THE GREAT MIMICKER

A RARE CASE OF DIFFUSE PLEURAL MESOTHELIOMA

ATTENDING:

Erik Sylvin, MD

Board Certified General and Thoracic Surgeon

- Medical Degree: Drexel University College of Medicine, 2006
- Residency: General Surgery, NY Presbyterian Hospital / Columbia University, 2012
- Fellowship: Cardiothoracic Surgery, University of Pennsylvania, 2015
- Specialized Training: Robotic Thoracic Surgery, Lenox Hill Hospital and Research (Montefiore Medical Center)

PRESENTER:

Ashli Alexander, MD

Chief General Surgery Resident

- Medical Degree: University of the West Indies, Jamaica, 2018
- Currently Training Residency: University of Miami (Graduating 2027)
- MIS Fellowship: UC Davis (Start 2027)

UHealth
UNIVERSITY OF MIAMI HEALTH SYSTEM

MESOTHELIOMA: HISTORY & RISK FACTORS

A Global Disease Shaped by Asbestos

WHAT IS DIFFUSE PLEURAL MESOTHELIOMA?

- Uncommon, aggressive malignancy of the pleura
- Accounts for ~1–2% of thoracic malignancies
- Poor prognosis; median survival 12–18 months
- Strongly linked to asbestos exposure

HISTORY OF MESOTHELIOMA

1960
Wagner et al. described the link between diffuse pleural mesothelioma and crocidolite (blue asbestos) exposure in South Africa.

1940s–1970s
Widespread industrial and commercial use of asbestos worldwide.

1980s
Regulatory action begins: Australia (1983), UK (1985) ban or restrict asbestos use.

2000s–Present
Many countries have banned asbestos, but mesothelioma remains due to long latency.

Latency period: typically **30–50 years** between exposure and diagnosis.

GLOBAL INCIDENCE

UNITED STATES
2,500 – 3,000
new cases per year
(CDC, 2022)

WORLDWIDE
30,000 – 40,000
new cases per year
(GLOBOCAN 2022)

COUNTRIES WITH HIGHEST INCIDENCE

Age-Standardized Rate (per 100,000)	
Australia	2.5 – 3.5
United Kingdom	2.0 – 3.0
Netherlands	~2.0
Italy	1.5 – 2.0
Belgium	1.5 – 2.0
United States	~0.6 – 0.7

★ Incidence correlates with historical asbestos use, particularly amphibole asbestos (crocidolite, amosite).

MAJOR RISK FACTORS

- **Asbestos exposure** (dominant risk factor)
- **Occupational exposures** (shipbuilding, construction, mining, insulation, manufacturing, military)
- **High cumulative dose and long duration of exposure**
- **Smoking** (associated with worse outcomes)
- **Environmental / household exposures** (secondary exposure less common)

KEY TAKEAWAY: Asbestos is the dominant preventable risk factor for diffuse pleural mesothelioma, with disease often emerging **decades after exposure**.

UHealth
UNIVERSITY OF MIAMI HEALTH SYSTEM

EXPOSURE ——— 30–50 YEARS ——→ DIAGNOSIS

Asbestos exposure
(occupational / environmental)

LONG LATENCY PERIOD

Mesothelioma typically develops decades after exposure—often 30 to 50 years later.

Mesothelioma diagnosis
(e.g., diffuse pleural mesothelioma)

MESOTHELIOMA: HISTORY & RISK FACTORS

A Global Disease Shaped by Asbestos

WHAT IS DIFFUSE PLEURAL MESOTHELIOMA?

- Uncommon, aggressive malignancy of the pleura
- Accounts for ~1–2% of thoracic malignancies
- Poor prognosis; median survival 12–18 months
- Strongly linked to asbestos exposure

HISTORY OF MESOTHELIOMA

1960
Wagner et al. described the link between diffuse pleural mesothelioma and crocidolite (blue asbestos) exposure in South Africa.

1940s–1970s
Widespread industrial and commercial use of asbestos worldwide.

1980s
Regulatory action begins: Australia (1983), UK (1985) ban or restrict asbestos use.

2000s–Present
Many countries have banned asbestos, but mesothelioma remains due to long latency.

Latency period: typically **30–50 years** between exposure and diagnosis.

GLOBAL INCIDENCE

UNITED STATES
2,500 – 3,000
new cases per year
(CDC, 2022)

WORLDWIDE
30,000 – 40,000
new cases per year
(GLOBOCAN 2022)

COUNTRIES WITH HIGHEST INCIDENCE

Age-Standardized Rate (per 100,000)	
Australia	2.5 – 3.5
United Kingdom	2.0 – 3.0
Netherlands	~2.0
Italy	1.5 – 2.0
Belgium	1.5 – 2.0
United States	~0.6 – 0.7

★ Incidence correlates with historical asbestos use, particularly amphibole asbestos (crocidolite, amosite).

MAJOR RISK FACTORS

- **Asbestos exposure** (dominant risk factor)
- **Occupational exposures** (shipbuilding, construction, mining, insulation, manufacturing, military)
- **High cumulative dose and long duration of exposure**
- **Smoking** (associated with worse outcomes)
- **Environmental / household exposures** (secondary exposure less common)

KEY TAKEAWAY: Asbestos is the dominant preventable risk factor for diffuse pleural mesothelioma, with disease often emerging **decades after exposure**.

UHealth
UNIVERSITY OF MIAMI HEALTH SYSTEM

Why this case matters

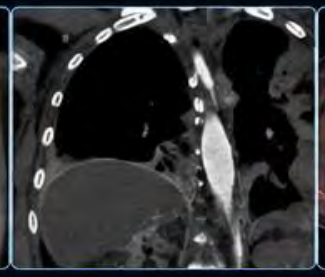
> "How many diagnoses would you consider before malignant mesothelioma in a patient with recurrent pleural effusions?"

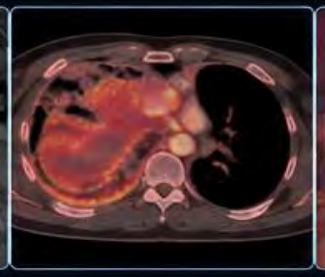
LEARNING OBJECTIVES

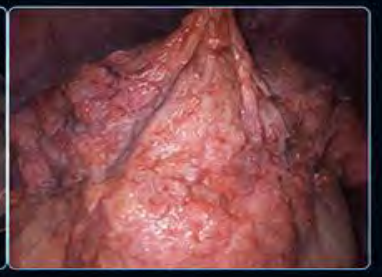
- Recognize atypical presentations of pleural mesothelioma.
- Review diagnostic workup.
- Discuss operative biopsy strategy.
- Review current staging.
- Discuss when surgery is appropriate.

CENTRAL MESSAGE

Mesothelioma rarely presents as a straightforward diagnosis. This case demonstrates how multiple factors can obscure the underlying disease and delay the path to diagnosis.







CASE DESCRIPTION

71-YEAR-OLD MALE

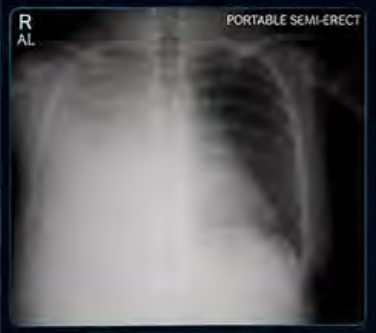
- Former smoker
- Morbidly obese (BMI 37)
- Occupational exposure: Print shop for several years
- History of anal cancer Treated with definitive chemoradiation – in remission

INITIAL PRESENTATION

Acute hypoxic respiratory failure secondary to a massive recurrent right pleural effusion

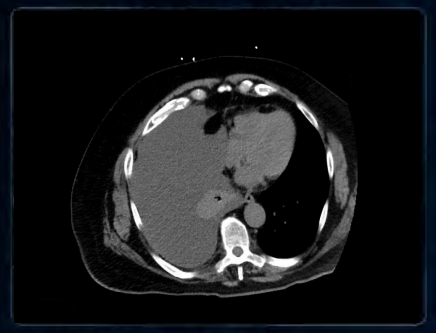
INITIAL IMAGING

1. CXR (Initial)



Complete opacification of the entire right hemithorax.

2. CT Chest (Initial)



Large right pleural effusion, significant lower lobe atelectasis, and pleural nodularity along the visceral and parietal pleura.

