Primary Malignant Deciduoid Mesothelioma

A Challenging Diagnosis

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Primary malignant deciduoid mesothelioma is a rare subtype of epithelioid mesothelioma that was first described in the peritoneum in young women without a history of asbestos exposure. It was thought to be a distinct clinicopathologic entity with ominous prognosis; recent studies have better characterized this entity. On morphology, primary malignant deciduoid mesothelioma is characterized by cytomorphologic features resembling decidualized tissue. Pleomorphism is variable. The immunoprofile is similar to other epithelioid mesotheliomas. The prognosis is the same as other epithelioid mesotheliomas and seems to depend on histological grade.

Primary malignant deciduoid mesothelioma (PMDM) is an extremely rare variant of primary mesothelioma representing less than 5% of mesotheliomas.1 It was first described in 1985 by Talerman et al.2 However, the term deciduoid was first used in 1994 by Nascimento.3 This uncommon variant is characterized by cytomorphologic features resembling decidualized tissue3 and was initially thought to behave more aggressively than other epithelioid mesotheliomas.3

CLINICAL FEATURES

The first reported cases of PMDM suggested that this variant affects young women without a history of asbestos exposure and is exclusively located in the peritoneum.4 Some cases of PMDM that occurred during or after pregnancy suggested a potential role for hormonal changes.5 However, more-recent reviews showed that PMDM occurs in both sexes with a slight male predominance.4 Pleural, pericardial, and paratesticular deciduoid mesothelioma have been described; the pleural location was more common than in the peritoneum.4 In addition, this variant has been reported in a wide age range (8–75 years) and has also been associated with asbestos exposure.1,6–8

Clinical presentation and imaging are not specific. In most cases, patients presented with abdominal distension, chest pain, and anorexia. On imaging, pleural effusion with thickening of the pleura and ascites are the most common findings. Some cases were diagnosed on autopsy.1

HISTOLOGY

Decidual morphology can be focal, predominant, or seen in the entire tumor.1,9 Cells in PMDM are large, round or polygonal, with well-defined borders. They are arranged in solid sheets, trabeculae, and pseudopapillary structures. Their cytoplasm is typically abundant, glassy, and eosinophilic. The nucleus is vesicular with prominent nucleolus.7,9,10 Binucleation and multinucleation are not uncommon.9 Nuclear pleomorphism and pseudoinclu-
sions can be seen (Figure 1).1 The stroma is often fibrous or edematous.9 Mitotic activity varies as does the presence of abnormal mitotic figures.1

Some unusual features such as focal clear cytoplasm foamy cells; rhabdoid cells, or mucinous stroma have been reported.1

ANCILLARY STUDIES

Immunocytochemistry

The immunoprofile of PMDM is the same as other epithelioid mesotheliomas; cells usually have cytoplasmic expression for cytokeratin AE1/AE3, cytokeratin 7, and cytokeratin 5/6. Expression of cytokeratin AE1/AE3 and cytokeratin 7 is diffuse and strong.

Cytokeratin 7 results were negative in only 2 reported cases.4,11 Expression of cytokeratin 5/6 is usually patchy (Figure 2). Nuclear expression of Wilms tumor 1 is usually strong. Cells also express epithelial membrane antigen, podoplanin (D2-40) (Figure 3), and mesothelin; the expression is membranous. Calretinin expression is both cytoplasmic and nuclear (Figure 4).1,12,13

Cytogenetics

Cytogenetic studies performed on patients with PMDM showed band aberrations on 1p, 12q, 17, 8q, 19, and 20,14 which are mostly chromosomal gains. Dominak et al.11 reported the first case of translocation with 2 balanced translocations: t(1p;12q) and t(16p;16p).
Electron Microscopy

On ultrastructural examination, PMDM cells show characteristic mesothelial microvilli.\textsuperscript{1,8,11,12} Electron microscopy also reveals many intermediate filaments; those filaments give a glassy eosinophilic appearance to the cytoplasm on hematoxylin-eosin slides. It also demonstrates the cytoplasmic nature of the nuclear pseudoinclusions.\textsuperscript{7,12}

**DIFFERENTIAL DIAGNOSIS**

Immunochemistry combined with morphology is a valuable tool for ruling out diseases in the differential diagnosis. Indeed, PMDM can be confused with a subset of tumors including carcinomas, melanoma, anaplastic large cell lymphomas, rhabdomyosarcoma, and gastrointestinal stromal tumors. A panel of 2 mesothelioma markers and 2 negative markers depending on the differential diagnosis being considered is recommended.\textsuperscript{13}

Trophoblastic neoplasia and pseudotumoral deciduosis should also be considered in the differential diagnosis in women with peritoneal PMDM.

