Epithelioid Malignant Mesothelioma Metastatic to the Skin: A Case Report and Review of the Literature

Short Title: Metastatic Malignant Mesothelioma

Authors:

Rachel Elizabeth Ward, M.D.,[1] Stefanie Ann Ali, M.D.,[2] Matthew Kuhar, M.D. [3,4]

Affiliation:

[1]Department of Dermatology, Wayne State University, Detroit, MI

[2]Dermatology and Plastic Surgery Associates, Lombard, IL

[3]Department of Dermatology, Indiana University School of Medicine, Indianapolis, IN

[4]Department of Pathology, Indiana University School of Medicine, Indianapolis, IN

Corresponding Author: Rachel Elizabeth Ward, M.D.

Address: 18100 Oakwood Boulevard, Suite 300, Dearborn, Michigan 48124

Email: rward@med.wayne.edu

Phone: 313-429-7845

Fax: 313-429-7992

Key Words: mesothelioma, cutaneous, metastasis, histopathology, immunohistochemistry

---

Introduction

Mesothelioma is a rare form of cancer arising from a monolayer of mesothelial cells that form the lining of the internal body cavities and organs, with the vast majority of cases arising from the pleura (65-80%), less commonly from the peritoneum (10-30%), and rarely from the pericardium and tunica vaginalis testis (1-2%).(1-3) Malignant mesothelioma (MM) is aggressive and is known to be locally invasive and have a propensity for metastasis to distant organs, rarely including metastasizing to the skin. Cutaneous involvement by MM can occur through three main routes: regional spread via lymphatics, direct extension within surgical scars, and distant metastasis via hematogenous spread.(4, 5) The most common route, direct extension in the form of needle track metastasis (NTM), can occur after placement of intraperitoneal catheters in the treatment of MM or through the contamination of surgical sites.(5-10) Few reports have noted true cutaneous metastasis of MM, with less than twenty cases found in the literature.(1, 2, 4, 6-9, 11-27)

Case Report

A 75-year-old retired automobile mechanic who specialized in brake repair presented to the Emergency Department with rapidly progressive dyspnea. A chest radiograph was performed, which showed a large left-sided pleural effusion. Evaluation of thoracentesis fluid showed reactive mesothelial cells without evidence of malignancy. Over the next few months, he experienced increasing dyspnea, hemoptysis, anorexia, and persistent hemorrhagic pleural effusions. A video-assisted thoracoscopic surgery (VATS) was performed, and multiple biopsies showed marked pleural thickening with a mixed infiltrate of tumor nests and necrotic debris. Immunohistochemical stains were positive for cytokeratin (CK) 5/6, CK7, Calretinin, D2-40

(podoplanin), p53, GLUT-1, with focal positivity of MOC-31, and negative for thyroid transcription factor (TTF)-1, CK20, caudal-related homeobox gene 2 (CDX2), BerEP4, and Napsin A (Fig. 1). The diagnosis of malignant mesothelioma of the pleura, stage II, was made. Due to his significant co-morbidities, he was not a candidate for systemic chemotherapy.

Four months later, he presented with a new single firm, pink cutaneous nodule measuring 6 x 8 mm on his upper back (Fig. 2). A shave biopsy was performed, which revealed a reasonably well-circumscribed nodular dermal proliferation of atypical epithelioid tumor cells forming pseudoglandular structures with numerous mitoses. The well-circumscribed and nodular growth pattern within the dermis as well as lack of surgical scars in the surrounding area favored metastasis over direct extension. Immunohistochemical stains showed immunoreactivity for CK5/6, CK7, Calretinin, and D2-40 and negative staining for TTF-1, CK20, GLUT-1, and prostate-specific antigen (PSA) (Fig. 3). The collective findings supported a diagnosis of epithelioid malignant mesothelioma metastatic to the skin. Unfortunately, the patient succumbed to his disease within a week following his biopsy.