CLINICAL COURSE

Initial management

- Thoracentesis: ~2L of amber fluid removed
- Interval worsening liver disease, concerning for cirrhosis

Lobulated liver contour with left lobe hypertrophy and right lobe atrophy

Recurrent effusions

- Required 2 additional large volume thoracenteses
- PleurX catheter placed for recurrent effusion

Pleural fluid cytology

- Undifferentiated malignant cells suspicious for malignant mesothelioma

Discharged

- Improved after drainage
- Outpatient thoracic surgery follow-up for pleural biopsy was missed

Readmission

- Extensive subcutaneous emphysema
- Malfunctioning PleurX (side hole external to pleural space) causing persistent air leak
- Catheter removed

Complication

- Upper GI bleed
- EGD: bleeding duodenal ulcer – treated endoscopically
- Hemodynamically stable

Operative intervention

- After optimization, underwent RIGHT thoracoscopic pleural biopsy
- Two ports used to minimize risk of tumor seeding
- Multiple biopsy sites obtained
- Chest tube placed postoperatively

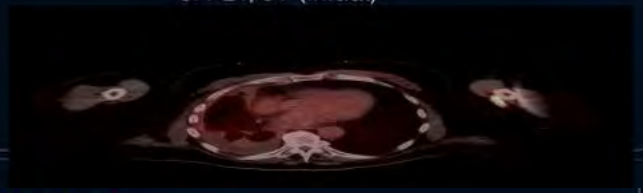
PATHOLOGY

- Epithelioid malignant diffuse pleural mesothelioma
- Calretinin+, EMA+, D2-40 (weak focal)+, WT1+
- p40–, TTF-1–

Further staging

- EBUS with mediastinal lymph node sampling – performed
- PET/CT: No convincing FDG avid malignancy; minor FDG activity in right pleural effusion/pleura (nonspecific)
- MRI Brain planned – patient declined due to psychosocial stressors

3. PET/CT (Initial)



KEY DIAGNOSTIC CHALLENGES

- ☑ Recurrent effusions with multiple potential etiologies (malignancy, liver disease, infection, heart failure)
- ☑ Cytology suspicious but not diagnostic
- ☑ Missed follow-up delayed tissue diagnosis
- ☑ Complications diverted clinical course

TEACHING POINT

Mesothelioma is a great mimicker. It often hides behind more common diagnoses and can be delayed by patient and system factors.

DIAGNOSIS

Epithelioid malignant diffuse pleural mesothelioma

PRINT SHOP EXPOSURE

AND THE QUESTION OF MESOTHELIOMA RISK

There is **no strong evidence** that print shops themselves are an established mesothelioma risk factor, unlike shipbuilding, insulation work, construction, mining, or asbestos manufacturing.

HOWEVER:

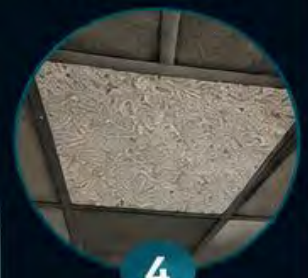
Older print shops (particularly **before the 1980s**) sometimes contained:

1 ASBESTOS-INSULATED DRYERS AND PRESSES

2 ASBESTOS BRAKE LININGS IN MACHINERY

3 PIPE INSULATION

3 BOILER INSULATION



4 BUILDING MAULATION

KEY POINT

While working in a print shop is not an established high-risk occupation, **incidental asbestos exposure** from older equipment and building materials is biologically plausible and should not be everlooked in occupational histories.

TAKEAWAY: A thorough occupational history remains essential—even in jobs not classically linked to asbestos.

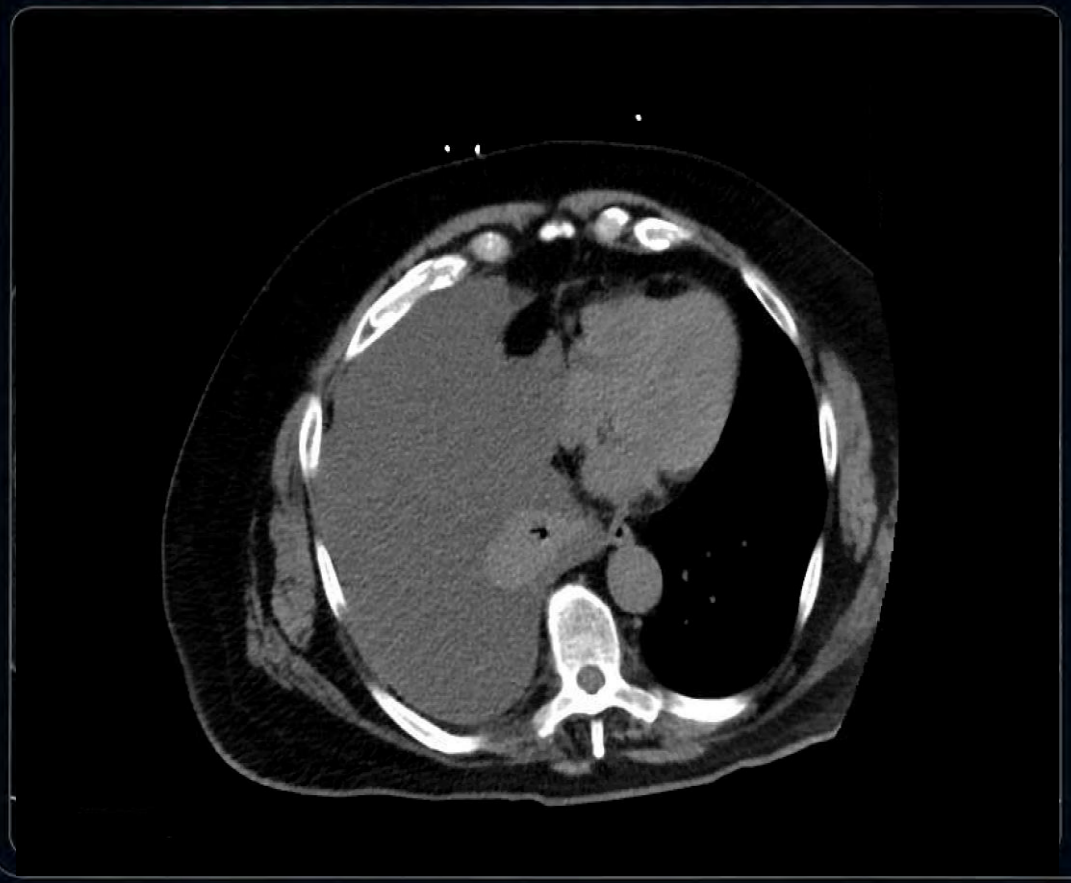
INITIAL IMAGING

THE FIRST CLUES

FIGURE A CHEST X-RAY (CXR)

FINDING: COMPLETE OPACIFICATION OF THE ENTIRE RIGHT HEMITHORAX

FIGURE B CT CHEST WITH CONTRAST



DIFFERENTIAL

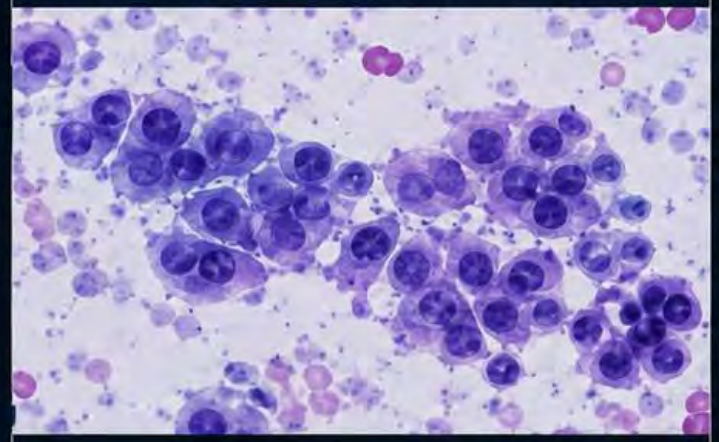
- Metastatic disease
- Empyema
- Tuberculosis
- Lymphoma
- Mesothelioma
- Pleural carcinomatosis

PLEURAL EFFUSION WITH PLEURAL NODULARITY...
WHAT IS YOUR DIFFERENTIAL?

CYTOLOGY & IHC: CONSISTENT WITH MALIGNANT MESOTHELIOMA

Integrating cytology, immunohistochemistry, and molecular findings confirms the diagnosis.

PLEURAL FLUID CYTOLOGY
(REPRESENTATIVE IMAGE)



IHC: POSITIVE FOR MALIGNANT CELLS

The cytologic and immunophenotypic features including loss of BAP1 by IHC and positive FISH analysis for CDKN2A/B (p16) deletion is consistent with a malignant mesothelioma.

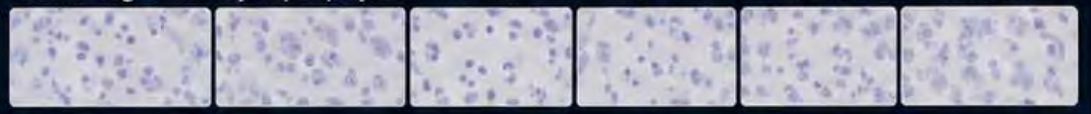
Case reviewed intradepartmentally. Clinical correlation is recommended.

