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ORIGINAL ARTICLE – CLINICAL ONCOLOGY

Clinical, pathological and radiologic features of minute pulmonary meningothelial-like nodules

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Abstract

Objectives Reports about the radiologic features of minute pulmonary meningothelial-like nodules are sparse. This study aims to investigate the radiologic features of minute pulmonary meningothelial-like nodules.

Method From January 2016 to April 2019, 7589 patients underwent pulmonary resections at Fudan University Shanghai Cancer Center. Postoperative pathology records were reviewed retrospectively. Fifty-nine patients with minute pulmonary meningothelial-like nodule were included. The identification of minute pulmonary meningothelial-like nodules in pathology specimen included pathologically confirmed in resected nodules, and discovery in the peripheral tissue of other resected nodules incidentally. We went back and checked all the pre-operative scans of patients to analyze surgical decision and observe any change of visible minute pulmonary meningothelial-like nodule over time. Clinic, radiologic and pathological features were collected.

Result Fifty-nine patients included 10 men and 49 women, with a mean age of 57.7. Five patients had history, while 54 patients were non-smokers. 79 min pulmonary meningothelial-like nodules was found. Of them, 36 nodules were not visible on computed tomography scan. 43 nodules were visible on computed tomography scan, with an average size of 5.3 mm in 29 patients. Computed tomography appearance included pure ground-glass opacity in 36, mixed in 2, and solid nodules in 5. Nearly half of patients had a pre-operative follow-up more than 6 months (13/29, 44.8%). The median pre-operative radiologic follow-up was 4.9 months. Approximately 90% of patients underwent pulmonary surgery because of other malignant nodule on chest computed tomography scan (52/59, 88.1%).

Conclusion Most minute pulmonary meningothelial-like nodules tend to present as ground-glass opacity, especially pure ground-glass opacity. Continuous computed tomography monitoring revealed no radiologic change over time. Continuous computed tomography monitoring was necessary part of management of minute pulmonary meningothelial-like nodule.

Keywords GGO · Benign nodule · Minute pulmonary meningothelial-like nodule

Introduction

Minute pulmonary meningothelial-like nodules (MPMNs) are identified in autopsy or resected lung specimens (Matsuoka et al. 2012). These benign pulmonary nodules are usually asymptomatic, which do not require surgical treatment. However, with the development and popularization of thin-section chest CT scan, some MPMNs can visible on chest CT scan and presented as malignant nodules. Few studies had reported radiologic appearance of MPMNs. In this study, we collected 59 cases of MPMNs, described their features, and discussed their management.

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Methods

Patients and diagnostic criteria

From January 2016 to April 2019, 7589 patients underwent pulmonary resections at the departments of Thoracic Surgery Fudan University Shanghai Cancer Center. To recognize patients with MPMN, their postoperative pathology records were reviewed retrospectively. Two pathologists blindly and independently rechecked the slides. Fifty-nine patients and seventy-nine MPMNs which met the diagnostic criteria according to Gaffey's report (Gaffey et al. 1988) were included. Clinic features were collected, including sex, age, and smoking history.

This study was approved by the Committee for Ethical Review of Research (Fudan University Shanghai Cancer Center IRB 2008223-9). Due to the retrospective nature of this study, informed consent was waived.

Pathology specimen and chest CT scan

The identification of MPMNs in pathology specimen contained two different scenarios. Some MPMNs were pathologically confirmed in resected nodules, and the other MPMNs were identified in the peripheral tissue of other resected nodules incidentally. In the first scenario, MPMNs could be seen and located on chest CT scan, while in the second scenario, MPMNs were not visible on chest CT scan. We went back and rechecked all pre-operative scans of patients to analyze surgical decision and to observe any change of visible MPMNs over time. Radiologic and pathological features were collected, including location of nodules, diameter of nodules on CT scan, CT appearance of nodules, and pathological reports.

Results

Patient characteristics

Fifty-nine patients included 10 men and 49 women, with a mean age of 57.7. Five patients had a smoking history, while 54 patients were non-smokers. Main diagnosis was minute pulmonary meningothelial-like nodules in 14 patients, adenocarcinoma in 42 patients, atypical adenomatous hyperplasia in 2, and metastatic lung cancer in 1. 46 patients had single-minute pulmonary meningothelial-like nodule, and 13 patients had more than one nodules (Table 1).

