

Epidemiology, prognosis, presentation, and management of Diffuse pulmonary meningotheiomatosis

Diffuse pulmonary meningotheiomatosis primarily affects middle-aged to elderly women, presenting with mild or no symptoms, following a stable course without progression, and typically managed conservatively.

Abstract

Diffuse pulmonary meningotheiomatosis occurs almost exclusively in middle-aged to elderly women (most patients in their 50s to 70s) and is noted for its indolent clinical course. The papers describe computed tomography findings of multiple bilateral small nodules—often ground-glass, micronodular, or miliary in configuration and typically less than 5–8 mm in size. Patients may be asymptomatic or report mild respiratory symptoms such as cough, dyspnea, or chest discomfort. Histopathological confirmation, frequently obtained via video-assisted thoracoscopic, transbronchial, or cryobiopsy, reveals bland epithelioid or spindle cells arranged in whorled patterns, with immunohistochemical positivity for markers such as epithelial membrane antigen, vimentin, and, in isolated cases, pan-tropomyosin receptor kinase.

Follow-up over periods ranging from 6 months to over 2 years consistently shows stable disease without evidence of progression or malignant transformation. Conservative management predominates, with surgical intervention performed primarily to secure a diagnosis.

Paper search

Using your research question "Epidemiology, prognosis, presentation, and management of Diffuse pulmonary meningotheiomatosis", we searched across over 126 million academic papers from the Semantic Scholar corpus. We retrieved the 498 papers most relevant to the query.

Screening

We screened in sources that met these criteria:

- **Human Subjects:** Does the study report on human subjects (not animals or in vitro research)?
- **Disease Confirmation:** Is there pathologically confirmed diagnosis of diffuse pulmonary meningotheiomatosis?
- **Study Type:** Is the study one of the following: case report, case series, cohort study, cross-sectional study, systematic review, or meta-analysis?
- **Clinical Content:** Does the study describe at least one of the following: clinical presentation/symptoms, diagnostic methods/findings, disease progression/outcomes, or treatment approaches/effectiveness?
- **Patient Data:** Does the study report essential patient demographics and clinical characteristics?
- **Information Depth:** Does the study provide substantial clinical information beyond just an incidental mention of the condition?
- **Disease Focus:** Does the study include pulmonary involvement (not solely focused on other types of meningotheelial proliferation)?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Data extraction

We asked a large language model to extract each data column below from each paper. We gave the model the extraction instructions shown below for each column.

- **Patient Demographics:**

Extract the following patient characteristics:

- Number of patients in the study
- Gender distribution (number of males/females)
- Age range or mean age
- Smoking history (if reported)
- Occupational exposure history (if reported)

If information is incomplete or partially missing, note "NR" (Not Reported) for that specific characteristic. If multiple studies are reported in the same paper, extract data for each patient group separately.

- **Clinical Presentation and Symptoms:**

List all reported clinical symptoms, specifically:

- Respiratory symptoms (cough, dyspnea, shortness of breath)
- Duration of symptoms
- Other systemic symptoms

Prioritize symptoms explicitly mentioned in the text. If no symptoms are reported, write "Asymptomatic" or "No specific symptoms noted".

- **Diagnostic Methods:**

Extract:

- Imaging techniques used (CT, X-ray, etc.)
- Biopsy type (transbronchial, open lung, CT-guided fine needle)
- Specific imaging findings (nodule characteristics, distribution)

If multiple diagnostic methods were used, list all in order of occurrence. Note the specific characteristics of pulmonary nodules (size, distribution, appearance).

- **Pathological and Immunohistochemical Findings:**

Document:

- Histological cell characteristics
- Immunohistochemical stain results (e.g., EMA, progesterone receptor, pan-TRK)
- Presence of any cellular atypia
- Additional molecular/genetic testing results

If multiple stains or findings are reported, list all with their specific results.

- **Disease Progression and Follow-up:**

Extract:

- Duration of follow-up

- Changes in lung lesions over time
- Any interventions or treatments
- Long-term patient outcomes

If follow-up information is limited, clearly state the duration and any observed changes. If no follow-up was reported, write "No follow-up data available".

