Myxoid variant of peritoneal epithelioid malignant mesothelioma. A case report

Barbara Goldová[1], Pavel Dundr[1], Michal Zikán[2] , Věra Tomancová[3]

[1] Department of Pathology, First Faculty of Medicine and General University Hospital, Charles University in Prague, Czech Republic
[2] Oncogynecological Centre, Department of Obstetrics and Gynecology, First Faculty of Medicine and General University Hospital, Charles University in Prague, Czech Republic
[3] Department of Oncology, First Faculty of Medicine and General University Hospital, Charles University in Prague, Czech Republic

SUMMARY

The myxoid variant of a diffuse malignant epithelioid mesothelioma is a rare tumor. To the best of our knowledge, only three cases of this type of mesothelioma involving the peritoneum have been reported in the literature to date. Although it is rare in the peritoneal cavity, it should be included in the differential diagnosis of the more common myxoid/mucinous abdominal lesions (e.g. mucinous carcinomas or pseudomyxoma peritonei), which can myxoid MM mimic. We report the case of a 60-year-old female with a myxoid variant of malignant peritoneal mesothelioma. Histologically, the tumor consisted of medium-sized to large epithelioid cells with a moderate to abundant amount of eosinophilic cytoplasm. Some of the tumor cells contained intracytoplasmic, optically clear vacuoles. The nuclei were irregular with coarse chromatin and some exhibited prominent nucleoli. Some of the cells were multinucleated. Mitotic figures were rare. Most of the tumor cells were located within an ample myxoid background. Immunohistochemically, the tumor cells showed a diffuse positivity for cytokeratin cocktail AE1/AE3, calretinin, D2-40, and cytokeratin 7. Vimentin, HBME-1 and WT-1 were only focally positive. Progesterone receptors showed positivity in rare tumor cells (up to 5%). Other markers examined, including cytokeratin 20, estrogen receptors, BerEP4, CEA, TTF-1, GCDFP-15, and CD15 were negative.

Keywords: malignant mesothelioma – myxoid variant – peritoneum

Myxoidní varianta epiteloidního maligního mezoteliomu peritonea. Popis případu.

SOUHRN

Myxoidní varianta difuzního epiteloidního maligního mezoteliomu je vzácná. Ke dnešnímu datu byly popsané pouze tři případy tohoto typu mezoteliomu, který postihoval peritoneum. Přestože jde o vzácný tumor v peritoneální dutině, měl by být zahrnutý do diferenciální diagnózy myxoidních / mucinózních břišních lézí, které myxoidní MM můžou imitovat. Uvádíme případ 60-ti leté pacientky s myxoidní variantou maligního mezoteliomu peritonea. Histologicky nádor sestával ze středně velkých až velkých epiteloidních buněk se středním až hojným množstvím eosinofilní cytoplasmy. Některé z buněk obsahovali intracytoplasmaticky opticky prázdné vakuoly. Jádra buněk byla nepravidelná s hrubým chromatinem, některá obsahovala prominentní jadérka. Některé z buněk byly vícejaderné. Mitózy byly patrné řídce. Většina buněk byla rozprostřená na myxoidním pozadí. Imunohistochemicky nádorové buňky vykazovali difuzní pozitivitu koktejlu cytokeratinů AE1/AE3, kalretininu, D2-40 a cytokeratinu 7. Vimentin, HBME- 1 a WT-1 byly pozitivní jen fokálně. Progesteronové receptory vykazovali pozitivitu v ojedinělých buňkách (do 5%). Ostatné vyšetřované markery jmenovitě cytokeratin 20, estrogenové receptory, BerEP4, CEA, TTF-1, GCD-FP-15 a CD15 byly negativní.

Klíčová slova: maligní mezoteliom – myxoidní varianta – peritoneum

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Malignant mesothelioma (MM) is a rare tumor that usually occurs in the pleura or peritoneum (1). On rare occasions, this tumor can be found in the tunica vaginalis of the paratesticular region, hernia and hydrocoele sacs, or in the pericardial cavity (2,3). The morphology of MM is very heterogeneous and various subtypes have been described, including one with prominent myxoid change. Myxoid MM is rare, however, and only 23 cases of this type of tumor has been reported to date, including one series of 19 cases and four single case reports (2,4-6). Most of the reported cases involved the pleural cavity (5), but one occurred in the pericardium (4), and another three in the peritoneum (4,6). The survival rate of patients with myxoid MM appears to be better than that of epitheloid MM in general (5). We have described an additional case of a primary peritoneal epitheloid MM with a prominent myxoid change, including its clinico-pathological and immunohistochemical features.

