image. MPR (Multi-Planar Reconstruction) is the multi-planar reconstruction mode.*

After 1 and 2 years, only multiple miliary-like foci of the lungs remained on chest CT; a series of CT scans over 3 years showed no changes (Figure 2). The patient was consulted by a phthisiologist; she had only light dry cough; the Diaskin test and Quantiferon test were negative; acid-fast microorganisms were not detected in the sputum, i.e. no data for active pulmonary tuberculosis were found.

The patient did not smoke and denied occupational hazards. Over the past 2 years, she had the aforementioned COVID-19 and acute bronchitis (*Mycoplasma pneumoniae*).

On physical examination, the chest corresponded to the normosthenic constitution, participated evenly in breathing, pulmonary sounds were heard on percussion, and vesicular breathing was heard on auscultation. The respiratory rate was 14/min, SpO_2 97% in air at rest. The borders of the heart were not dilated, heart sounds were muffled, the pulse was 76 beats per 1 minute, the rhythm was regular. Blood pressure was 120 and 80 mm Hg. No visible pathology was found in other organs and systems.

The general blood and urine test, coagulogram were within reference values. The biochemical blood test showed an isolated increase of uric acid levels - 452.9 μmol /l; C-reactive protein (CRP) - 6.6 mg/l. The total levels of IgA, IgM, IgG, IgE were normal.

Pulmonary functional test (PFT) did not reveal any ventilation disorders: the volume of forced expiration in the first second (FEV_1) was 115% of pred., the forced vital capacity of the lungs (FVC) was 119% of pred, FEV_1/FVC was 79%. The test with salbutamol was negative.

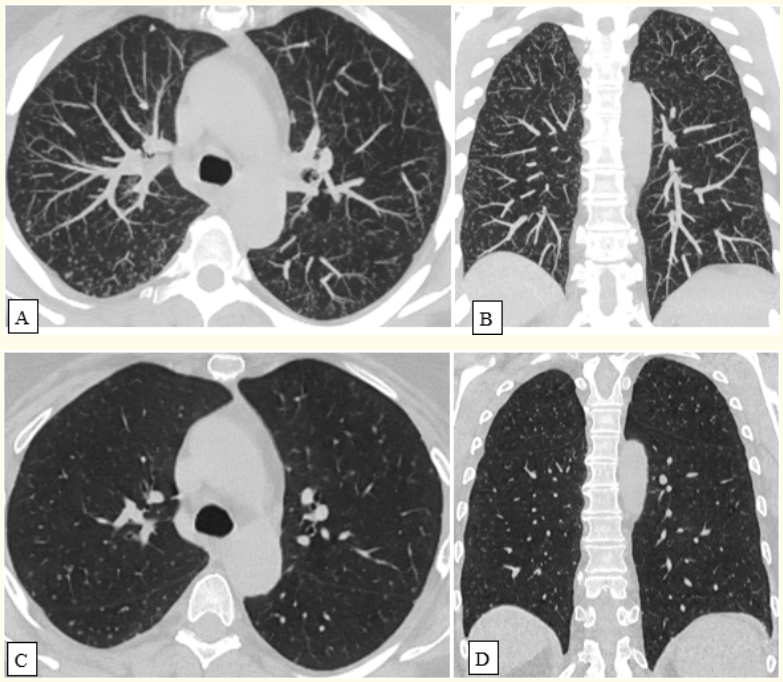

Figure 2: *In all segments of both lungs, diffusely located multiple foci, both perilymphatic and centrilobular, up to 3 mm in size, are preserved, without dynamics of size, quantity and prevalence: A - Axial plane, MIP mode; B - Frontal plane, MIP mode; C - Axial plane, MPR mode; D - Frontal plane, MPR mode.*

The patient underwent diagnostic bronchoscopy, cryobiopsy of the 2nd segment of the right lung and bronchoalveolar lavage (BAL).

Cytological analysis of BAL: cytosis - 0.22 x10^6/ml, alveolar macrophages - 73%, lymphocytes - 9%, neutrophils - 18%, acid-fast mycobacteria did not detected. In BAL DNA of atypical microorganisms (*Mycoplasma pneumoniae*, *Chlamydophila pneumoniae*), viruses (Herpes simplex virus types 1,2,6, Epstein - Barr virus, Cytomegalovirus), *Mycobacterium tuberculosis* (*Mycobacterium tuberculosis* complex) did not detected, microbiological analysis did not show any etiologically significant growth.

