

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

Diffuse pulmonary meningotheliomatosis 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 meningotheliomatosis 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 meningotheliomatosis", 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 meningotheliomatosis?
- **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 meningothelial 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 meningotheliomatosis 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 meningotheliomatosis | 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 meningotheliomatosis in malignancy/immunosuppression | 61-year-old female, asymptomatic, diffuse nodules, stable at 1 year | No |
| Karakas et al., 2023 | Case report | 1 | Diffuse pulmonary meningotheliomatosis 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 meningotheliomatosis 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 meningothelial-like nodules, 13 diffuse pulmonary meningotheliomatosis | Comparative analysis | Diffuse pulmonary meningotheliomatosis: all female, mean age 51.4, higher lung function, stable at 1 year | Yes |
| Jesus et al., 2023 | Case report | 1 | Diffuse pulmonary meningotheliomatosis 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 meningothelial-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 meningotheliomatosis with histology/immunohistochemistry | 60- and 73-year-old females, one non-smoker, miliary nodules, chemotherapy, 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 meningotheliomatosis 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 meningotheliomatosis 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 meningotheliomatosis 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 meningotheliomatosis as micronodular pattern | 60s–70s, gender not reported, micronodular pattern, no follow-up | No |
| Jayaschandran et al., 2017 | Case report | 1 | Diffuse pulmonary meningotheliomatosis 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.

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 meningotheliomatosis: mean 51.4; minute pulmonary meningothelial-like nodules: mean 57.9 | Diffuse pulmonary meningotheliomatosis: 0 male:13 female; minute pulmonary meningothelial-like nodules: 35 male:132 female | Diffuse pulmonary meningotheliomatosis: 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.

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.

Disease Course and Prognosis

Key Findings:

- In the included studies, follow-up data, where available, indicated that diffuse pulmonary meningotheliomatosis 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 meningotheliomatosis was sometimes mistaken for metastatic disease, but did not appear to impact cancer outcomes in the included studies.

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