IMMUNOHISTOCHEMISTRY (CELL BLOCK)

POSITIVE

LOSS OF EXPRESSION

NEGATIVE



Ki-67 PROLIFERATION INDEX: ~5–10%

MOLECULAR FINDINGS

IHC	FISH
BAP1 LOSS OF EXPRESSION	CDKN2A/B (p16) DELETION POSITIVE

NCCN INSIGHT

Patients with pleural mesothelioma with loss of BAP1 by IHC and retained p16 expression by IHC have prolonged survival in both univariate and multivariate analysis.

PATIENT PROGNOSTIC INSIGHT

Patients with mesothelioma with germline BAP1 mutation have prolonged survival.

TEACHING POINTS

- Cytology alone is insufficient to exclude mesothelioma (sensitivity ~30–60%).
- A comprehensive IHC panel is essential to establish the diagnosis.
- Loss of BAP1 by IHC and CDKN2A/B (p16) deletion by FISH support mesothelioma.
- Prognostic biomarkers (BAP1 loss with p16 retention or germline BAP1 mutation) are associated with improved survival.

KEY TAKEAWAY

The integration of cytology, IHC, and molecular findings confirms malignant mesothelioma and provides important prognostic information.

WHY WAS DIAGNOSIS DELAYED?

THE GREAT MIMICKER

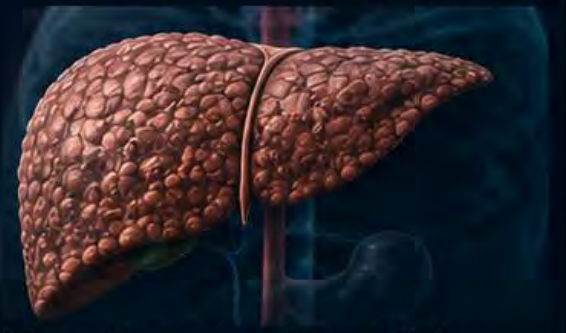
RECURRENT PLEURAL EFFUSIONS

Symptoms attributed to recurrent effusions managed with thoracentesis and PleurX.

PRIOR MALIGNANCY

History of anal cancer created diagnostic anchoring toward metastatic disease.

POSSIBLE CIRRHOSIS



Liver disease and potential hepatic hydrothorax provided a competing explanation.

MISSED FOLLOW-UP

Missed thoracic surgery appointment delayed definitive tissue diagnosis.

MULTIPLE COMPETING DIAGNOSES OBSCURED THE UNDERLYING DISEASE.

ADDITIONAL CONTRIBUTING FACTORS

- Subcutaneous emphysema from malpositioned PleurX and persistent air leak
- Upper GI bleed from duodenal ulcer requiring endoscopic treatment
- Multiple hospital re-admissions and procedural setbacks
- Patient-level factors including psychosocial stressors

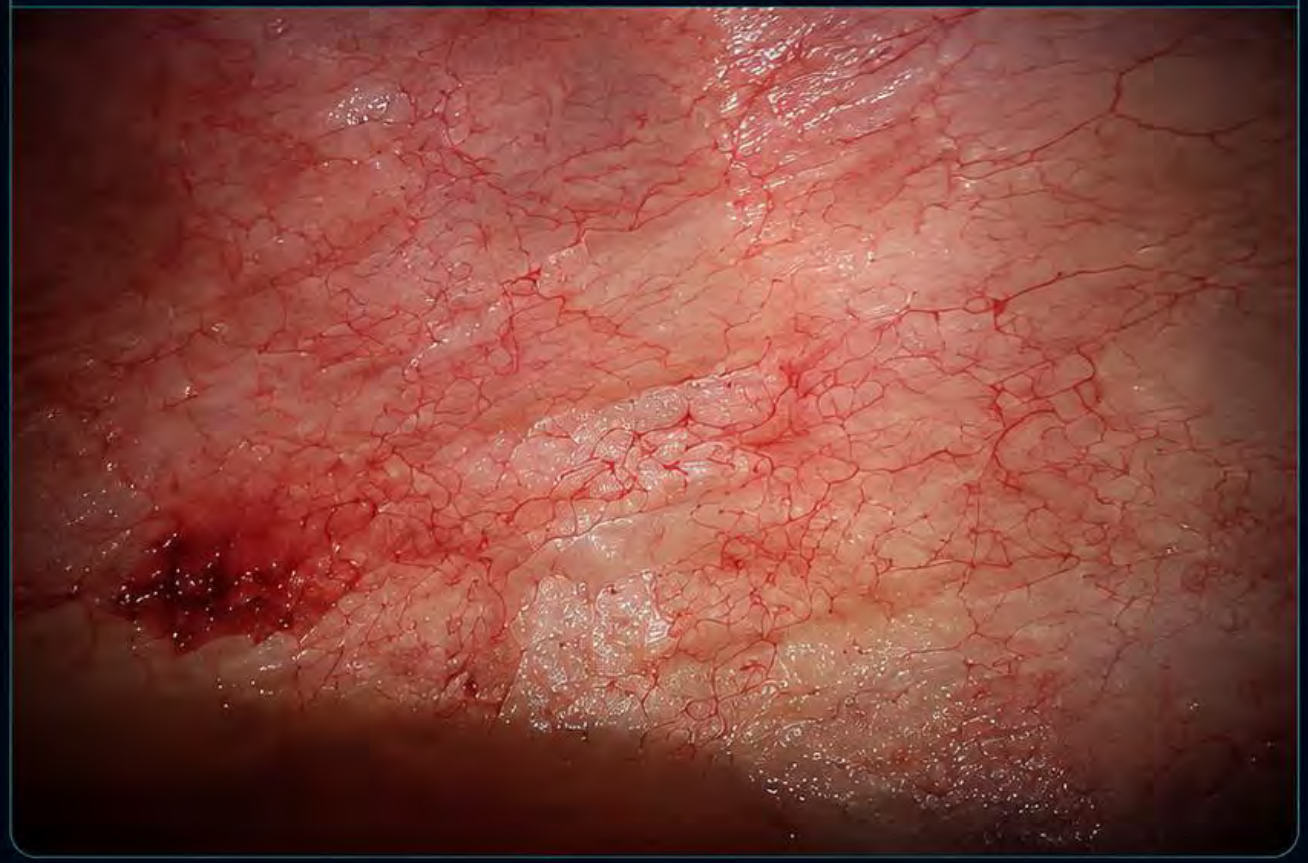
KEY TAKEAWAY

Mesothelioma was not missed because there were no clues, but because several plausible alternatives and intervening events took precedence.

OPERATIVE DECISION MAKING

THORACOSCOPY

PLEURAL PLAQUES



OPERATIVE PEARLS

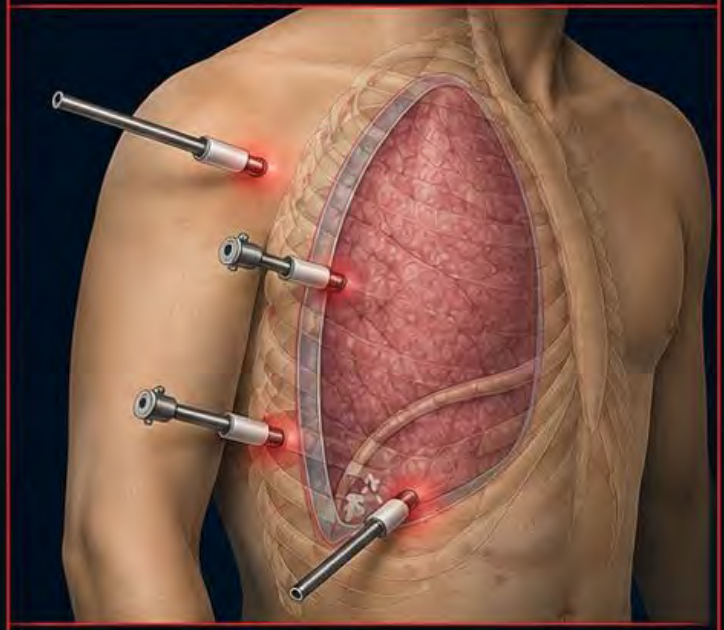
- Thoracoscopic biopsy preferred
- Multiple representative biopsies
- Avoid excessive port placement
- Avoid traversing future incision sites
- Chest tube placement away from biopsy
- Specimens for pathology + immunohistochemistry

MINIMAL TRAUMA. MINIMAL TRACTS. MAXIMAL INFORMATION.

WHY ONLY 2 PORTS?