Discussion

The results of a literature search of cases of cutaneous metastasis of malignant mesothelioma are summarized in Table 1.(2, 4, 6-9, 11, 12, 17-21, 23-27) There were nineteen previously reported cases of MM metastatic to the skin, three of which predated the availability of immunohistochemical stains. We excluded cases in which the cutaneous presentation was due to direct extension or regional spread. Importantly, as the umbilicus is an embryological remnant of the vitelline duct and retains a connection to the peritoneal cavity (22), we excluded cases of umbilical presentations of MM as we consider it to be a direct extension.(14, 16, 22) The average

age at presentation of cutaneous metastasis was 56.5 years (range: 25-77). Excluding one outlier (12), the average time from original diagnosis of MM to presentation of cutaneous metastasis was six months, with seven individuals receiving their diagnosis of MM at or shortly after the time of their cutaneous biopsy. MM primary to the pleura accounted for 85% of reported cases of cutaneous metastases, and peritoneal MM accounted for 15% of reported cases. The most commonly reported site of cutaneous metastasis was the face, followed by the scalp and chest. All peritoneal MM cases were of the epithelioid subtype. Approximately 60% of cases of pleural MM were of the epithelioid subtype, 23% were of the sarcomatoid subtype, and 17% were of the biphasic subtype. The majority of reports demonstrated positive staining with calretinin, cytokeratins (especially CK 5/6 and CK 7), vimentin, epithelial membrane antigen (EMA), thrombomodulin, HMBE-1, and Wilms' Tumor (WT)-1. Commonly used negative stains included carcinoembryonic antigen (CEA), S100, TTF-1, Leu M1, Factor VIIIRA, cluster of differentiation (CD)-31, CD34, B72.3, and human melanoma black (HMB)-45.

The diagnosis of MM can be challenging for several reasons, including delayed and non-specific presentation, relative paucity of sensitive diagnostic techniques, and histologic similarity to other neoplasms. Primary MM has a very long latency period, often presenting up to four or five decades post-exposure, and is linked to asbestos exposure (including automobile brakes, which formerly contained asbestos) in up to 90% of cases of pleural MM.(1, 5, 6, 20, 28-31) Due to the delay from exposure to onset of symptoms, the disease is typically far progressed at the time of diagnosis, with metastases typically appearing at a late stage of the disease.(3, 9, 25, 32, 33) Additionally, diagnosis can be delayed because the symptoms for both pleural and peritoneal MM are vague and non-specific, including chest pain, dyspnea for pleural MM and abdominal pain, weight loss, and increased abdominal girth for peritoneal MM.(1, 3, 20, 26) Recurrent

pleural effusions and ascites are common in pleural and peritoneal MM, respectively. However, sampling of body cavity fluid cytology is oftentimes non-diagnostic, with reports estimating the sensitivity to be between 33 and 84%.(21, 32) Clinically, cutaneous metastases of MM can appear as violaceous nodules or papules (as is seen in the present case), erythematous eruptions, or inflammatory and infiltrative plaques.(5, 9)

There are three main histologic subtypes of MM: epithelioid (60%), sarcomatoid (10-20%), and biphasic or mixed (20-30%), which has both epithelioid and sarcomatoid components.(3, 5, 8, 29) The epithelioid subtype is comprised of trabecular cords of cuboidal, oval, or polygonal cells that are usually clumped together with visible, elongated nuclei and abundant eosinophilic cytoplasm and may have various secondary patterns, including tubulopapillary, micropapillary, acinar, adenoid cystic, clear cell, signet ring, solid, small and large cell patterns, and pleomorphic.(1, 5) The sarcomatoid subtype, the least common yet most aggressive subtype, is comprised of spindle cells arranged in fascicles with enlarged and elongated nuclei, which may have desmoplastic, lymphohistiocytic, fibrosarcomatous, chondrosarcomatous, osteosarcomatous, and malignant fibrous histiocytoma-like secondary patterns.(5, 34, 35) MM can be difficult to diagnose histologically, as the tumor can resemble features of benign reactive mesothelial proliferations, metastatic adenocarcinoma (especially neoplasms from the gastrointestinal tract, breast, lung, prostate, kidney, or thyroid), sarcoma (especially epithelioid angiosarcoma, which can develop from prior radiation exposure), lymphoma, and melanoma (adenoid or pseudopapillary subtypes).(1, 6-9, 12, 20, 23, 24, 26, 28) As such, immunohistochemistry plays a pivotal role in diagnosis. However, no specific unique immunohistochemical or genetic marker has been elucidated to allow for prompt, efficient

diagnosis. Therefore, the diagnosis of MM is typically one of exclusion and relies heavily on patterns of positive and negative stains.(3, 28, 35)