Table 1 Clinical features of 59 patients

Clinical features	
Age (years)	
Mean	57.7
Range	41–74
Gender	
Male	10 (16.9)
Female	49 (83.1)
Smoking history	
Present/former	5 (8.5)
Never	38 (91.5)
Main diagnosis	
MPMN	14 (23.7)
AAH	2 (3.4)
AIS/MIA	21 (35.6)
Invasive adenocarcinoma	21 (35.6)
Metastatic lung cancer	1 (1.7)
Numbers of MPMN	
1	46 (78.0)
2	7 (11.9)
3	6 (10.1)

HE staining and immunohistochemical results

Minute pulmonary meningothelial-like nodules consist of cells resembled meningothelial cells and arranged in nests, microscopically (Fig. 1a and b). In addition to immunohistochemical staining, totally 24 specimens were tested. 22 of 23 specimens (95.7%) tested positive for EMA, 21 of 21 specimens (100.0%) tested positive for PR, 18 of 18 specimens (100.0%) tested positive for VIM, and 17 of 18 specimens (94.4%) tested positive for CD56, while 13 of 16 (81.3%) specimens tested negative for TTF-1 and 11 of 11 specimens (100.0%) tested negative for Syn (Table 2).

Radiologic features of MPMN and follow-up

Seventy-nine minutes pulmonary meningothelial-like nodules were enrolled. Of them, 36 nodules were not visible on CT scan, because they were incidentally discovered in resected lung specimens. 43 nodules could be observed on chest CT scan, with an average size of 5.3 mm in 29 patients. CT appearance included pure ground-glass opacity in 36, mixed in 2, and solid nodules in 5 (Table 3). For those 29 patients with measurable nodules on CT scan, nearly half of patients had a pre-operative follow-up more than 6 months (13/29, 44.8%). The median pre-operative radiologic follow-up was 4.9 months. Approximately 90% of patients underwent pulmonary surgery because of other malignant nodule on chest CT scan (52/59, 88.1%). Five patients underwent surgery on account of malignant finding of MPMN (5/59, 8.5%) (Table 4). Owing to long-term CT-scan follow-up revealed no change in size, two patients underwent resection of MPMN (2/59, 3.4%).

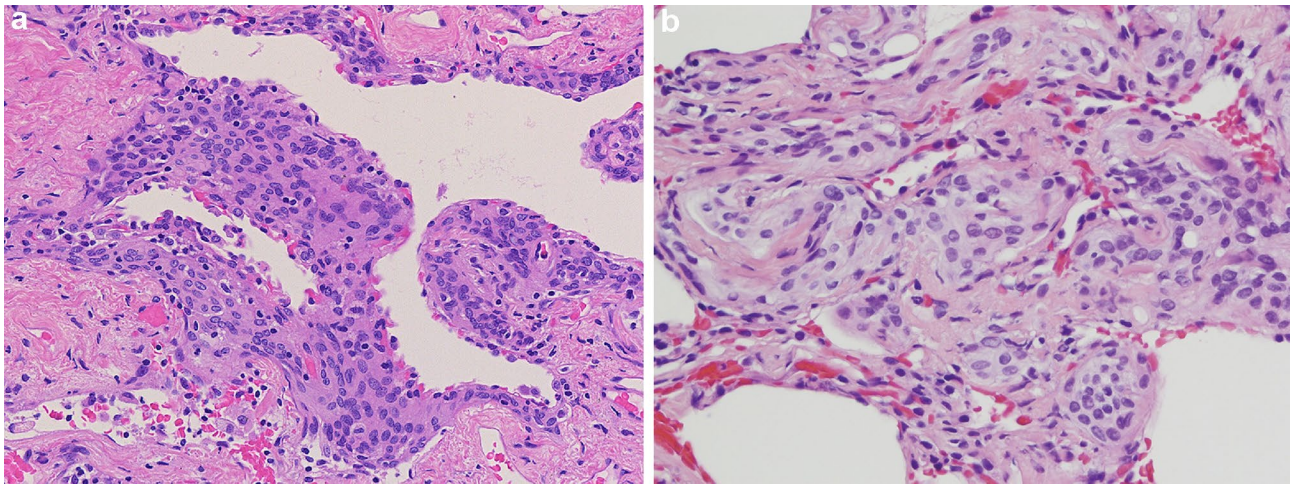

Fig. 1 **a** Photomicrograph of MPMN, it showed cells arranged in nests (hematoxylin and eosin staining, 200×). **b** Photomicrograph of MPMN, and it showed cells resembled meningothelial cells (hematoxylin and eosin staining, 400×)