LESS TRAUMA. LOWER RISK. SOUND ONCOLOGIC PRINCIPLE

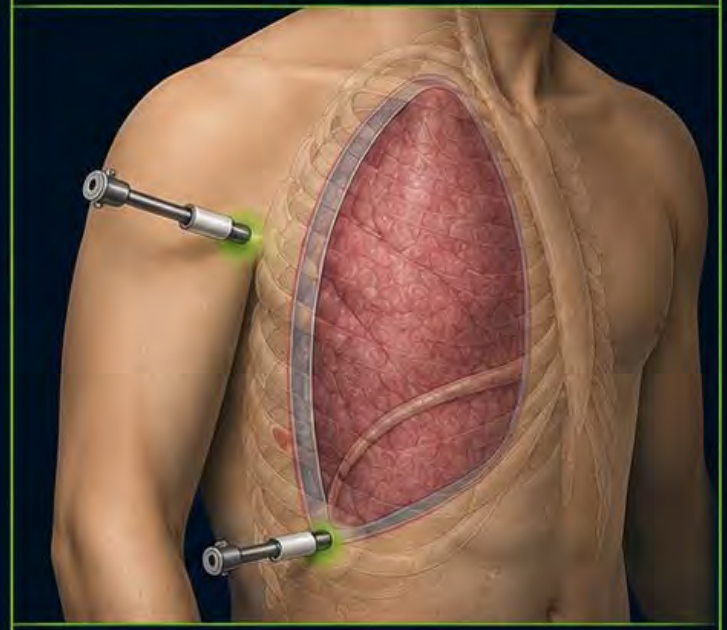
BAD
4 PORTS



Multiple chest wall implantation sites

VS

GOOD
2 PORTS



Minimal tract creation

THE EVIDENCE

Mesothelioma demonstrates **tumor tract seeding** after invasive pleural procedures.

Although prophylactic radiation is no longer routinely recommended, **minimizing unnecessary chest wall violations remains standard surgical practice.**

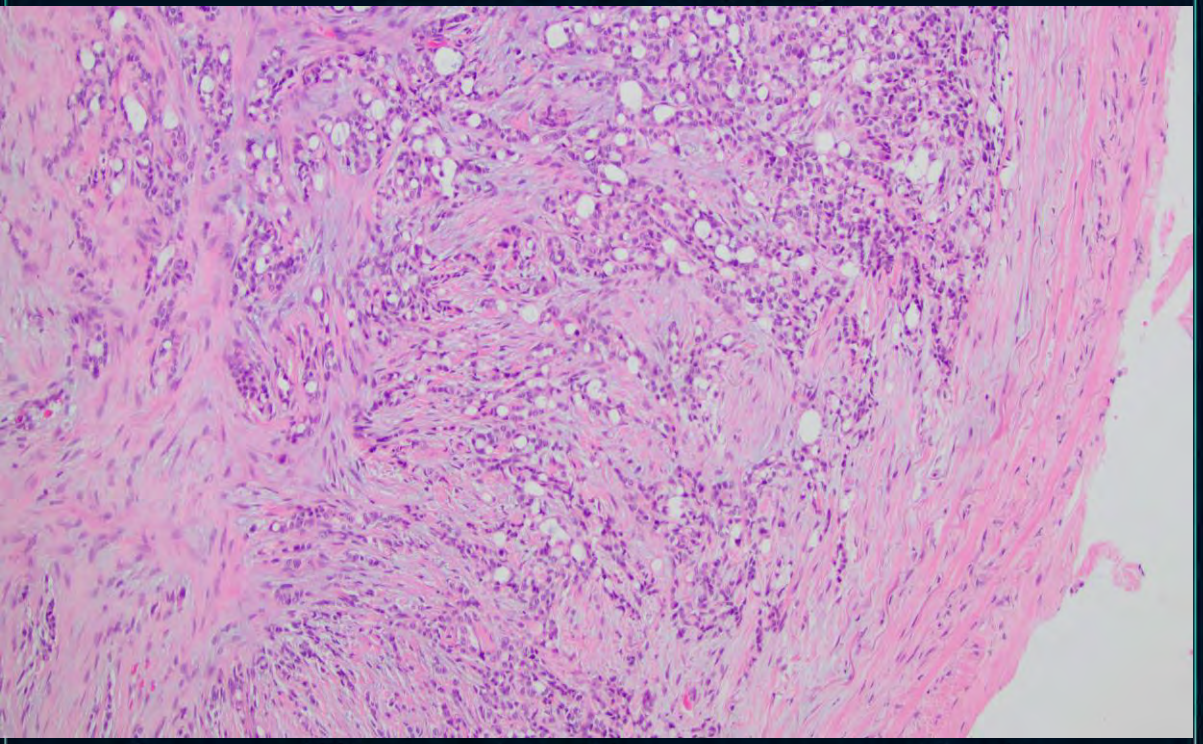
FEWER PORTS. FEWER TRACTS. SOUND ONCOLOGIC PRINCIPLE.

Use the fewest ports necessary to safely obtain an adequate diagnostic biopsy.

PATHOLOGY: THE DEFINITIVE ANSWER

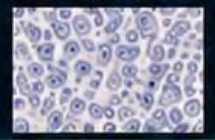
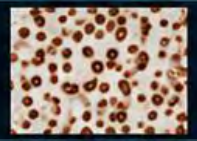
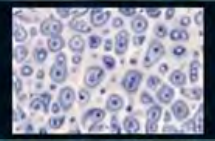
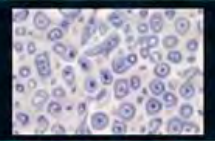
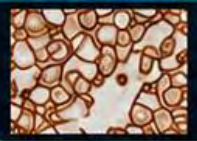
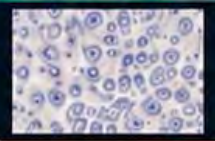
IMAGING RAISED SUSPICION. PATHOLOGY CONFIRMED THE DIAGNOSIS.

PLEURAL BIOPSY (H&E)



10x power, H&E stain slide of tumor showing proliferation of epithelioid cells infiltrating the pleura. Same power with a rim of external pleural surface.

IMMUNOSTAINING PROFILE

POSITIVE (supports mesothelial origin)		NEGATIVE (argues against carcinoma)	
	Calretinin ✓		CEA ✗
	WT-1 ✓		BerEP4 ✗
	CK5/6 ✓		MOC31 ✗
	D2-40 (focal) ✓		TTF-1 ✗

MOLECULAR FINDINGS: Loss of BAP1 expression by IHC and CDKN2A/B (p16) deletion by FISH support a malignant mesothelial proliferation.