✉ ***Correspondence address:***
Barbara Goldová, MD
Department of Pathology, First Faculty of Medicine and General University Hospital, Charles University in Prague, Studničkova 2, Prague 2, 12800, Czech Republic
phone: +420224968665, Fax: +420224911715
email: barbara.goldova@vfn.cz

CASE REPORT

A 60-year-old woman suffering from weight loss, abdominal pain and distension lasting for 4 months was referred to the Oncogynecological centre from the regional hospital. The serum CA 125 showed high levels (up to 154.2 kIU/l). A computerized tomography (CT) scan and an ultrasound revealed a left adnexal mass, a tumorous infiltration of the omentum (omental cake), and parietal carcinomatosis in the pelvis and on the diaphragm.

The adnexal mass was considered to be of potential primary origin and the patient was referred to open surgery (laparotomy), with no radiotherapy or chemotherapy beforehand. A macroscopic finding in the abdominal cavity confirmed the presence of ascites (5000 ml), omental cake and a tumor mass in the abdominal wall in the left lower quadrant (described on im-

aging as an "ovarian" mass), a massive nodular spread (nodules up to 1 cm) over the diaphragm, visceral and parietal peritoneum in the entire abdominal cavity and on both ovaries. A frozen section during the procedure revealed a malignant tumor of uncertain origin. A hysterectomy with bilateral oophorectomy and total omentectomy were performed as debulking, and a nodular carcinomatosis had been left as a residual disease.

After the final diagnosis of the malignant mesothelioma, the patient was referred to a clinical oncologist and received two cycles of chemotherapy. Presently, she is alive eight months after the diagnosis with signs of generalized disease and on symptomatic treatment only.

MATERIALS AND METHODS

Sections from formalin-fixed, paraffin-embedded tissue blocks were stained with hematoxylin-eosin. Immunohistochemical staining was performed using the avidin-biotin complex method with antibodies directed against the following antigens: cytokeratin cocktail AE1/AE3 (1:50, Dako, Glustrup, Denmark), calretinin (1:50, Dako), cytokeratin 7 (1:200, Dako), cytokeratin 20 (1:100, Dako), vimentin (1:50, Dako), TTF-1 (1:100, NeoMarkers, Fremont, CA, USA), MIB-1 (1:50, Dako), HBME-1 (1:50, Dako), WT-1 (1:100, Thermo scientific), D2-40 (1:100, Dako), progesterone receptors (1:100, Novocastra), estrogen receptors (1:20, Novocastra), BerEP4 (1:50, Dako), CEA (1:100, Dako), GCDFP-15 (1:40, Signet), and CD15 (1:40, Dako).

RESULTS

Grossly, the resected specimen consisted of part of the omentum (size 40 x 20 x 5-10 mm), which was replaced by a gelatinous tumor. In the cross section, some cystic spaces were filled with mucoid substance.

Histologically, the tumor consisted of dyscohesive medium-sized to large epithelioid cells with a moderate to abundant amount of eosinophilic cytoplasm (Fig. 1). Some of the tumor cells contained intracytoplasmic, optically clear vacuoles. The nuclei were irregular with coarse chromatin and some exhibited prominent nucleoli (Fig. 2). Some of the cells were multinucleated. Mitotic figures were rare (up to 1/10 HPF). Most of the tumor cells were located within an ample myxoid background, which was alcian blue positive (Fig. 3).

Immunohistochemically, the tumor cells showed diffuse positivity for cytokeratin coctail AE1/AE3, D2-40 (Fig. 4), cytokeratin 7, and calretinin (Fig. 5). Vimentin, HBME-1 and WT-1 were only focally positive. Progesterone receptors showed positivity in rare tumor cells (up to 5 %). Other markers examined, including cytokeratin 20, estrogen receptors, BerEP4, CEA, TTF-1, GCDFP-15, and CD15 were negative. Examination of proliferative activity with a monoclonal antibody MIB-1 showed nuclear positivity in only 2-3% of the tumor cells.