Histological examination of the biopsy revealed fragments of lung tissue with small (up to 2 mm) nodules in the form of nests of monomorphic oblong cells of medium size with oval nuclei, with a fragment of a lymph node with an accumulation of macrophages in one of the biopsy specimens (Figure 3).

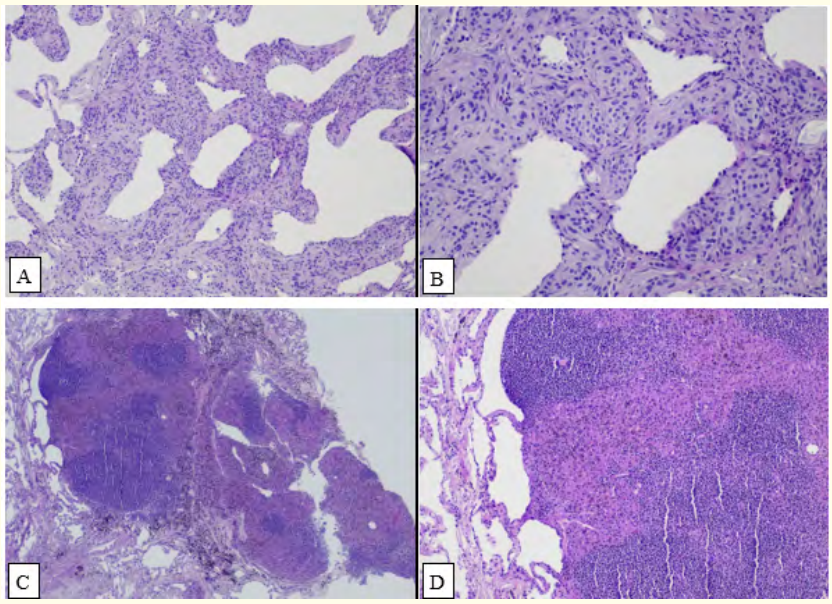

Figure 3: *Morphological examination of a biopsy of the right lung, stained with hematoxylin and eosin: A, B - A small formation, the histological picture of which resembles the "cellular whorls" of meningothelial meningiomas; C, D - Lymph node, located next to the formation, with sinus histiocytosis - macrophages with black pigment in the cytoplasm.*

Immunohistochemistry (IHC) demonstrated, that all cells of the "nodules" expressed Vimentin, progesterone receptors (PR), membrane marker of NK cells (CD 56), and did not express Chromogranin A, Synaptophysin, antigens to cytokeratin 5/6 (CK5/6), receptors to estrogen (ER), pan cytokeratin monoclonal antigens (PanCK AE1/3). The marker of proliferative activity (Ki-67) is positive in less than 1% of cells - proliferative activity is very low (Figure 4).

Thus, taking into account the results of the IHC, the diagnosis of neuroendocrine tumor, epithelioid tumor, spindle cell carcinoma is rejected. The morphological picture and immunophenotype in lung samples were characteristic of MPMN and in our case - DPM.

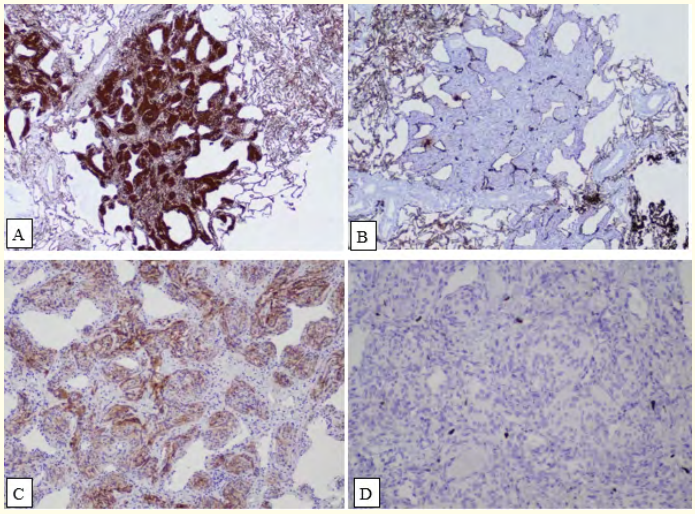

Figure 4: *Immunohistochemistry of a biopsy of the right lung: A - Positive reaction with vimentin; B - Negative reaction with pan cytokeratin antigens (PanCK AE1/3); C - Positive membrane reaction with the differentiation cluster CD56; D - Nuclear reaction with the proliferative activity marker Ki-67 - single cells express antibodies to this marker..*

Discussion

MPMN are usually asymptomatic nodules, ranging in size from 100 μm to 3 mm, often discovered incidentally during examination of surgical or autopsy material, and can be single or multiple. The incidence rate, according to various researchers, is 0.07 - 13.8%. The term diffuse pulmonary meningotheliomatosis (DPM) is used to denote multiple bilateral changes [2-4].