Results

Characteristics of Included Studies

Study	Study Design	Population Size	Study Focus	Key Findings	Full text retrieved
Ding et al., 2019	Case report and literature review	11	Clinical features, diagnosis, differential diagnosis	Diffuse pulmonary meningothe-liomatosis is rare, female-predominant, presents as diffuse small nodules, biopsy required for diagnosis, stable on follow-up	No
Nadrous et al., 2023	Retrospective case series	11	Long-term follow-up of biopsy-confirmed diffuse pulmonary meningothe-liomatosis	All female, median age 58, 46% prior cancer, 80% stable disease, possible hormone replacement therapy link	No
Gleason et al., 2017	Literature review	25	Demographics, presentation, imaging, histology	92% female, median age 59.5, 60% asymptomatic, 44% with malignancy, diagnosis by biopsy	No

Study	Study Design	Population Size	Study Focus	Key Findings	Full text retrieved
Alkurashi et al., 2020	Case report	1	Clinical and radiological presentation	55-year-old female, dry cough and chest discomfort, ground-glass nodules, stable at 1 year	No
Trieu et al., 2020	Case report	1	Diagnosis by transbronchial cryobiopsy	67-year-old female, non-smoking, asymptomatic, diffuse nodules, stable at 1 year	No
Suster and Moran, 2007	Case series	5	Clinical, radiological, pathological features	4 females and 1 male, 54–75 years, dyspnea/shortness of breath, ground-glass nodules, no significant change at 1 year	Yes
Virk et al., 2023	Case report	1	Diffuse pulmonary meningothe-liomatosis in malignancy/immunosuppression	61-year-old female, asymptomatic, diffuse nodules, stable at 1 year	No
Karakas et al., 2023	Case report	1	Diffuse pulmonary meningothe-liomatosis with pan-tropomyosin receptor kinase (pan-TRK) expression	59-year-old female, chronic cough, pan-TRK positive, no progression	Yes
Forsythe et al., 2022	Case report	1	Clinical, radiological, pathological features	57-year-old female, chronic cough, ground-glass nodules, no follow-up data	No

Study	Study Design	Population Size	Study Focus	Key Findings	Full text retrieved
Healy et al., 2023	Case report	1	Diffuse pulmonary meningothe-liomatosis as rare cause of nodules	Female in her 50s, ex-smoker, recurrent infections, minute nodules, no follow-up data	No
Li et al., 2023	Case series	167 minute pulmonary meningotheelial-like nodules, 13 diffuse pulmonary meningothe-liomatosis	Comparative analysis	Diffuse pulmonary meningothe-liomatosis: all female, mean age 51.4, higher lung function, stable at 1 year	Yes
Jesus et al., 2023	Case report	1	Diffuse pulmonary meningothe-liomatosis in prior lung adenocarcinoma	81-year-old female, asymptomatic, ground-glass micronodules, stable at 2 years	Yes
Audisho et al., 2018	Case report	1	Minute pulmonary meningotheelial-like nodules with congestive heart failure	55-year-old female, cough and chest pain, congestive heart failure, ground-glass nodules, managed for heart failure	No
Morresi-Hauf et al., 2015	Case reports	2	Diffuse pulmonary meningothe-liomatosis with histology/immunohistochemistry, no follow-up	60- and 73-year-old females, one non-smoker, miliary nodules, histology/immunohistochemistry, no follow-up	Yes
Niemierko et al., 2024	Case report and review	Not reported in abstract	Radiological/pathological features	52-year-old female example, dyspnea, random small nodules, no follow-up	No

Study	Study Design	Population Size	Study Focus	Key Findings	Full text retrieved
Dzian et al., 2021	Case report	1	Diffuse pulmonary meningothe-liomatosis by video-assisted thoracoscopic surgery biopsy	60-year-old male, asymptomatic, bilateral nodules, no follow-up	No
Yun et al., 2020	Case report and review	1	Diffuse pulmonary meningothe-liomatosis with imaging review	80-year-old female, no symptoms mentioned, ground-glass nodules, no follow-up	No
Oh et al., 2024	Case report	1	Diffuse pulmonary meningothe-liomatosis with short-term follow-up	57-year-old female, chest discomfort and dyspnea, centrilobular nodules, stable at 6 months	No
Huang et al., 2015	Case report	1	Cytological diagnosis	57-year-old female, no symptoms mentioned, minute nodules, no follow-up	No
Fernández Sarabia et al., 2010	Case report	1	Diffuse pulmonary meningothe-liomatosis as micronodular pattern	60s–70s, gender not reported, micronodular pattern, no follow-up	No
Jayaschandran et al., 2017	Case report	1	Diffuse pulmonary meningothe-liomatosis as miliary pattern	74-year-old female, asymptomatic, small nodules, stable for more than 2 years	Yes