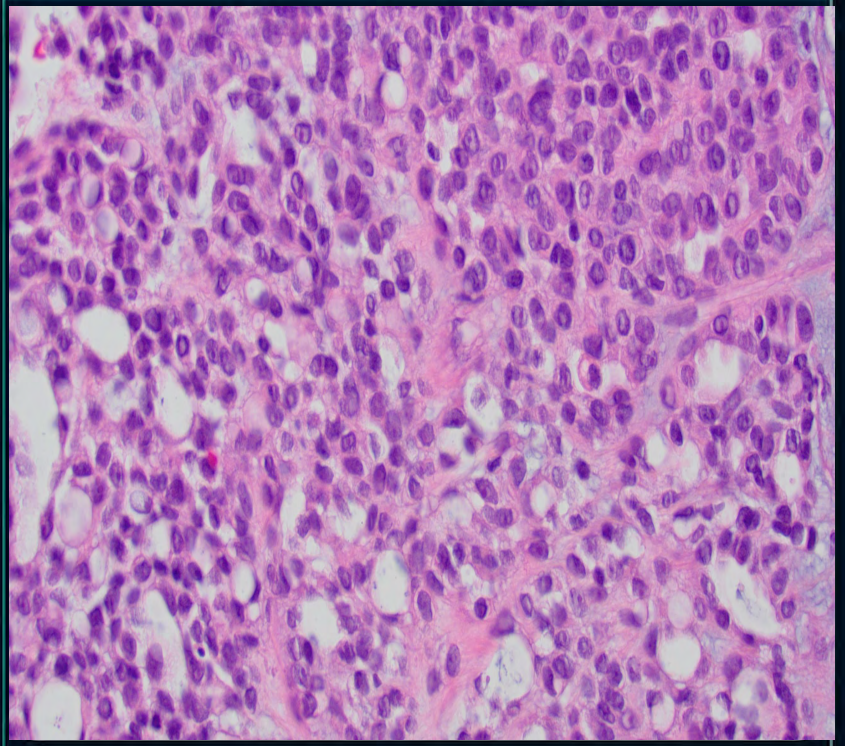
DIAGNOSIS

DIFFUSE EPITHELIOID PLEURAL MESOTHELIOMA

PATHOLOGY: THE DEFINITIVE ANSWER

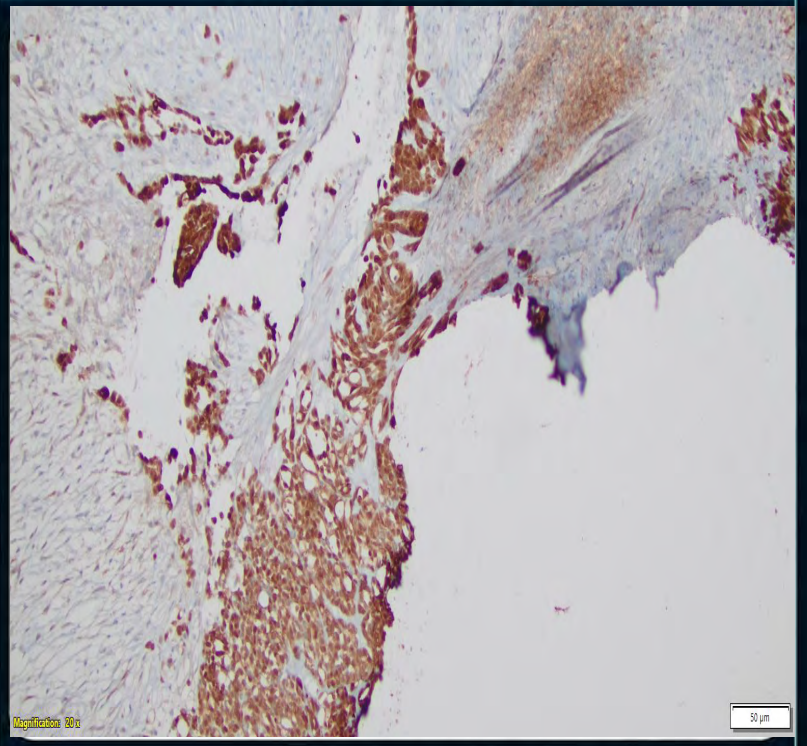
IMAGING RAISED SUSPICION. PATHOLOGY CONFIRMED THE DIAGNOSIS.

H&E – HIGH POWER



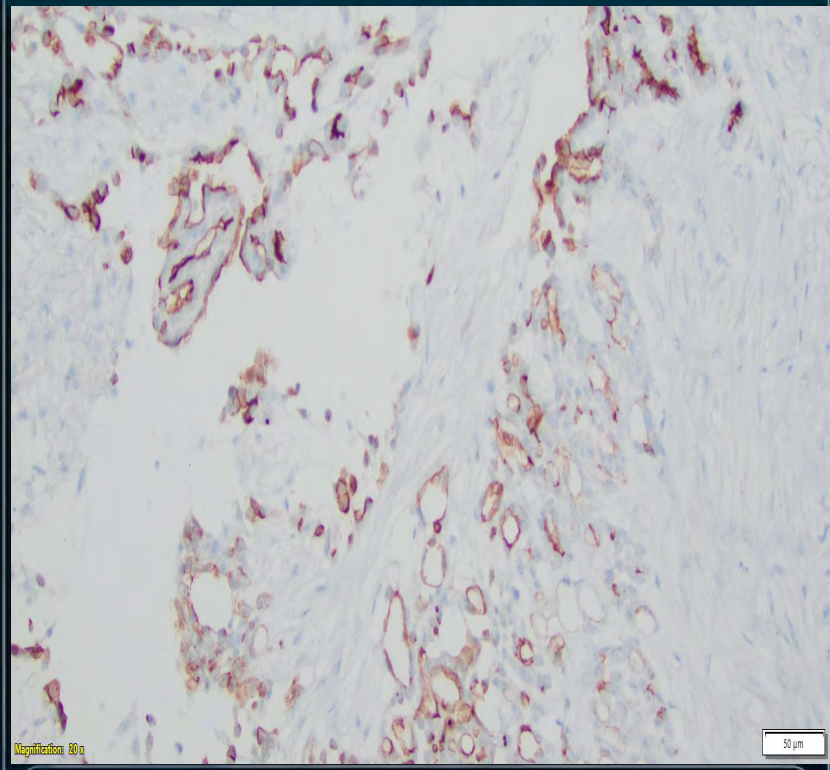
40x MAGNIFICATION
Demonstrates cell detail and pseudoglandular structures.