Table 2 Immunohistochemical results

No.	EMA	PR	VIM	CD56	TTF-1	Syn
1	++	++	NE	NE	–	–
2	++	++	++	+	–	–
3	++	++	++	++	NE	NE
4	++	NE	NE	NE	–	NE
5	++	++	NE	NE	++	NE
6	+	++	++	++	NE	–
7	++	++	NE	++	NE	NE
8	+	+	++	++	+	–
9	++	++	++	++	NE	NE
10	+	++	++	++	–	–
11	NE	+	++	+	–	NE
12	++	++	++	NE	–	NE
13	++	++	++	++	NE	NE
14	+	++	++	NE	–	NE
15	+	++	NE	+	NE	–
16	++	++	NE	++	NE	–
17	+	NE	++	++	–	–
18	+	++	++	++	+	NE
19	–	++	++	–	–	–
20	++	NE	++	+	–	NE
21	++	+	++	++	–	NE
22	++	++	++	NE	–	NE
23	+	++	++	++	–	–
24	+	++	++	++	NE	–

EMA epithelial membrane antigen, *PR* progesterone receptor, *VIM* vimentin, *Syn* Synaptophysin, – negative, + weak positive. ++ positive

Table 3 Radiologic features of 43 nodules (29 patients)

Radiologic features	
Size(mm)	
Mean	4.5
Range	1.9–12.6
Location	
RUL	3 (7.0)
RML	2 (4.7)
RLL	19 (44.2)
LUL	5 (11.6)
LLL	14 (32.6)
Appearance	
Pure	36 (83.7)
Mixed	2 (4.7)
Solid	5 (11.6)

Table 4 Reasons of surgical decision (59 patients)

Reasons of surgical decisions	
Other malignant nodule	52 (88.1)
Malignant finding of MPMN	5 (8.5)
Long-term CT-scan follow-up	2 (3.4)

Fig. 2 An MPMN located in right lower lobe presents as ground-glass opacity on chest CT scan

Fig. 3 An MPMN located in left lower lobe presents as solid nodule on chest CT scan

Discussion

Minute pulmonary meningothelial-like nodules (MPMN) were first described by Korn in 1960 (Korn et al. 1960). Since this kind of lesion was composed of nests of epithelioid, similar to "carotid body tumors" and associated with pulmonary vessels, Korn named them "pulmonary chemodectomas". However, subsequent studies showed a series of different opinions about MPMNs (Gaffey et al. 1988; Churg and Warnock 1976; Niho et al. 1999; Ionescu et al. 2004; Weissferdt et al. 2015). Warnock and Gaffey reported "pulmonary chemodectomas" had similar structural and immunohistochemical features of meningothelial cells (Gaffey et al. 1988; Churg and Warnock 1976). And a new item "minute meningothelioid nodule" was accepted. Mukai reported some MPMN immunostaining positive for myosin and vimentin, suggested its origin from muscle cells (Niho et al. 1999). Weissferdt reported that MPMN was associated with CNS meningiomas in common genetic pathways (Weissferdt et al. 2015). However, Ionescu reported MPMN lacked mutational damage, while meningiomas showed high frequency of loss of heterozygosity, suggested its reactive origin (Ionescu et al. 2004). Not a common sense about mechanism of MPMN was reached, on the other hand, radiologic reports about MPMN were sparse.

Our study reported clinical, pathological and radiologic features of 59 cases of MPMN, and discussed management of these patients. Frequency of MPMN was 0.77%, lower than the previous studies based on operation (7.0–13.8%) (Niho et al. 1999; Mizutani et al. 2009; Mukhopadhyay et al. 2009). Actual number of frequency might be larger, because some MPMNs were discovered incidentally. Female was in the majority in our study (49/59, 83.1%), which was in accordance with the previous reports (Mizutani et al. 2009; Mukhopadhyay et al. 2009). 79 MPMNs were identified in pathology specimens. Of them, 36 nodules had no definite location on CT scan, because they were discovered in the peripheral tissue of other resected nodules incidentally. The remaining 43 nodules were visible on chest CT scan, with an average size of 4.5 mm. CT appearance included pure ground-glass opacity in 36, mix in 2 and solid nodules in 5. No specific imaging features were observed on chest CT scan. Though most