Study	Study Design	Population Size	Study Focus	Key Findings	Full text retrieved
Sakano et al., 2025	Case report	1	Diffuse pulmonary meningotheliomatosis mimicking metastases	64-year-old male, no symptoms mentioned, ground-glass nodules, no follow-up	No
Mizutani et al., 2020	Case report	1	Diffuse pulmonary meningotheliomatosis with immunohistochemistry	57-year-old female, no symptoms mentioned, tiny nodules, no follow-up	No
Noguchi-Konaka et al., 2022	Case report	1	Diffuse pulmonary meningotheliomatosis in breast cancer	77-year-old female, no symptoms mentioned, granular shadows, no follow-up	No
Rajadurai et al., 2019	Case report	1	Pulmonary meningioma metastases	Not reported, not reported, multiple metastases 13 years post-resection, no outcome data	No

Summary of Study Characteristics:

- Design: 21 case reports, 2 case series, 1 retrospective case series, and 2 literature reviews (some studies combined designs).
- Population: Most studies (20) reported on single cases; 1 study included 2 cases, 1 included 5 cases, 2 included 11 cases, 1 included 13 cases, and 1 included 25 cases.
- Gender: All-female populations in 10 studies; 12 additional studies reported only female cases. Three studies included male cases (totaling 3 males).
- Age: Mean or median age reported in 5 studies (range: 51.4 to 75 years); individual ages provided in 15 studies. We didn't find mention of age in 5 studies.
- Symptoms: 11 studies described asymptomatic cases; 8 studies described symptomatic cases (most commonly cough, dyspnea, or chest discomfort). In 6 studies, we didn't find clear mention of symptom status.
- Malignancy: 4 studies reported an association with prior malignancy or cancer; in the remaining 21 studies, we didn't find mention of malignancy.
- Imaging: Ground-glass nodules described in 7 studies; micronodules, minute, small, tiny, miliary, or granu-

lar nodules in 9 studies; diffuse or bilateral nodules in 3 studies; centrilobular nodules in 1 study; multiple metastases in 1 study.

- Diagnosis:Biopsy explicitly reported as the diagnostic method in 4 studies; immunohistochemistry in 2 studies; cytology in 1 study; in 18 studies, we didn't find mention of the diagnostic method.
 - Outcomes:11 studies reported stable disease at follow-up (6 months to more than 2 years); in 12 studies, we didn't find follow-up or outcome data. No studies reported disease progression. One study reported management of comorbid congestive heart failure.
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Thematic Analysis

Epidemiology and Demographics

Study	Age Distribution	Gender Ratio	Associated Conditions
Ding et al., 2019	51–75 years, mean 64±8	1 male:10 female	1 with thromboembolism, 8 with no lung disease
Nadrous et al., 2023	Median 58 (interquartile range 52.3–63.8)	0 male:11 female	46% prior cancer, 36% former smokers, 27% on hormone replacement therapy
Gleason et al., 2017	37–73 years, median 59.5	2 male:23 female	44% with malignancy
Alkurashi et al., 2020	55	0 male:1 female	Hypertension, hypothyroid, gastroesophageal reflux, impaired glucose
Trieu et al., 2020	67	0 male:1 female	Scleroderma
Suster and Moran, 2007	54–75	1 male:4 female	3 with prior malignancy
Virk et al., 2023	61	0 male:1 female	Breast ductal hyperplasia, thyroid cancer, common variable immunodeficiency
Karakas et al., 2023	59	0 male:1 female	Nonsmoker
Forsythe et al., 2022	57	0 male:1 female	No mention found
Healy et al., 2023	50s	0 male:1 female	Ex-smoker, livestock exposure
Li et al., 2023	Diffuse pulmonary meningotheiomatosis: mean 51.4; minute pulmonary meningotheial-like nodules: mean 57.9	Diffuse pulmonary meningotheiomatosis: 0 male:13 female; minute pulmonary meningotheial-like nodules: 35 male:132 female	Diffuse pulmonary meningotheiomatosis: higher lung function
Jesus et al., 2023	81	0 male:1 female	Prior lung adenocarcinoma

Study	Age Distribution	Gender Ratio	Associated Conditions
Audisho et al., 2018	55	0 male:1 female	Congestive heart failure, diabetes, hypertension, tobacco use
Morresi-Hauf et al., 2015	60, 73	0 male:2 female	Type 2 diabetes, hypertension, reflux
Niemierko et al., 2024	52 (example)	No mention found	No mention found
Dzian et al., 2021	60	1 male:0 female	No mention found
Yun et al., 2020	80	0 male:1 female	No mention found
Oh et al., 2024	57	0 male:1 female	No mention found
Huang et al., 2015	57	0 male:1 female	Nonsmoker
Fernández Sarabia et al., 2010	60s–70s	No mention found	Breast, rectal cancer
Jayaschandran et al., 2017	74	0 male:1 female	Nonsmoker
Sakano et al., 2025	64	1 male:0 female	Prostate cancer
Mizutani et al., 2020	57	0 male:1 female	No mention found
Noguchi-Konaka et al., 2022	77	0 male:1 female	Breast cancer
Rajadurai et al., 2019	No mention found	No mention found	Intracranial meningioma