CALRETININ STAIN

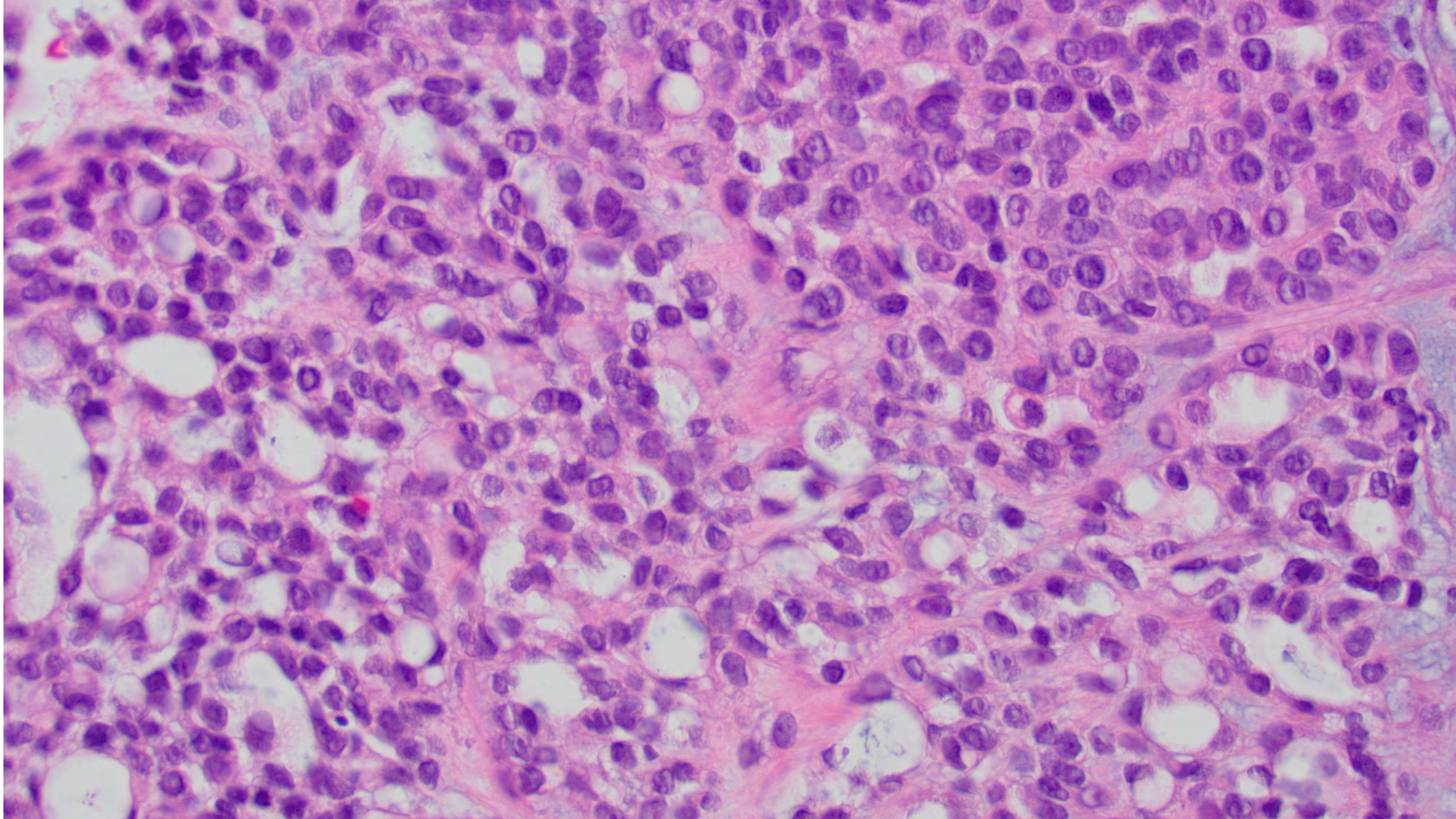


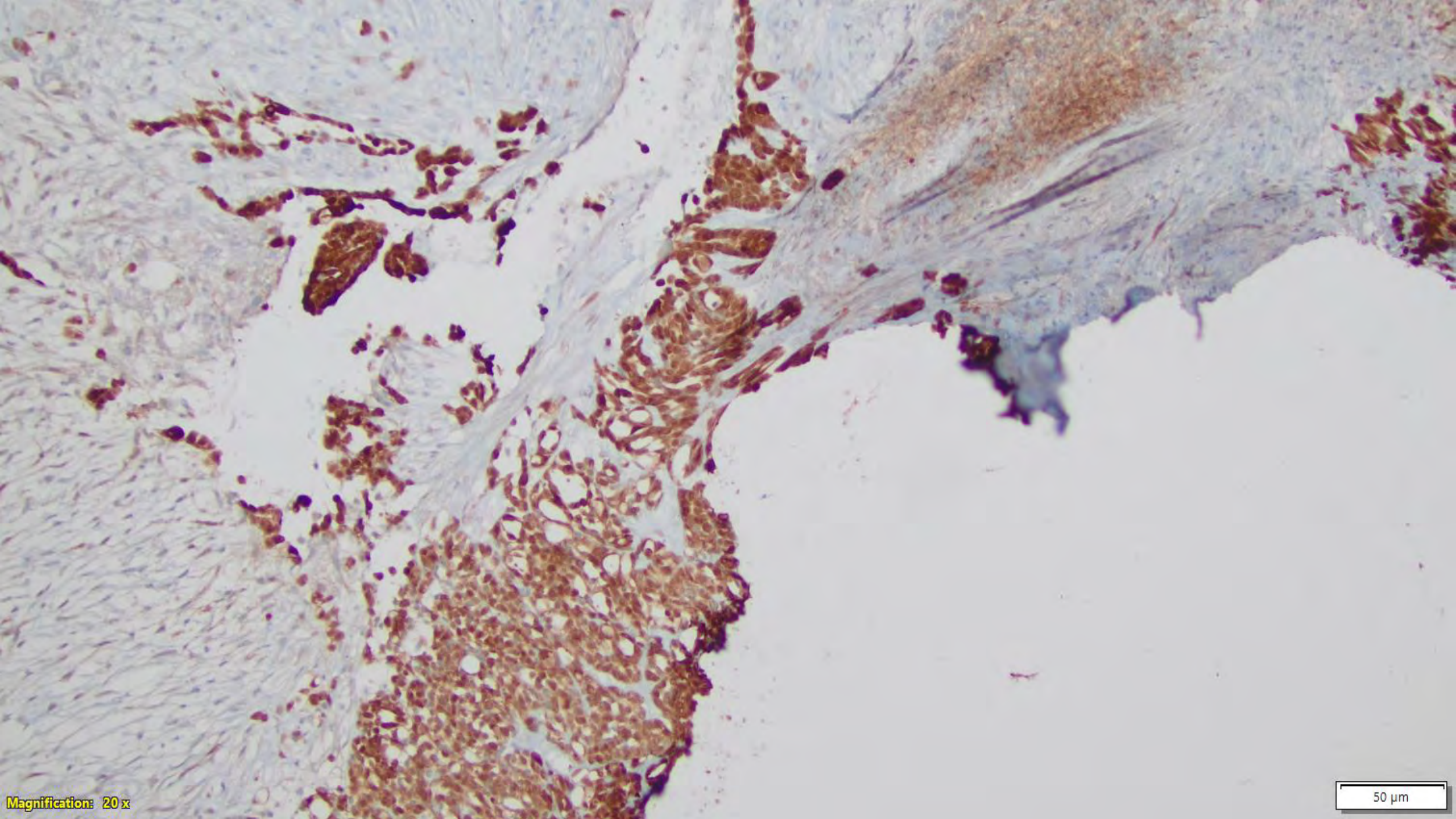
10x MAGNIFICATION
Positive calretinin immunostain supports mesothelial lineage.

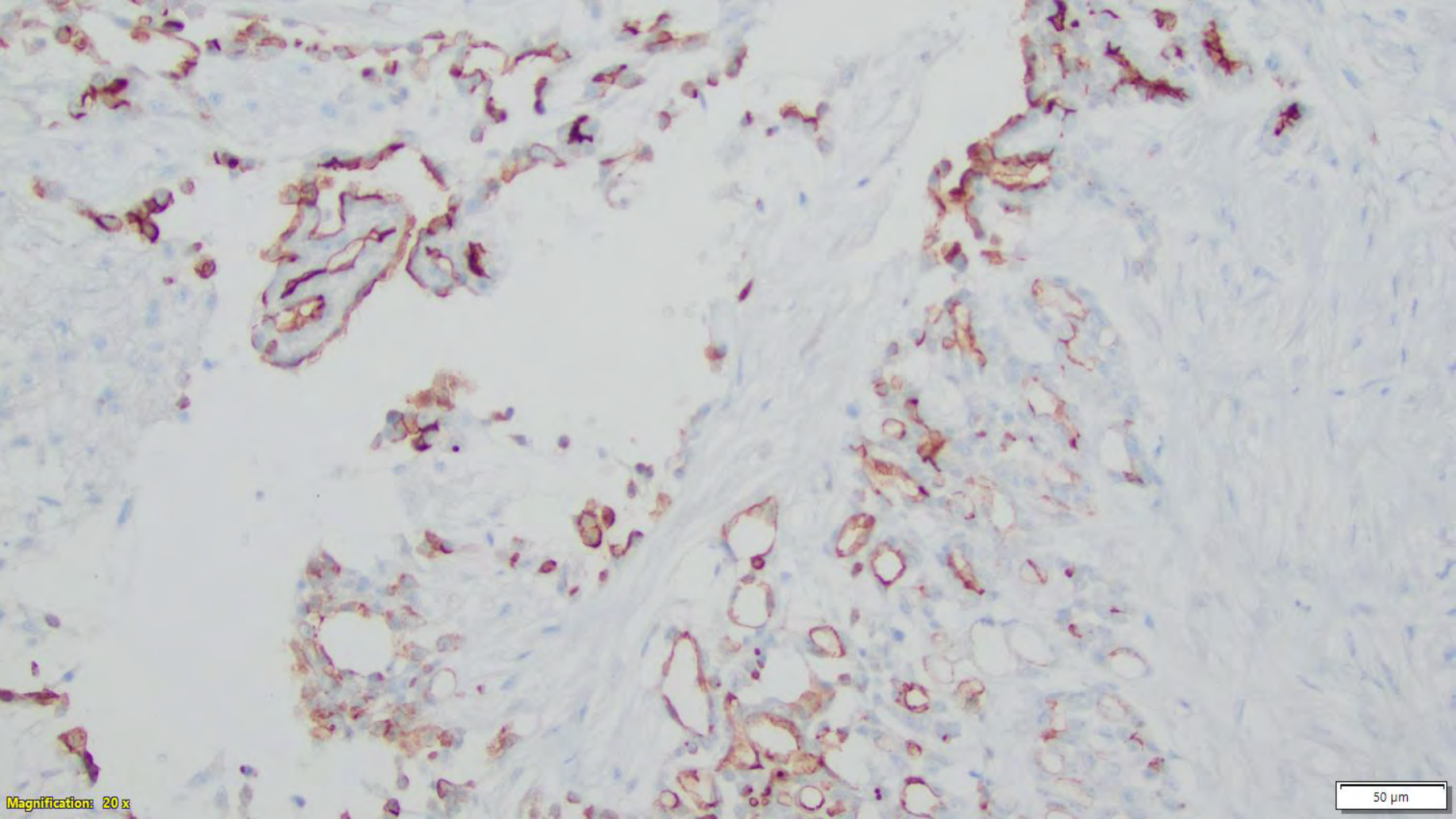
EMA STAIN



20x MAGNIFICATION
Positive EMA immunostain supports a diagnosis of malignant rather than benign mesothelial proliferation.