In 1960, Korn., *et al.* and in 1963, Zak FG and Canves A described multiple small formations in the lungs, consisting of nests of epithelioid cells located around venules in the interstitium of the lungs. Given the similarity of the histological picture with carotid body tumors and the perivascular location, scientists introduced the term "chemodectomatosis" to describe the identified formations [5,6].

In 1988, Gaffey., *et al*. studied the clinical and pathological features of these proliferations and noted their similarity to meningothelial cells, introducing a more precise term to designate them: small meningothelial-like nodules [7].

This pathology does not occur in childhood, which practically excludes the possibility of its "congenital" genesis. Basically, MPMN and DPM are diagnosed in women aged 50 - 70 years. Patients may complain of unproductive cough, shortness of breath, but more often MPMN and DPM are asymptomatic and are an accidental finding during radiological or histological studies [8,9].

Associations of MPMN with pulmonary embolism, pulmonary infarctions, breast and thyroid cancer, oncological diseases of the uterus, intestine, esophagus, and atypical adenomatous hyperplasia of the lungs are known. MPMN are also found in patients with hypersensitivity pneumonitis, pulmonary vasculitis, and chronic lung diseases, such as bronchial asthma [10-12]. Melocchi., *et al.* in a review described MPMN and DPM in patients with arterial hypertension, coronary heart disease, diabetes mellitus, obesity, gastroesophageal reflux disease, thyroid and kidney disease, and neurodermatitis [13].

MPMN are visualized on chest CT, as randomly located small "ground glass opacity" foci or diffuse small solid nodules of 2.0 - 8.0 mm, rarely with cavitation. DPM is characterized by bilateral lung damage, which was observed in our patient. PFT is usually not impaired, restrictive ventilation disorders are less often determined [14-16].

Histogenesis and immunohistochemical characteristics are currently under study.

Almost all researchers describe MPMN as multiple nodules with clear boundaries. Nodules can be located close to the pleura, but do not penetrate the pleura. Their shapes are predominantly round, oval or spindle-shaped, located in a nested order, more often in the peripheral parts of the lungs, can have a solid structure and red-brown or gray-red staining. The cells externally resemble meningeal epithelium, have medium-sized nuclei, there are no signs of atypia and mitotic figures. These proliferations are associated with the alveolar interstitium, a number of formations have a cyst-like structure, explained by thickening of the alveolar wall, as well as air in the alveolar cavity, vessels were detected along the edges of some nodules, but the connection between them is still unknown. Considering the smoothness and uniform thickness of the vascular wall, some authors assume the absence of invasion of formations into the vessel wall [5,6,16].

Immunohistochemistry of MPMN were revealed: positive reactions to epithelial cell membrane antigen (epithelial membrane antigen (EMA), vimentin, progesterone receptor (PR) and CD56, and negative reactions to thyroid transcription factor-1 (TTF-1), cytokeratin (CK), synapsin (Syn), system-specific biological protein S-100, androgen receptor (AR) and melanoma-associated antigen HMB-45. A positive reaction to progesterone may explain the most frequent detection of this pathology in women. The development of lung adenocarcinoma with MPMN is not excluded, this is indirectly confirmed by their simultaneous detection. A positive result is given by the use of somatostatin receptor 2a (SSTR2a) and insulinoma-associated protein 1 (INSM1), which can be used to distinguish MPMN from lung neuroendocrine tumors. Some authors describe a weak positive reaction to neuron-specific enolase (NSE), but non-specific, as well as a number of positive reactions for CD68 from KP1 and weakly positive reactions for CD68 by PG-M1. Mukhopadhyay., *et al.* advocate the need for reactions with chromogranin and synaptophysin for differential diagnosis with adenocarcinomas and note a positive reaction with CD56 and a negative reaction with TTF-1. TTF-1 in the human body is usually found in bronchial and alveolar epithelial cells. Negative TTF-1 reactions indicate that MPMN originates from tissues other than bronchial and alveolar tissues, however, at present there is no precise data on the origin of MPMN [3,17,18].