Key Findings:

- Age Distribution:
 - Age information was available for 24 of 25 studies.
 - Most common age group: 50s (12 studies)
 - Next most common: 60s (7 studies), 70s (6 studies), 80s (2 studies)
 - Mean or median age reported in 6 studies
- Gender Ratio:
 - Only female participants in 17 studies
 - Only male participants in 2 studies
 - Mixed gender ratio (with strong female predominance) in 4 studies
 - No mention of gender in 3 studies
- Associated Conditions:
 - Prior malignancy or cancer in 9 studies
 - Smoking status (former/ex-smoker, nonsmoker, or tobacco use) in 6 studies
 - Hormone replacement therapy in 1 study
 - Autoimmune or connective tissue disease in 1 study
 - Cardiovascular or metabolic comorbidities (hypertension, diabetes, congestive heart failure, impaired glucose) in 6 studies
 - Other conditions (hypothyroid, gastroesophageal reflux, immune deficiency, livestock exposure, breast ductal hyperplasia, common variable immunodeficiency) in 6 studies
 - No mention of associated conditions in 6 studies

- Non-obvious insight: There is a striking female predominance across nearly all studies, with only rare male cases reported.
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Clinical and Radiological Features

Study	Symptoms	Radiological Findings	Diagnostic Features
Ding et al., 2019	Cough, dyspnea, fatigue, duration over 3 years	Diffuse, bilateral, small solid or ground-glass nodules, less than 5 mm, some cavitated	Computed tomography, biopsy (video-assisted thoracoscopic surgery, open, transbronchial, fine needle aspiration)
Nadrous et al., 2023	Cough, dyspnea, chest discomfort, some incidental	Innumerable small (less than 5 mm) bilateral ground-glass nodules, "cheerio sign"	Computed tomography, biopsy, immunohistochemistry
Gleason et al., 2017	60% asymptomatic, 32% unexplained respiratory symptoms	Diffuse bilateral nodules on high-resolution computed tomography	Surgical or transbronchial biopsy
Alkurashi et al., 2020	Dry cough, chest discomfort, 4 months	Innumerable diffuse small ground-glass nodules	High-resolution computed tomography, video-assisted thoracoscopic surgery biopsy
Trieu et al., 2020	Asymptomatic	Diffuse bilateral nodules, mosaicism	Computed tomography, transbronchial cryobiopsy
Suster and Moran, 2007	Dyspnea, shortness of breath, cough, chest tightness	Ground-glass nodules, 2–8 mm, subpleural	X-ray, computed tomography, open or video-assisted thoracoscopic surgery biopsy
Virk et al., 2023	Asymptomatic	Sub 6 mm bilateral centrilobular ground-glass nodules, solid nodules	Computed tomography, transbronchial cryobiopsy
Karakas et al., 2023	Chronic cough, fatigue, night sweats	Multiple subcentimeter bilateral nodules, up to 5 mm	Computed tomography, transbronchial biopsy, pan-tropomyosin receptor kinase positive
Forsythe et al., 2022	Chronic cough	Bilateral multiple ground-glass nodules	Computed tomography, wedge resection
Healy et al., 2023	Recurrent infections	Multiple bilateral minute nodules	X-ray, computed tomography, video-assisted thoracoscopic surgery biopsy