Calretinin is considered to be one of the most specific stains for MM, as it strongly and diffusely stains both the nucleus and cytoplasm, is frequently expressed in all histologic subtypes of MM, and stains positively in less than ten percent of adenocarcinoma.(1, 5, 12, 36, 37) Other less specific markers for MM are considered to be WT1, CK 5/6, thrombomodulin, and HBME-1.(5, 24, 27) Pertinent negative stains for MM include CEA, CA-125, Leu M1 (CD15), BerEP4, MOC-31, TTF-1, B72.3, which stain positively in adenocarcinoma, S100 and HMB-45, which stain positively in melanoma, Factor VIII, vimentin, and CD31, which stain positively in angiosarcoma, and PSA, which stains positively in prostatic adenocarcinoma.(5, 21, 23, 24, 28) Current recommendations for diagnosing MM suggest initial screening panels to include positive staining for at least two MM markers (such as calretinin, WT1, CK5/6) and negative staining for at least two carcinoma markers (such as CEA, Leu M1, BerEP4, TTF-1).(28, 38) More recent research has shown promising results using fluorescence *in situ* hybridization (FISH) analysis to detect homozygous deletion of *p16* and immunohistochemistry to detect loss of nuclear staining of BRCA1-associated protein 1 (BAP1), independently or in combination, for difficult cases of MM.(38-40) This is especially useful in differentiating between malignant pleural mesothelioma and benign reactive mesothelial hyperplasia, which have cytologic and histologic similarities.(39, 41)

Though not approved for use at present, two serum markers, serum mesothelin-related protein (SRMP) and osteopontin, have been proposed to aid in diagnosis and monitor progression of MM. (26, 31, 42-44). Diagnosis can be challenging, but a thorough workup

including histologic, immunohistochemical, and molecular investigations, in combination with clinical and radiologic correlation, can aid in diagnosis.

References

1. Abban C, Viglione M. Peritoneal mesothelioma presenting as a skin nodule. Journal of Cutaneous Pathology. 2009;36(6):675-9.
2. Falkenstern-Ge RF, Kimmich M, Bode-Erdmann S, Friedel G, Ott G, Kohlhaufl M. Pleural mesothelioma presenting as periumbilical metastasis: the first clinical documentation. Case reports in oncological medicine. 2013.
3. Sinon SH, Rich AM, Hussaini HM, Yoon HS, Firth NA, Seymour GJ. Metastases to the oral region from pleural mesothelioma: Clinicopathologic review. Head & neck. 2013;35(4):599-604.
4. Patel T, Bansal R, Trivedi P, Modi L, Shah MJ. Subcutaneous metastases of sarcomatoid mesothelioma with its differential diagnosis on fine needle aspiration--a case report. Indian journal of pathology & microbiology. 2005;48(4):482-4.
5. Shieh S, Grassi M, Schwarz JK, Cheney RT. Pleural mesothelioma with cutaneous extension to chest wall scars. Journal of Cutaneous Pathology. 2004;31(7):497-501.
6. Cassarino DS, Xue W, Shannon KJ. Widespread cutaneous and perioral metastases of mesothelioma. Journal of Cutaneous Pathology. 2003;30(9):582-5.
7. Dutt PL, Baxter JW, O'Malley FP, Glick AD, Page DL. Distant cutaneous metastasis of pleural malignant mesothelioma. Journal of Cutaneous Pathology. 1992;19(6):490-5.
8. Müller CSL, Reichrath J, Tilgen W. Disseminated cutaneous metastasis of a biphasic pleural mesothelioma. Journal of the European Academy of Dermatology & Venereology. 2009;23:226-7.
9. Prieto VG, Kenet BJ, Varghese M. Malignant mesothelioma metastatic to the skin, presenting as inflammatory carcinoma. American Journal of Dermatopathology. 1997;19(3):261-5.
10. Shrestha RL, Wood BA, Lee YC. Pseudo-tumor mimicking indwelling pleural catheter tract metastasis in mesothelioma. Journal of bronchology & interventional pulmonology. 2014;21(4):350-2.
11. Bazex A, Miguères J, Dupré A, Christol B, Jover A, Cantala P. Métastases au niveau du cuir chevelu d'un mésothéliome pleural. Bulletin Société de Dermatologie et de Syphiligraphie. 1968;76:99-101.
12. Beer TW, Heenan PJ. Malignant mesothelioma presenting as a lip tumor: report of two cases with one unrecognized by 166 pathologists. The American Journal of dermatopathology. 2007;29(4):388-91.
13. Berkowitz RK, Longley J, Buchness MR, Silvers DN, Ozzello L, Grossman ME. Malignant mesothelioma: diagnosis by skin biopsy. Journal of the American Academy of Dermatology. 1989;21(5.2):1068-73.
14. Boyde AM, Attanoos RL. Sister Mary Joseph's nodule in malignant peritoneal mesothelioma. Histopathology. 2003;43(3):303-4.
15. Cartwright LE, Steinman HK. Malignant papillary mesothelioma of the tunica vaginalis testes: cutaneous metastases showing pagetoid epidermal invasion. Journal of the American Academy of Dermatology. 1987;17(5.2):887-90.
16. Chen KT. Malignant mesothelioma presenting as Sister Joseph's nodule. The American Journal of dermatopathology. 1991;13(3):300-3.
17. Edstrom LE, Dawson PJ, Kohler J, DeMeester TR. Malignant mesothelioma: a metastasis to the face. Journal of surgical oncology. 1980;14(3):251-4.