Pseudotumoral deciduosis is a rare, benign condition, most commonly seen in pregnant women with twins.\textsuperscript{15} It is associated with high progesterone levels. This condition can also be seen in postmenopausal women from adrenal secretion of progesterone.\textsuperscript{16} Cells in pseudotumoral deciduosis show less atypia and pleomorphism than does PMDM with no mitotic figures.\textsuperscript{1,9} Expression of estrogen and progesterone receptors and \(\alpha\)-inhibin by decidual cells in pseudotumoral deciduosis is also discriminative because those markers are negative in PMDM.\textsuperscript{1,14} Cytokeratin, however, is not a useful marker because it can be expressed in both PMDM and pseudotumoral deciduosis.\textsuperscript{17}

Although a subset of mesothelioma expresses human chorionic gonadotropin, no case of human chorionic gonadotropin–positive deciduoid mesothelioma has been reported. Thus, that marker helps differentiate between PMDM and trophoblastic neoplasia.\textsuperscript{1,18}

Large cells with eosinophilic cytoplasm can be seen in oxyphilic clear cell renal cell carcinomas. Positivity of PAX8, PAX2, and claudin 4 are suggestive of a renal origin.\textsuperscript{1,13} Metastatic adenocarcinomas, particularly pleomorphic lung

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**Figure 1.** Deciduoid mesothelioma. Tumor cells with distinct borders arranged in sheets, glassy and eosinophilic cytoplasm, and vesicular and pleomorphic nuclei with prominent nucleoli, and frequent binucleations and multinucleations (hematoxylin-eosin, original magnification \(\times 40\)).

**Figure 2.** Patchy expression of cytokeratin 5/6 (clone DS/16B4) (original magnification \(\times 40\)).

**Figure 3.** Membranous expression of podoplanin (clone D2-40) (original magnification \(\times 40\)).

**Figure 4.** Nuclear and cytoplasmic reactivity to calretinin (clone DAK-Calret1) (original magnification \(\times 40\)).
carcinoma, should also be included in the differential diagnosis. Immunohistochemistry stain with carcinoembryonic antigen, BER-EP4/EpCAM, thyroid transcription factor 1, and napsin A combined with mesothelial markers discriminates these 2 entities.\textsuperscript{1,13} The large polygonal cells with pleomorphic nuclei seen in anaplastic large cell lymphoma can mimic decidual mesothelioma cells especially when they lose CD45 expression and express epithelial membrane antigen.\textsuperscript{20} Epithelial membrane antigen–positive anaplastic large cell lymphoma is usually CD30- and anaplastic lymphoma kinase–positive and show the classic anaplastic lymphoma kinase translocation t(2;5)(p23;q35) in 80% of cases.\textsuperscript{20} However, pathologists remember that a small subset of mesotheliomas has shown a positive reactivity to CD30 and that anaplastic large cell lymphomas may rarely express cytokeratin (pan).\textsuperscript{18,21}

Additional markers can be tested when metastatic melanoma, rhabdomyosarcoma, or gastrointestinal stromal tumors are suspected. These include S100, human melanoma black 45, and Melan-A for metastatic melanoma; CD117 and DOG1 for gastrointestinal stromal tumors; and desmin, myogenin, and MYOD1 for rhabdomyosarcoma.\textsuperscript{1,9,13,22}

**CURRENT TREATMENT**

Treatment of patients with PMDM is the same as treatment of other subtypes of diffuse mesothelioma and is based on cytoreductive surgery combined with chemotherap\textsuperscript{22,23}. Cisplatin and pemetrexed are considered first-line treatment because they have shown significant survival advantage.\textsuperscript{24} Extensive debulking surgery with intraoperative chemotherapy is associated with better survival, especially in patients without lymph node metastases.\textsuperscript{7,25} Radiation therapy seems to be associated with less recurrence after surgery and could be a part of a trimodal therapy.\textsuperscript{29}

**PROGNOSIS**

Although it was thought that PMDM behaves more aggressively than conventional epithelioid mesotheliomas, it seems that this particular variant does not have a worse outcome.\textsuperscript{1,8} However, a subgroup of PMDM showing marked pleomorphism, decreased cell cohesion, atypical mitotic figures, and high mitotic rate (>5 mitosis/10 high-power fields) seems to have a highly aggressive clinical course.\textsuperscript{3} Hence, grading decidual mesothelioma and including that grade in the pathology report may best influence patient treatment and outcome.\textsuperscript{1,13}

**CONCLUSIONS**

We highlight a particular variant of epithelioid mesothelioma. Pathologists should be aware of this rare malignancy because high-grade PMDM can carry a poor outcome. It also can be easily confused with other neoplastic and nonneoplastic peritoneal lesions.

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