Study	Symptoms	Radiological Findings	Diagnostic Features
Li et al., 2023	Cough, shortness of breath, chest tightness	Diffuse pulmonary meningotheiomatosis: diffuse ground-glass nodules, 2–8 mm, 40–600+ per lung	High-resolution computed tomography, video-assisted thoracoscopic surgery biopsy
Jesus et al., 2023	Asymptomatic	Multiple bilateral micronodules, 2–5 mm, basal	Computed tomography, positron emission tomography, video-assisted thoracoscopic surgery biopsy
Audisho et al., 2018	Productive cough, chest pain, months	Innumerable bilateral small nodules, less than 0.1–0.7 cm	Computed tomography, video-assisted thoracoscopic surgery excision
Morresi-Hauf et al., 2015	No symptoms (1), mild limitation (1)	Multiple diffuse miliary nodules, peripheral	Computed tomography, video-assisted thoracoscopic surgery, cryobiopsy
Niemierko et al., 2024	Dyspnea (example)	Numerous small (less than 6 mm) ground-glass or solid nodules, random, "cheerio sign"	Computed tomography, surgical or transbronchial biopsy
Dzian et al., 2021	Asymptomatic	Multiple bilateral nodules	High-resolution computed tomography, video-assisted thoracoscopic surgery biopsy
Yun et al., 2020	No symptoms mentioned	Randomly distributed ground-glass nodules	Imaging, surgical biopsy
Oh et al., 2024	Chest discomfort, exertional dyspnea	Multifocal centrilobular ground-glass nodules	Computed tomography, thoracoscopic wedge resection
Huang et al., 2015	No symptoms mentioned	Multiple minute nodules	Computed tomography, fine needle aspiration, wedge resection
Fernández Sarabia et al., 2010	Asymptomatic	Micronodular pattern, both lungs	Computed tomography, biopsy
Jayaschandran et al., 2017	Asymptomatic	Small solid or ground-glass nodules, less than or equal to 5 mm, centrilobular, some cavitated	Computed tomography, transbronchial biopsy
Sakano et al., 2025	No symptoms mentioned	Multiple ground-glass nodules, bilateral	Imaging, surgical biopsy

Study	Symptoms	Radiological Findings	Diagnostic Features
Mizutani et al., 2020	No symptoms mentioned	Multiple tiny bilateral nodules	Computed tomography, video-assisted thoracoscopic surgery biopsy
Noguchi-Konaka et al., 2022	No symptoms mentioned	Multiple granular shadows, bilateral	Computed tomography, positron emission tomography, transbronchial or thoracoscopic biopsy
Rajadurai et al., 2019	No symptoms mentioned	Multiple metastases	Computed tomography, core biopsy

Symptoms:

- 8 of 25 studies described patients as asymptomatic.
- Cough was reported in 8 studies.
- Dyspnea or shortness of breath in 6 studies.
- Chest discomfort, pain, or tightness in 6 studies.
- Fatigue in 2 studies.
- Other symptoms (night sweats, recurrent infections, mild limitation) in 3 studies.
- In 6 studies, we didn't find mention of symptom status.

Radiological Findings:

- Ground-glass nodules described in 14 studies.
- Solid nodules in 4 studies.
- Cavitated nodules in 2 studies.
- Nodule size specified as less than 5 mm in 5 studies, 2–8 mm in 2 studies, less than 6 mm in 2 studies, and 2–5 mm in 1 study.
- Bilateral distribution in 19 studies.
- Diffuse distribution in 7 studies.
- Centrilobular distribution in 3 studies.
- Subpleural, basal, peripheral, and random distributions each described in 1–2 studies.
- Special radiological signs: "cheerio sign" (2 studies), mosaicism (1), miliary pattern (1), micronodular pattern (2), granular shadows (1), metastases (1).
- All studies provided at least some radiological description, which is notable given the rarity of the condition.

Diagnostic Approach and Management

Diagnostic Methods:

- High-resolution computed tomography was used to identify characteristic diffuse, small, bilateral nodules.
- Histopathological confirmation was obtained by:
 - Video-assisted thoracoscopic surgery biopsy

- Open lung biopsy
- Transbronchial biopsy (including cryobiopsy)
- Computed tomography-guided fine needle aspiration (rarely)
- Histology: Bland epithelioid or spindle cells, often in whorled patterns.
- Immunohistochemistry: Positivity for epithelial membrane antigen, vimentin, and progesterone receptor.
- Pan-tropomyosin receptor kinase positivity was reported as a novel finding in one recent case.
- Molecular testing was rarely performed.

Management:

- In the included studies, management was conservative in nearly all cases, with no specific therapy indicated.
 - Discontinuation of hormone therapy led to symptomatic improvement in rare cases.
 - Surgical intervention was used for diagnostic purposes only.
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Disease Course and Prognosis

Key Findings:

- In the included studies, follow-up data, where available, indicated that diffuse pulmonary meningotheiomatosis was generally indolent.
- Most patients showed stable disease over periods ranging from 6 months to more than 2 years.
- Rare cases demonstrated slow progression or development of new nodules, but no cases of malignant transformation were reported.
- Prognosis was favorable, and long-term outcomes were excellent with conservative management.
- In patients with comorbid malignancy, diffuse pulmonary meningotheiomatosis was sometimes mistaken for metastatic disease, but did not appear to impact cancer outcomes in the included studies.

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