18. Elbahaie AM, Kamel DE, Lawrence J, Davidson NG. Late cutaneous metastases to the face from malignant pleural mesothelioma: a case report and review of the literature. World journal of surgical oncology. 2009;7:84.
19. Fletcher SV, Laws DE, McCutcheon J, Perkins P. Mesothelioma – A change in the natural history?: Distant cutaneous and soft tissue metastases following chemotherapy. Respiratory Medicine CME. 2009;2(1):25-6.
20. Kanbay A, Oguzulgen KI, Ozturk C, et al. Malignant pleural mesothelioma with scalp, cerebellar, and finger metastases: a rare case. Southern Medical Journal. 2007;100(1):63-5.
21. Krishnaraj N, Leen GL, Kane P, Edge CJ, Murphy SA, Gribbin HR. Malignant mesothelioma presenting as stroke--a case report. European journal of cancer care. 2003;12(4):365-8.
22. Kwee WS, Veldhuizen RW, Vermorken JB, Golding RP, Donner R. Peritoneal mesothelioma presenting as umbilical tumor. Pathology, research and practice. 1982;174(1-2):159-65.
23. Maiorana A, Giusti F, Cesinaro AM, Conti A, Rossi G. Cutaneous metastases as the first manifestation of pleural malignant mesothelioma. Journal of the American Academy of Dermatology. 2006;54(2):363-5.
24. Ordóñez NG, Smith J, Jr. Peritoneal malignant mesothelioma with multiple distant skin metastases. Archives of Dermatology. 1983;119(10):827-30.
25. Pappa L, Machera M, Tsanou E, et al. Subcutaneous metastasis of peritoneal mesothelioma diagnosed by fine-needle aspiration. Pathology Oncology Research. 2006;12(4):247-50.
26. Samedi V, White S, Zimarowski MJ, Harris A, Saffitz J, Wang HH. Metastatic peritoneal mesothelioma in the setting of recurrent ascites: a case report. Diagnostic cytopathology. 2010;38(9):675-81.
27. Terada T. Skin Metastasis of Pleural Epithelioid Malignant Mesothelioma. Applied Immunohistochemistry & Molecular Morphology. 2011;19(1):92-3.
28. Kerger BD, James RC, Galbraith DA. Tumors that mimic asbestos-related mesothelioma: time to consider a genetics-based tumor registry? Frontiers in genetics. 2014;5:151.
29. Moser S, Beer M, Damerau G, Lubbers HT, Gratz KW, Kruse AL. A case report of metastasis of malignant mesothelioma to the oral gingiva. Head & neck oncology. 2011;3:21.
30. Nickell LT, Jr., Lichtenberger JP, 3rd, Khorashadi L, Abbott GF, Carter BW. Multimodality imaging for characterization, classification, and staging of malignant pleural mesothelioma. Radiographics : a review publication of the Radiological Society of North America, Inc. 2014;34(6):1692-706.
31. Tsao AS, Wistuba I, Roth JA, Kindler HL. Malignant pleural mesothelioma. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2009;27(12):2081-90.
32. Gunday M, Erinanc H, Geredeli C. Unusual region for pericardial malignant mesothelioma: cutaneous manifestation in a Turkish woman. Rare tumors. 2013;5(3):142-3.
33. Lester T, Xu H. Malignant pleural mesothelioma with osseous metastases and pathologic fracture of femoral neck. Applied immunohistochemistry & molecular