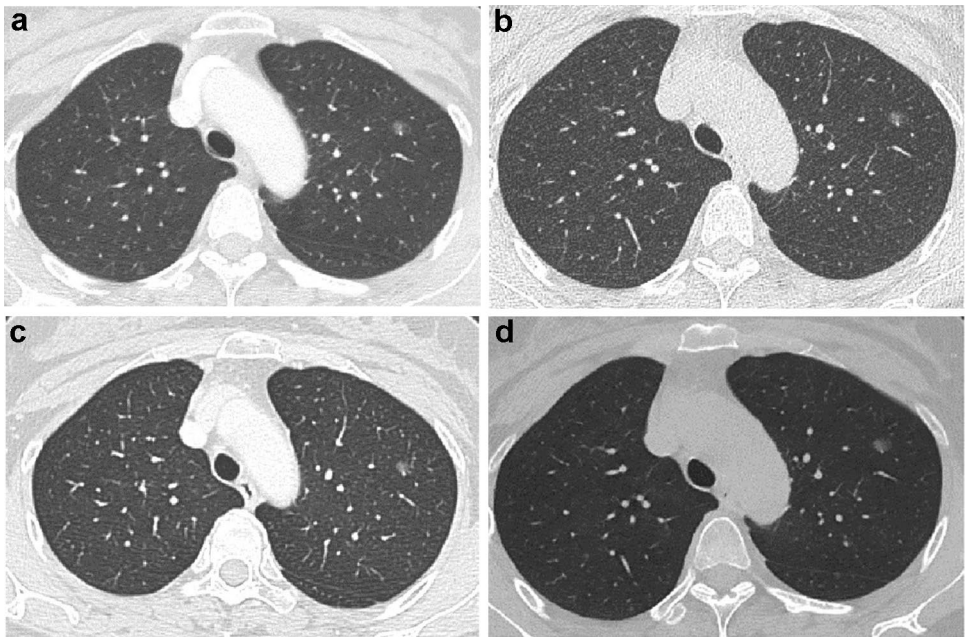

Fig. 4 **a** A 50-aged female patient was first examined a pure ground-glass opacity in June, 2016. **b** Continuous CT chest scans were conducted in Sept, 2017. **c** Next continuous CT chest scans were conducted in July, 2018. **d** Latest continuous CT chest scans were conducted in Mar, 2019

MPMNs presented as pure ground-glass opacity (36/43, 83.7%), some MPMNs could still simulate malignant nodules (Figs. 2, 3). Considering little was known about the mechanism of MPMN, there was no means to identify benign meningothelial-like lesions which can be ignored rather than resected by CT scan. It was still difficult to differentiate MPMNs from malignant nodules based on CT appearance.

In fact, most patients with MPMN underwent surgery because of other malignant nodule on chest CT scan (52/59, 88.1%) instead of MPMN itself; that means the resection of MPMNs were additional. Those malignant nodules on chest CT scan were confirmed as lung cancer pathologically, which explained the majority of patients' main diagnosis was malignant cancer (43/59, 72.9%). Long-term CT-scan follow-up for two patients revealed persistent ground-glass opacity, and no change of size on chest CT scan. Finally, two patients underwent resection of MPMNs (Figs. 4, 5). Moreover, five patients underwent resections in consequence of malignant finding of MPMN.

That arouse a requirement about the management of MPMN or suspected MPMN. Surgical decision partly based on continuous monitoring of nodules. For those 29 patients with visible MPMNs on chest CT scan, nearly 50% patients had a pre-operative follow-up more than 6 months (13/29, 44.8%). Part of other benign lesions presented as ground-glass opacity such as inflammatory lesion, which may disappear on chest CT scan over time. Therefore, to avoid unnecessary pulmonary resections, CT surveillance would be helpful for the management of MPMN. Considering the fact that smaller GGN which was radiologically stable for more than 5 years still had possibility of growth (Lee et al. 2019), the management of MPMN may include long-term CT surveillance. Furthermore, finding a means of CT imaging to differentiate MPMN from other kind of nodule would play a big role in establishing the standard management of MPMN.

This study has several limitations. Due to the occasionality of some MPMNs, some patients may miss diagnosis. Furthermore, we selected patients underwent pulmonary surgery, so patients with MPMN choose CT follow-up instead of surgical treatment were not included.