Li H., *et al*. suggest 2 hypotheses for the pathogenesis of MPMN:

1. MPMN is a type of reactive hyperplasia. This hypothesis is supported by the absence of MPMN in children, the identified association with embolism, chronic diseases and lung tumors [3]. The genetic aspects of oncogenicity meningiomas and their genetic similarity with MPMN revealed the absence of the process of loss of heterozygosity (LOH) in MPMN compared to meningiomas. Allelic imbalance of meningioma is mainly located in chromosomes 22q, 14q, 1p and was practically not detected in MPMN, only isolated cases were recorded. In contrast, multiple LOH events were recorded in DPM (33% of cases affecting 7 genomic loci), which allowed considering DPM as a transitional form between reactive and neoplastic hyperplasia [19].

Also, Niho S., *et al*. in a study of MPMN clonality based on the polymorphic marker associated with the X chromosome, the human androgen receptor gene (HUMARA), confirmed the absence of histological differences between monoclonal and polyclonal MPMN. Given that monoclonality is one of the main properties of neoplasia, the reactive nature of MPMN is assumed [20].

2. MPMN are associated with meningiomas of the central nervous system. Primary pulmonary meningioma (PPM) is a rare neoplasm, characterized by a benign and asymptomatic course, slow growth. Malignant PPM with aggressive growth and distant metastases are extremely rare [21,22]. Histologically, primary meningiomas are characterized by spindle-shaped nests of cells located in the form of bundles or whorls. IHC gives identical positive reactions with epithelial membrane antigen (EMA), progesterone receptor (PR), somatostatin receptor 2 (SSTR 2) [22].

Yang B., *et al*. distinguish three types of pleuropulmonary meningothelial proliferations, including metastatic pulmonary meningiomas, PPM and MPMN. MPMN have IHC similar to meningiomas. In addition, MPMN have similar chromosomal abnormalities affecting

chromosomes 1p, 14q, 9p, 10, 17 and 22q.33,34, loss of the NF2 gene on chromosome 22q. Cases are known about the simultaneous coexistence of MPMN and PPM in the same sample, which suggests the possibility of their common origin, as well as the possibility of progression of MPMN to DPM, and subsequently to pleural or pulmonary meningiomas [8,23].

A similar radiographic picture of pulmonary meningioma and metastases of intracranial meningioma with MPMN has been described [1,3,5,7,13].

The differential diagnosis of diffuse nodular lesions is complex, particularly in the presence of cavitation. DPM can mimic many diseases, including hematogenous spread of infection or tumor to the lungs, sarcoidosis, other granulomatosis, diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH), pulmonary Langerhans cell histiocytosis, multifocal micronodular pneumocytic hyperplasia, multiple adenocarcinomas, metastases of various sarcomas [13,19,25,26]. Therefore, the diagnosis can only be confirmed morphologically.

The clinical course of DPM is benign, not requiring therapeutic and surgical interventions, which was observed in our patient. Zhang Y., *et al*. when observing patients with confirmed DPM for 1-3-6 years, did not reveal new changes or an increase in the size of existing nodules on CT of the chest. The patients did not have any clinical symptoms. However, given the frequent occurrence of this pathology in patients with malignant diseases, it is necessary to conduct a thorough oncologists search, excluding concomitant meningioma. Due to the expression of somatostatin receptors (SSTR2a), there is a hypothesis about the possible use of somatostatin treatment in cases of DPM progression [1,11,13,27].

We observed in this clinical case diffuse bilateral changes, with thickening in the subpleural areas, which are an accidental finding and are not accompanied by any significant clinical manifestations. Given the postmenopausal period, the absence of smoking history, clinical and laboratory signs of infectious diseases, tuberculosis, the absence of neurological symptoms, obvious oncopathology, morphological diagnostics of changes in the lungs was carried out. Histological and immunohistochemistry confirmed the rare diagnosis of diffuse pulmonary meningotheliomatosis, which requires further monitoring.

Conclusion

In conclusion, DPM should be considered as one of the conditions in the differential diagnosis of disseminations in the lungs. Given its probable relationship, especially with oncology, it is necessary to carefully examine patients. Further studies are needed that can clarify the nature of DPM.

Conflict of Interest

The authors declare no conflict of interest.

Bibliography

1. Zhang Y., *et al*. "Minute pulmonary meningothelial-like nodules: associations between computed tomography and pathology features". *Quantitative Imaging in Medicine and Surgery* 13.1 (2023): 462-470.

2. Masago K., *et al*. "Is primary pulmonary meningioma a giant form of a meningothelial-like nodule? A case report and review of the literature". *Case Reports in Oncology* 5.2 (2012): 471-478.

3. Li H., *et al*. "[Recent advances and controversies in minute pulmonary meningothelial-like nodules]". *Zhongguo Fei Ai Za Zhi* 26.8 (2023): 621-629.