morphology : AIMM / official publication of the Society for Applied Immunohistochemistry. 2008;16(5):507-9.
34. Klebe S, Brownlee NA, Mahar A, et al. Sarcomatoid mesothelioma: a clinical-pathologic correlation of 326 cases. Modern Pathology. 2010;23(3):470-9.
35. Sporn T, Roggli VL. Mesothelioma. Pathology of Asbestos-Associated Diseases. 2 ed. New York: Springer-Verlag 2004. p. 104-68.
36. Marchevsky AM. Application of immunohistochemistry to the diagnosis of malignant mesothelioma. Archives of pathology & laboratory medicine. 2008;132(3):397-401.
37. Sugarbaker PH, Acherman YI, Gonzalez-Moreno S, et al. Diagnosis and treatment of peritoneal mesothelioma: The Washington Cancer Institute experience. Seminars in oncology. 2002;29(1):51-61.
38. Husain AN, Colby T, Ordonez N, et al. Guidelines for pathologic diagnosis of malignant mesothelioma: 2012 update of the consensus statement from the International Mesothelioma Interest Group. Archives of pathology & laboratory medicine. 2013;137(5):647-67.
39. Hida T, Hamasaki M, Matsumoto S, et al. BAP1 immunohistochemistry and p16 FISH results in combination provide higher confidence in malignant pleural mesothelioma diagnosis: ROC analysis of the two tests. Pathology international. 2016;66(10):563-70. Epub 2016/09/12.
40. Hwang HC, Sheffield BS, Rodriguez S, et al. Utility of BAP1 Immunohistochemistry and p16 (CDKN2A) FISH in the Diagnosis of Malignant Mesothelioma in Effusion Cytology Specimens. The American journal of surgical pathology. 2016;40(1):120-6. Epub 2015/10/09.
41. Cigognetti M, Lonardi S, Fisogni S, et al. BAP1 (BRCA1-associated protein 1) is a highly specific marker for differentiating mesothelioma from reactive mesothelial proliferations. Mod Pathol. 2015;28(8):1043-57. Epub 2015/05/30.
42. Robinson BW, Creaney J, Lake R, et al. Mesothelin-family proteins and diagnosis of mesothelioma. Lancet. 2003;362(9396):1612-6.
43. Robinson BW, Creaney J, Lake R, et al. Soluble mesothelin-related protein--a blood test for mesothelioma. Lung cancer (Amsterdam, Netherlands). 2005;49 Suppl 1:S109-11.
44. Pass HI, Lott D, Lonardo F, et al. Asbestos exposure, pleural mesothelioma, and serum osteopontin levels. The New England journal of medicine. 2005;353(15):1564-73.

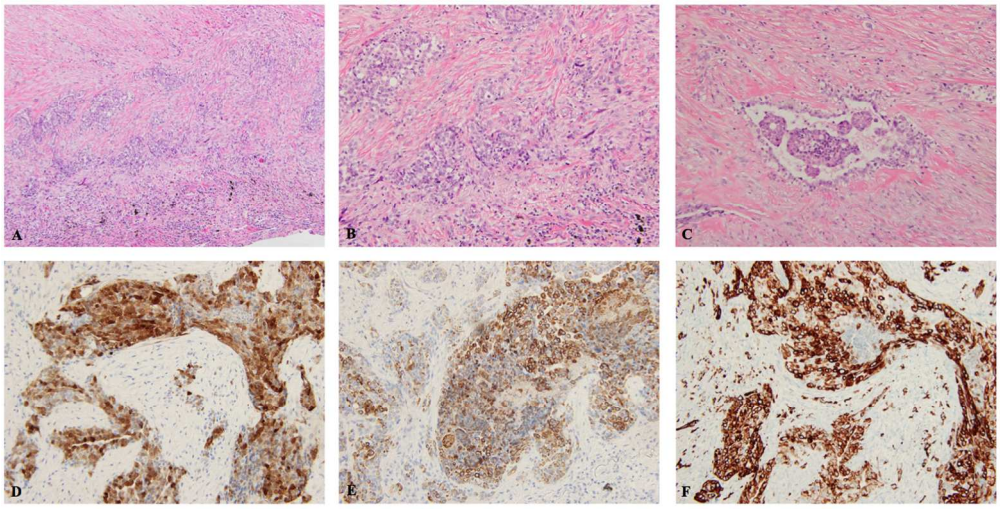

Fig. 1. Hematoxylin and eosin staining of the pleural biopsy revealed marked thickening and a fibroblastic reaction to infiltrative tumor nests and pseudoglandular structures (A: x40). The tumor cells are mildly pleomorphic with increased mitotic activity (B and C: x100 and x200). Immunohistochemical staining showed positivity for calretinin (D: x200), CK 5/6 (E: x200), and CK7 (F: x200).