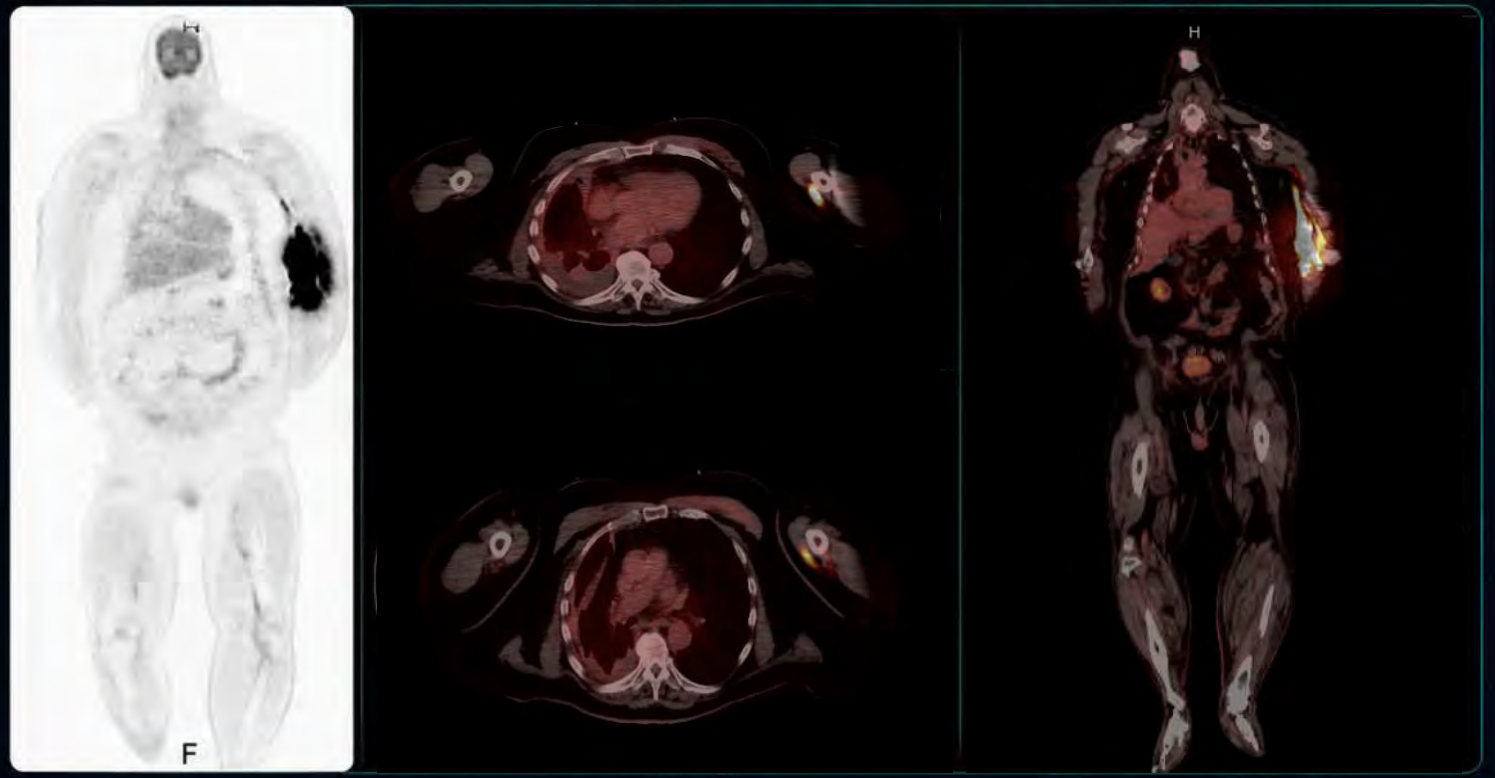

Magnification: 20 x
50 µm


Magnification: 20 x
50 µm

STAGING WORKUP

A SYSTEMATIC APPROACH AFTER DIAGNOSIS

- DIAGNOSIS
- PET/CT
- EBUS
- MRI BRAIN (SELECTED PATIENTS)
- MULTIDISCIPLINARY REVIEW



STAGE

T1N0M0

AJCC 8th EDITION

- **T1** Ipsilateral pleural involvement, no visceral pleural involvement
- **N0** No regional lymph node metastasis
- **M0** No distant metastasis

EARLY STAGE POTENTIALLY ELIGIBLE FOR DEFINITIVE SURGERY

TEACHING POINT

PET showed **little FDG activity** despite biopsy-proven disease.

TNM STAGING FOR PLEURAL MESOTHELIOMA

T (TUMOR)
Describes extent of pleural involvement (parietal, visceral, chest wall, diaphragmatic involvement, or contralateral disease).

N (NODES)
Assesses regional lymph node involvement (ipsilateral, contralateral mediastinal, supraclavicular).

M (METASTASIS)
Determines presence or absence of distal metastatic disease (non-regional organs, distant nodal disease).

Stage guides prognosis and management strategy.

MESOTHELIOMA SURGERY: MORE IS *NOT* ALWAYS BETTER

HISTORICAL EXPERIENCE AND RANDOMIZED TRIALS

BRIGHAM & WOMEN'S / SUGARBAKER EXPERIENCE

- 529 epithelioid patients undergoing EPP (1988–2011)
- Median OS: 18 months (all patients)
- N0 patients: median OS 26 months
- Showed selected patients could have long-term survival
- Highly selected surgical cohort — not randomized

MARS 1 (2011)

- 50 patients randomized (24 EPP vs 26 no EPP)
- Adjusted HR for death: 2.75 favoring no EPP
- Higher perioperative morbidity and mortality with EPP
- → Led to a decline in routine EPP

MARS 2 (2024)

- 335 patients with resectable mesothelioma randomized to:
  - Extended pleurectomy/decortication + chemo
  - Chemotherapy alone
- Median survival:
  - 19.3 months (surgery + chemo)
  - 24.8 months (chemo alone)
- More serious adverse events with surgery
- → No survival benefit from lung-sparing surgery

WHAT THIS MEANS FOR OUR PATIENT

Our patient:

- Epithelioid histology
- T1 disease
- N0
- M0

→ Anatomically resectable disease → ≠ SURGERY IMPROVES SURVIVAL

KEY TAKEAWAYS

- Technically resectable does not automatically mean surgery improves survival.
- Decision-making should be multidisciplinary.
- Consider systemic therapy.
- If definitive cytoreductive surgery is contemplated, evaluate at a high-volume mesothelioma center.

RESECTABLE ≠ SURGERY INDICATED

HITHOC: THE "HIPEC" OF THE CHEST?

HEATED INTRATHORACIC CHEMOTHERAPY IN MALIGNANT PLEURAL MESOTHELIOMA

Rationale: After macroscopic cytoreductive surgery, heated chemotherapy is perfused throughout the hemithorax to eradicate microscopic residual pleural disease.

HEATED CHEMOTHERAPY
- Most commonly cisplatin-based (41–43°C)

CIRCULATING PERFUSATE
60–90 minutes of perfusion

WHERE HITHOC FITS IN MULTIMODAL SURGICAL THERAPY

1. MACROSCOPIC CYTOREDUCTION
(Pleurectomy/ Decortication)

2. HITHOC PERFUSION
Heated cisplatin-based chemotherapy

3. TARGETS MICROMETASTATIC DISEASE
High local drug concentration + hyperthermia effect

GOALS

- ✓ Deliver high local drug exposure
- ✓ Hyperthermia may enhance cytotoxicity and penetration
- ✓ Treat microscopic residual pleural disease

WHAT DOES THE DATA SHOW?

2021 SYSTEMATIC REVIEW & META-ANALYSIS[1]

- 11 observational studies
- 762 patients
- 3 studies had non-HITHOC comparison groups
- Pooled analysis favored HITHOC for overall survival

HR 0.61 (95% CI 0.46–0.81)

OTHER KEY FINDINGS

- Median OS in HITHOC studies: ~19–36 months
- Greatest potential benefit in epithelioid histology
- Acceptable morbidity in experienced centers, but not negligible

THE CATCH:

No randomized phase III trials.
Significant heterogeneity in patient selection, surgical technique, chemotherapy, temperature, and perfusion protocols.

COMMONLY USED REGIMENS

CISPLATIN
Most common agent (100–225 mg/m²) at 41–43°C

SOMETIMES COMBINED WITH:
- Doxorubicin
- Mitomycin C
- Pemetrexed

PATIENT SELECTION IS CRUCIAL

- Epithelioid histology
- Good performance status
- Achievable macroscopic cytoreduction
- Treatment in high-volume centers with mesothelioma expertise

PROMISING ≠ PROVEN

Consider HITHOC only in highly selected patients as part of a multimodal approach at experienced mesothelioma centers or within clinical protocols.

Not established standard of care.
Long-term benefit remains to be proven by prospective randomized trials.

Multidisciplinary evaluation is essential to determine appropriateness for aggressive multimodal therapy.

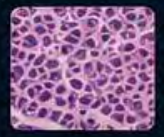
1. Yan TD, et al. Heated intrathoracic chemotherapy for malignant pleural mesothelioma: A systematic review and meta-analysis. J Thorac Dis. 2021;13(5):2847-2860.
2. Ratto GB, et al. Intraoperative heated intrathoracic chemotherapy in the multimodality treatment of pleural mesothelioma. Eur J Cardiothorac Surg. 2016;49(3):e83-e89.

CURRENT MANAGEMENT: WHERE DOES SURGERY FIT?

TREATMENT DECISIONS IN MALIGNANT PLEURAL MESOTHELIOMA ARE COMPLEX AND INDIVIDUALIZED

NCCN National Comprehensive Cancer Network®

DIAGNOSIS
Biopsy-proven mesothelioma

HISTOLOGY

Epithelioid
(most favorable subtype)

CLINICAL STAGING
T1N0M0
(No nodal or distant metastasis on EBUS/PET)

MULTIDISCIPLINARY EVALUATION
Thoracic surgery, medical oncology, radiation oncology, pathology, radiology, pulmonology, nephrology, nutrition, palliative care

ANATOMICALLY RESECTABLE
BUT IS HE OPERABLE?