In summary, most minute pulmonary meningothelial-like nodules tend to present as ground-glass opacity, especially pure ground-glass opacity. Continuous CT monitoring revealed no radiologic change over time. Continuous CT monitoring was necessary part of management of MPMN.

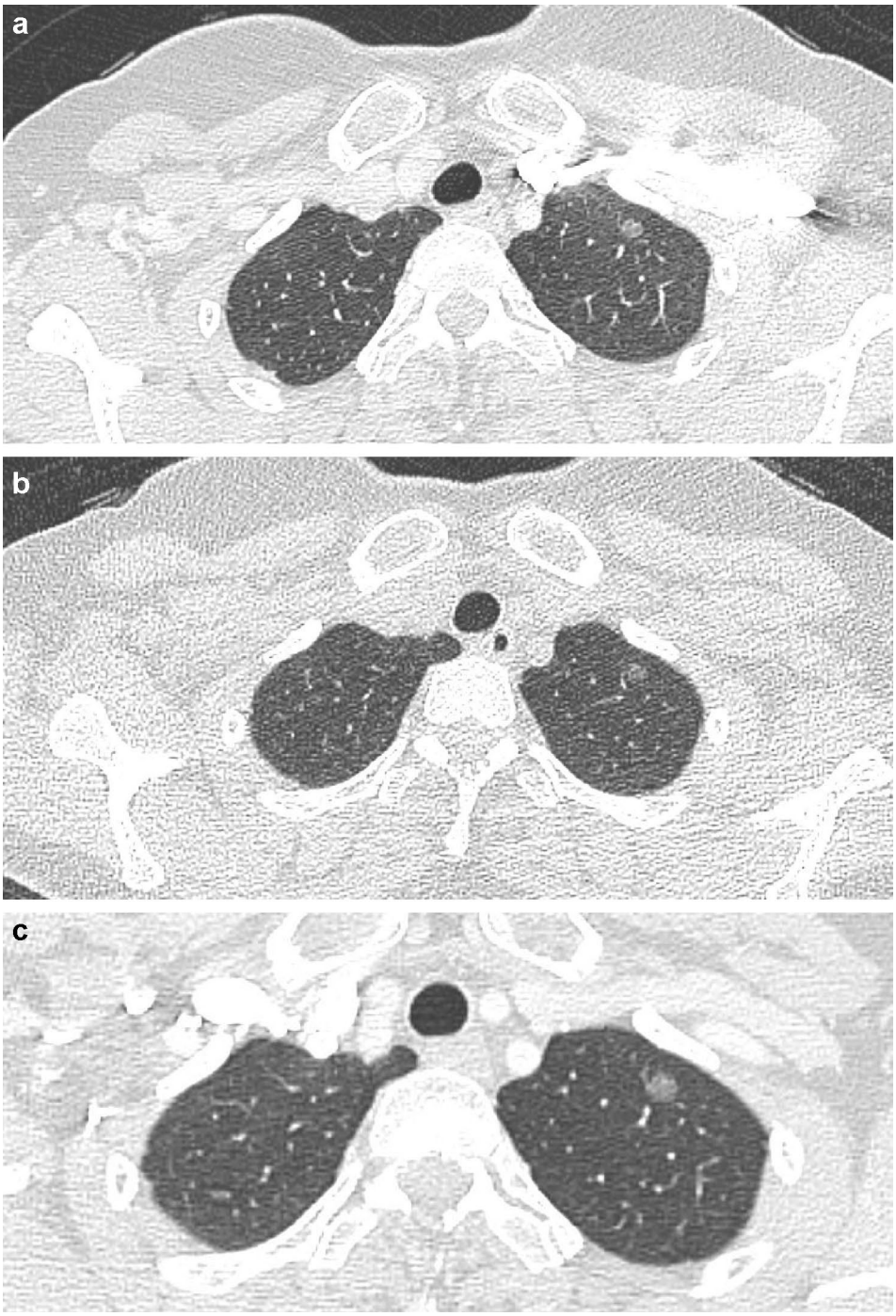

Fig. 5 **a** A 47-aged female patient was first examined a pure ground-glass opacity in Oct, 2014. **b** Continuous CT chest scans were conducted in Jan, 2015. **c** Latest continuous CT chest scans were conducted in June, 2018

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval The research was approved by the Committee for Ethical Review of Research (Fudan University Shanghai Cancer Center IRB# 090977-1). Informed consent was waived because of the retrospective nature of this research.

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