Fig. 2. A clinical image shows a single firm, pink cutaneous papule on the upper trunk.

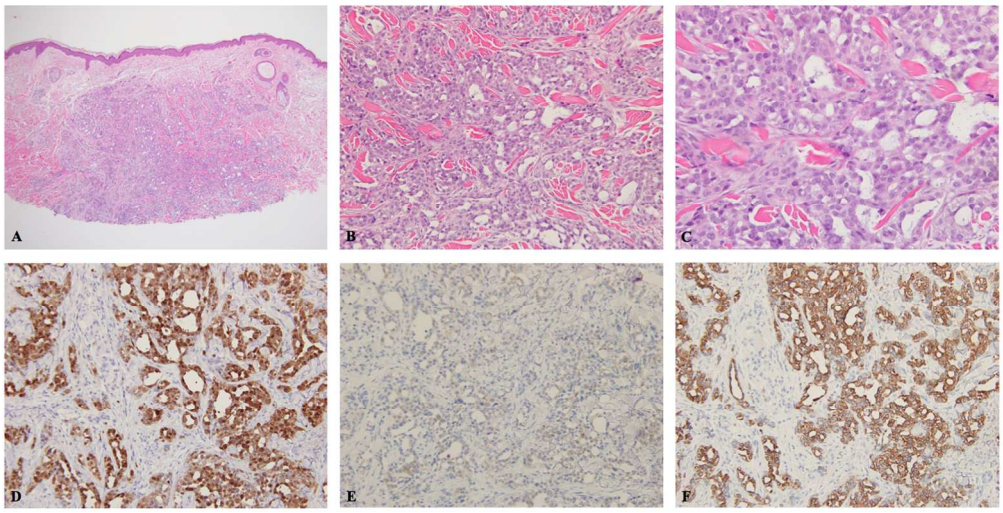

Fig. 3. Hematoxylin and eosin staining of the cutaneous nodule shows a fairly well-circumscribed nodular proliferation of epithelioid cells within the dermis (A: x40). The tumor forms pseudoglandular structures with cytologic atypia and mitoses (B and C: x200 and x400). Immunohistochemical stains with positive results include calretinin (D: x200), CK 5/6 (E: x200), and CK7 (F: x200).

Table 1. Details of reported cases of cutaneous metastases of malignant mesothelioma

Case	Year of Publication, Reference	Age (years) at Presentation / Gender	Location of cutaneous mets	Time from original diagnosis of MM to met presentation	Positive Stains	Negative Stains	Type of Mesothelioma	Subtype of Cutaneous Metastasis	Treatment	Outcome/follow up
1	1968 [11]	65/M	Scalp	2 mths	Not Reported	Not Reported	Pleural	Sarcomatoi	Not Reported	Not Reported
2	1980 [17]	50/M	Chest, face	16 mths, 21 mths	Not Reported	Not Reported	Pleural	Biphasic*	Chemotherapy (cyclophosphamide, doxorubicin, MTX x4 mths), Radiation	Deceased within 23 mths
3	1983 [24]	54/M	Neck, thorax, flank, abdomen	3 mths	Not Reported	Not Reported	Peritoneal	Epithelioid*	Chemotherapy (4 cycles: Cycles 1 & 2: vincristine, dacarbazine, cyclophosphamide Cycle 3: doxorubicin, dacarbazine, cyclophosphamide Cycle 4: (2 doses): MTX,	Deceased within 11 mths
4	1992 [7]	60/M	Cheek	At time of biopsy	Cytokeratin, Vimentin, EMA, Orthokeratin	Leu M1, CEA, S100, Factor VIIIRA, UE	Pleural	Epithelioid	Not Reported	Deceased shortly after biopsy
5	1997 [9]	50/M	Chest wall	12 mths	Cytokeratin (AE1/AE3, MNF116, CAM 5.2), EMA	Leu M1 (CD15), CEA, CD34, Factor VIIIRA, UE	Pleural	Epithelioid	Radiation	Not Reported
6	2003 [6]	64/M	Lip, flank, pubis, calf	9 mths	Calretinin, Cytokeratin (CK19 & AE1/AE3), HBME-1	Leu M1, CEA, BerEP4, B72.3, S100, HMB-45, MART-1,	Pleural	Epithelioid	Radiation	Not Reported
7	2003 [21]	64/M	Chin	At time of biopsy	Cytokeratin (MNF116)	Not Reported	Pleural	Sarcomatoid	Radiation	Not Reported
8	2005 [4]	25/F	Back, upper & lower extremities	3 mths	Not Reported	Not Reported	Pleural	Sarcomatoid	Surgery, chemotherapy (6 cycles), radiation	Progressive disease on subsequent imaging
9	2006 [23]	53/M	Flank	At time of biopsy	Calretinin, Cytokeratins (MNF116), CK5/6 (weak), CK7	CEA, CD31, CD34, S100, CK20	Pleural	Epithelioid	Chemotherapy, radiation, pleural sclerotherapy	Alive at 28 mths, but with progressive disease
10	2006 [25]	60/F	Chest wall	6 mths	Not Reported	Not Reported	Peritoneal	Not	Chemotherapy	Not Reported