OUR PATIENT
T1N0M0 EPITHELIOID – ANATOMICALLY RESECTABLE
BUT MULTIPLE FACTORS MAKE HIM A POOR SURGICAL CANDIDATE

MORBID OBESITY
BMI 37 – increases perioperative pulmonary complications and mortality.

MULTIPLE COMORBIDITIES
CAD, HTN, OSA, deconditioning – high baseline perioperative risk.

AKI ON CKD
Recent AKI on chronic kidney disease – increases risk of renal failure and complications.

ACTIVE DUODENAL ULCER
Recent bleeding ulcer with endoscopic control – high risk of re-bleeding, requires time for healing and optimization.

COMPLEX RECENT HOSPITALIZATION
Pleural sepsis, respiratory failure, prolonged recovery – poor physiologic reserve.

POOR PATIENT MOTIVATION / ENGAGEMENT
Missed follow-up, limited motivation for aggressive treatment and prolonged recovery.

PATIENT GOALS & VALUES
Quality of life, recovery burden, and personal priorities must guide decisions.

EARLY STAGE ≠ GOOD SURGICAL CANDIDATE
Treatment decisions must integrate tumor biology, physiologic reserve, and patient goals.

NCCN GUIDELINE PRINCIPLES
- Individualized, patient-centered approach
- Based on histology, stage, performance status, and patient goals
- Care should be delivered in experienced multidisciplinary centers
- Consider clinical trials for all eligible patients

TREATMENT PATHWAYS

UNRESECTABLE OR MEDICALLY INOPERABLE
SYSTEMIC THERAPY
- ✓ Immunotherapy-Based Regimens (e.g., nivolumab + ipilimumab)
- ✓ Platinum-Pemetrexed–Based Chemotherapy
- ✓ Clinical Trials
- ✓ Best Supportive / Palliative Care

POTENTIALLY RESECTABLE & HIGHLY SELECTED PATIENTS
CONSIDERATION OF SURGERY
- ✓ Extended Pleurectomy/Decortication (P/D) in experienced centers ONLY
- ✓ NOT recommended outside dedicated mesothelioma programs
- ✓ Must follow induction therapy and restaging
- ✓ Discuss expected morbidity, recovery time, and uncertain survival benefit

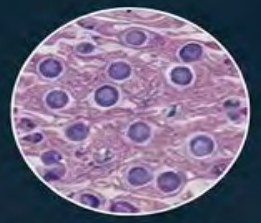
After MARS 1 and MARS 2, surgery has **NOT** shown a survival advantage over chemotherapy alone, even in resectable disease, and is associated with higher morbidity.

KEY TAKEAWAY: For this patient, the burden and risks of aggressive surgery outweigh the uncertain benefit. A multidisciplinary, patient-centered approach focusing on systemic therapy, optimization of comooorbidities, and supportive care best aligns with his disease and his goals.

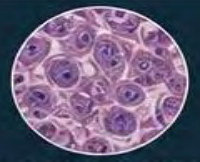
SYSTEMIC THERAPY

MALIGNANT PLEURAL MESOTHELIOMA

HISTOLOGY



EPITHELIOID



NON-EPITHELIOID (BIPHASIC OR SARCOMATOID)

FIRST-LINE THERAPY

PREFERRED

- (Carboplatin or Cisplatin)/Pemetrexed[1-4] (category 1)
- (Carboplatin or Cisplatin)/Pemetrexed + Bevacizumab[c,5-7] (category 1)
- (Carboplatin or Cisplatin)/Pemetrexed + Pembrolizumab[d,8] (category 1)
- Ipilimumab + Nivolumab[9] (category 1)

USEFUL IN CERTAIN CIRCUMSTANCES

- (Carboplatin or Cisplatin)/Gemcitabine[10-12]
- Pemetrexed[13]
- Vinorelbine[14]

PREFERRED

- Ipilimumab + Nivolumab[9] (category 1)
- (Carboplatin or Cisplatin)/Pemetrexed + Pembrolizumab[d,8] (category 1)

PRINCIPLES OF SYSTEMIC THERAPY[a,b]

PROGRESSION

SUBSEQUENT THERAPY

PREFERRED (IF CHEMOTHERAPY FIRST LINE)[e]

- Nivolumab[f,15,16]
- Ipilimumab + Nivolumab[15,17]

PREFERRED (IF IPILIMUMAB + NIVOLUMAB FIRST LINE)

- (Carboplatin or Cisplatin)/Pemetrexed[1-4]
- (Carboplatin or Cisplatin)/Pemetrexed + Bevacizumab[c,5-7]

OTHER RECOMMENDED

- Pemetrexed (category 1)[18,19]
- Gemcitabine[20,21]
- Gemcitabine + Ramucirumab[22]
- Vinorelbine[23,24]

PREFERRED (IF IPILIMUMAB + NIVOLUMAB FIRST LINE)

- (Carboplatin or Cisplatin)/Pemetrexed[1-4]
- (Carboplatin or Cisplatin)/Pemetrexed + Bevacizumab[c,5-7]

Goals: Prolong survival, maintain quality of life, manage symptoms.

Treatment decisions based on histology, performance status, comorbidities, and patient goals.

[a] Multidisciplinary evaluation is essential.
[b] Clinical trial participation is encouraged at all stages.
[c] Bevacizumab is category 2B for nonepithelioid histology.
[d] Pembrolizumab is category 2B for nonepithelioid histology.
[e] Subsequent therapy options depend on prior treatment and patient factors.

References: [1-24] See NCCN Guidelines for Malignant Pleural Mesothelioma (Latest Version)

TAKE HOME POINTS

WHAT THIS CASE TEACHES US ABOUT DIFFUSE PLEIOMA MESOTHELIOMA

1. **RARE BUT DEADLY.** Diffuse pleural mesothelioma is an aggressive, asbestos-related cancer with a long latency and **poor overall prognosis.**

2. **DIAGNOSIS TAKES HIGH SUSPICION.** Recurrent effusions with negative cytology do not exclude mesothelioma—definitive diagnosis often requires **invasive tissue sampling.**

3. **STAGE IS NOT THE WHOLE STORY.** Even early-stage (T1N0M0) disease may still carry substantial risk, and treatment must be **individualized to the patient**, not the stage alone.

4. **SURGERY IS NO LONGER THE DEFAULT.** MARS 1 and MARS 2 failed to show a survival advantage for routine radical surgery, highlighting the need for **careful patient selection.**

5. **HITHOC IS PROMISING, NOT PROVEN.** Heated intrathoracic chemotherapy may enhance local control in selected patients, but definitive **randomized evidence is lacking.**

6. **SYSTEMIC THERAPY HAS EVOLVED.** Immunotherapy—alone or in combination with chemotherapy—has expanded first-line options. Renal dysfunction should **inform, but not eliminate**, chemotherapy choices.

7. **THE PATIENT COMES FIRST.** Comorbidities, physiologic reserve, and **patient goals** must drive decisions. Technically resectable does not always mean worth operating.

THE BIG TAKEAWAY

Diffuse pleural mesothelioma management is complex and evolving.

THERE IS NO ONE-SIZE-FITS-ALL APPROACH.

- Ask the right questions.
- Use the best evidence.
- Treat the whole patient.

OUR ROLE IS TO GUIDE, NOT JUST TREAT.

"Stage tells us where the cancer is. | Evidence tells us what might help. | Judgment and compassion tell us what is right.

THAT IS HOW WE HONOR OUR PATIENTS.

REFERENCES

1. NCCN Clinical Practice Guidelines in Oncology: **Pleural Mesothelioma** *(latest version)*
2. WHO Classification of Thoracic Tumours *(5th edition)*
3. British Thoracic Society Guideline for Investigation of Pleural Disease *(2023)*
4. European Respiratory Society/European Society of Thoracic Surgeons Statement on Pleural Mesothelioma
5. International Mesothelioma Interest Group (IMIG) recommendations
6. ESTS Guidelines for Malignant Pleural Mesothelioma Surgery
7. Society of Thoracic Surgeons (STS) Expert Consensus on Malignant Pleural Mesothelioma
8. WHO Thoracic Tumours
9. International Mesothelioma Panel Immunohistochemistry Recommendations
10. NCCN Pleural Mesothelioma
11. IASLC Staging Manual
12. IMIG Staging System

ASCO Clinical Practice Guideline for Malignant Pleural Mesothelioma

"Evidence-based guidelines and multidisciplinary collaboration are essential for accurate diagnosis, staging, and optimal management of pleural mesothelioma."

THANK YOU

Thank you for your time
and attention.
I appreciate your questions.

Advancing care. Improving outcomes.
Together for our patients.

EVIDENCE
guides us.

COMPASSION
drives us.

PATIENTS
inspire us.

Committed to better outcomes in diffuse pleural mesothelioma.