4. Zhang Y., *et al*. "Minute pulmonary meningothelial-like nodules: rare lesions appearing as diffuse ground-glass nodules with cyst-like morphology". *Quantitative Imaging in Medicine and Surgery* 11.7 (2021): 3355-3359.

5. Zak FG and Chabes A. "Pulmonary chemodectomatosis". *Journal of the American Medical Association* 183 (1963): 887-889.

6. Korn D., *et al*. "Multiple minute pulmonary tumors resembling chemodectomas". *American Journal of Pathology* 37.6 (1960): 641-672.

7. Gaffey MJ., *et al*. "Minute pulmonary meningothelial-like nodules. A clinicopathologic study of so-called minute pulmonary chemodectoma". *American Journal of Surgical Pathology* 12.3 (1988): 167-175.

8. Mukhopadhyay S., *et al*. "Pulmonary meningothelial-like nodules: new insights into a common but poorly understood entity". *American Journal of Surgical Pathology* 33.4 (2009): 487-495.

9. Fadl SA., *et al*. "Minute pulmonary meningothelial-like nodules". *Radiology: Cardiothoracic Imaging* 3.5 (2021): e210219.

10. Mizutani E., *et al*. "Minute pulmonary meningothelial-like nodules: clinicopathologic analysis of 121 patients". *Human Pathology* 40.5 (2009): 678-682.

11. Morresi-Hauf AT., *et al*. "Diffuse pulmonale Meningotheliomatose [Diffuse pulmonary meningotheliomatosis]". *Pneumologie* 69.9 (2015): 553-559.

12. Suster S and Moran CA. "Diffuse pulmonary meningotheliomatosis". *American Journal of Surgical Pathology* 31.4 (2007): 624-631.

13. Melocchi L., *et al*. "Diffuse pulmonary meningotheliomatosis: Clinic-pathologic entity or indolent metastasis from meningioma (or Both)?" *Diagnostics (Basel)* 13.4 (2023): 802.

14. Kuroki M., *et al*. "Minute pulmonary meningothelial-like nodules: high-resolution computed tomography and pathologic correlations". *Journal of Thoracic Imaging* 17.3 (2002): 227-229.

15. Ding YL., *et al*. "[Diffuse pulmonary meningotheliomatosis: a case report and literature review]". *Zhonghua Jie He He Hu Xi Za Zhi* 42.1 (2019): 24-29.

16. Li N., *et al*. "Clinical, radiological, and pathological features of minute pulmonary meningothelial-like nodules and diffuse pulmonary meningotheliomatosis". *Frontiers in Medicine (Lausanne)* 10 (2023): 1209491.

17. Jayaschandran V., *et al*. "An uncommon cause of miliary pattern of pulmonary nodules-diffuse pulmonary meningotheliomatosis". *Respirology Case Reports* 5.4 (2017): e00238.

18. Peng XX., *et al*. "Benign disease prone to be misdiagnosed as malignant pulmonary nodules: Minute meningothelioid nodules". *Thoracic Cancer* 10.5 (2019): 1182-1187.

19. Ionescu DN., *et al*. "Pulmonary meningothelial-like nodules: a genotypic comparison with meningiomas". *American Journal of Surgical Pathology* 28.2 (2004): 207-214.

20. Niho S., *et al*. "Immunohistochemical and clonal analysis of minute pulmonary meningothelial-like nodules". *Human Pathology* 30.4 (1999): 425-429.

21. Huang X., *et al*. "Multiple primary pulmonary meningioma: A case report and literature review". *Thoracic Cancer* 13.15 (2022): 2257-2259.

22. Zhang DB and Chen T. "Primary pulmonary meningioma: A case report and review of the literature". *World Journal of Clinical Cases* 10.13 (2022): 4196-4206.

23. Yang B and Qiu J. "Primary pulmonary meningioma with associated multiple micronodules: a case report and literature review". *Surgical Case Reports* 2 (2023): rjad034.

24. Korn D., *et al*. "Multiple minute pulmonary tumors resembling chemodectomas". *American Journal of Pathology* 37.6 (1960): 641-672.

25. Radzikowska E. "Update on pulmonary Langerhans cell histiocytosis". *Frontiers in Medicine (Lausanne)* 7 (2021): 582581.

26. Kfoury H., *et al*. "Mimicry of minute pulmonary meningothelial-like nodules to metastatic deposits in a patient with infiltrating lobular carcinoma: a case report and review of the literature". *Korean Journal of Pathology* 46.1 (2012): 87-91.

27. Tzilas V and Bouros D. "A 58-year-old woman with lung nodules and chronic cough". *Chest* 160.3 (2021): e285-e288.

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