11	2007 [12]	67/M	Lip, scalp	12 years	Calretinin, CK5/6, CK7, EMA, HBME-1	TTF-1	Pleural	Epithelioid	Chemotherapy (pemetrexed, cisplatin, gemcitabine)	Alive at 31 mths, but with progressive disease
12	2007 [12]	77/M	Lip	At time of biopsy	Calretinin, Cytokeratin (CAM 5.2, AE1/AE3), CK7	BerEP4	Pleural	Epithelioid	Not Reported	Deceased within 6 mths
13	2007 [20]	47/M	Scalp, finger	Not Reported	Calretinin, CK5/6, Vimentin	Not Reported	Pleural	Biphasic	Chemotherapy (3 cycles vinorelbine before stopping treatment due progressive disease)	Deceased within 6 mths
14	2009 [18]	61/M	Face, posterior auricular	4 years	Calretinin (focally), Vimentin, CD10, Cytokeratin (CAM 5.2), SMA (focally)	CEA, TTF-1	Pleural	Sarcomatoid	Chemotherapy (6 cycles: pemetrexed, cisplatin), Radiotherapy	>37 mths disease free
15	2009 [19]	54/M	Scalp	8 mths	Calretinin, CK5/6	Not Reported	Pleural	Epithelioid*	Chemotherapy (pemetrexed, cisplatin x5 mths)	Not Reported
16	2009 [8]	65/M	Face, scalp, trunk	At time of diagnosis	Cytokeratin (MNF116), Vimentin	CEA, CD31, CD34, S100	Pleural	Biphasic	Not Reported	Deceased shortly after biopsy
17	2010 [26]	72/M	Abdomen	At time of biopsy	Calretinin, Pan-cytokeratin, WT1, CK7, CK20 (focal, weak)	B72.3, CDX2, Hep Par1, S100, MART-1, HMB-45. PAX2	Peritoneal	Epithelioid	Not Reported	Deceased shortly after biopsy
18	2011 [27]	75/M	Chest wall	8 mths	Calretinin, pan-cytokeratin, CK5/6, thrombomodulin, vimentin, HMBE-1, EMA, WT1, BerEP4	CEA, B72.3, MOC-1, SMA, CA125	Pleural	Epithelioid	Chemoradiation	Deceased within 19 mths
19	2013 [2]	55/M	Abdominal wall	At time of biopsy	Calretinin, CK5/6, CK7, WT1	TTF-1, EA, Napsin	Pleural	Epithelioid	Chemotherapy (6 cycles: pemetrexed, cisplatin)	Not Reported
20	Current Case (2017)	75/M	Upper back	4 mths	Calretinin, CK5/6, CK7, D2-40	TTF-1, CK20, Glut-1, PSA	Pleural	Epithelioid	Not Reported	Deceased within a week following cutaneous biopsy

*Subtype was inferred based on histologic description

Abbreviations: EMA, Epithelial Membrane Antigen; SMA, Smooth Muscle Actin; WT, Wilms' Tumor; CEA, Carcinoembryonic Antigen; UE, Ulex Europaeus lectin; HMB, Human Melanoma Black; MART, Melanocytic Antigen Recognized by cytotoxic T lymphocytes; TTF, Thyroid Transcription Factor; CDX, Caudal-related homeobox gene; PAX, Paired-box; CA, Cancer Antigen; PSA, Prostate-Specific Antigen; MTX, methotrexate; FU, fluorouracil