DISCUSSION

Malignant mesothelioma represents a tumor with a heterogeneous morphology. Based on histological features, MM can be divided into three main categories: epithelioid, sarcomatoid, and biphasic (mixed) types (7-9). Epithelioid MM shows several growth patterns, including tubulo-papillary, acinar, adenomatoid (microcystic), sheet-like, with psammomatous microcalcifications and diffuse (4,7). Less common variants of the epithelioid MM include deciduoid, small cell, clear cell, signet ring (lipid-rich), adenoid cystic type, glomeruloid and myxoid (10). Variants of the

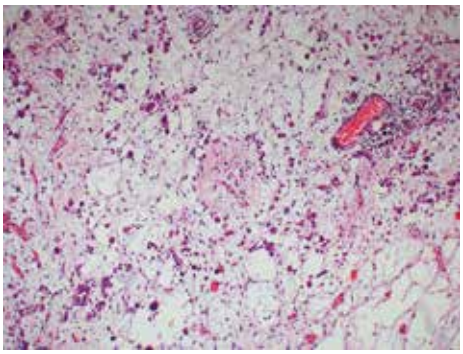

Fig. 1. Myxoid malignant mesothelioma consisted of dyscohesive medium-sized to large epitheloid cells (H&E, 100x).

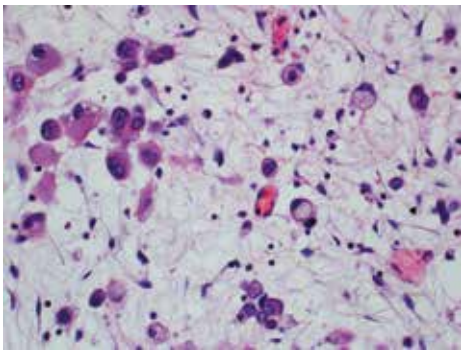

Fig. 2. Tumor cells with a moderate to abundant amount of eosinophilic cytoplasm. Note the irregular nuclei and focal cytoplasmic vacuolalisation (H&E, 400x).

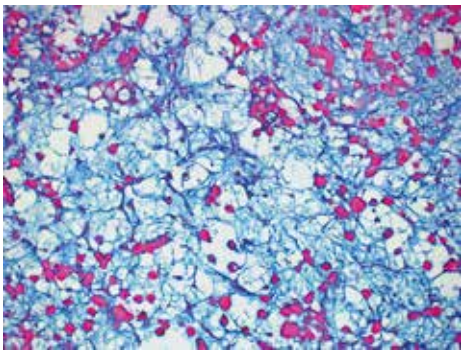

Fig. 3. Tumor cells located in ample myxoid alcian blue positive background (200x).

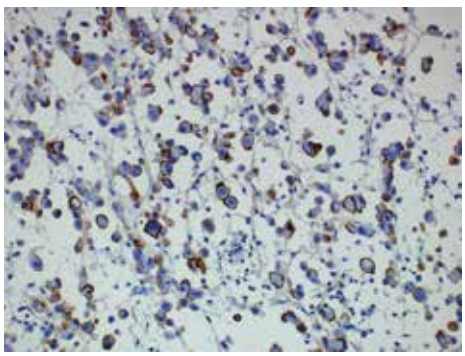

Fig. 4. Tumor cells showing membranous immunopositivity for D2-40 (200x).

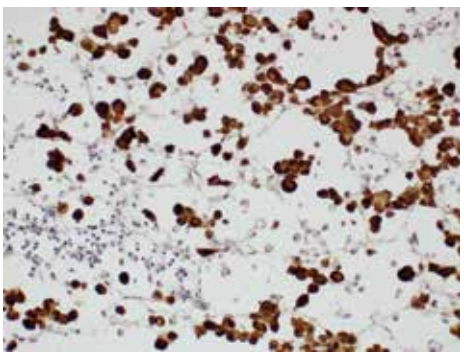

Fig. 5. Tumor cells immunopositivity for calretinin (200x).

sarcomatoid histotype include fibrosarcomatous or malignant fibrous histiocytoma-like, MM with divergent differentiation (e.g. osteochondroid, myogenous, rhabdoid and angiomatoid), lymphohistiocytoid (lymphoma-like), and desmoplastic (10). Moreover, a rare pleomorphic variant associated with highly aggressive clinical behavior was described (11). Other unusual features of MM are lymphoid follicles, prominent foamy histiocytes and striking vascular proliferation (pseudovascular) (4,7). The myxoid variant of epitheloid MM is rare; only 23 cases of myxoid MM have been reported to date. One of them was a localized form of tumor in the pericardium (2), 19 were found in the pleural cavity (5), and only two were found in the peritoneum (4). Moreover, one report described a single case of benign papillary mesothelioma of the peritoneum with prominent myxoid change (6). Myxoid mesotheliomas have retained the secretory activity of normal mesothelium, and one characteristic feature of all reported cases, as well as our own, is the presence of an ample myxoid background, which is Alcian blue positive.

The heterogeneous morphology of MM may raise a broad differential diagnosis and these tumors are difficult to diagnose by morphological features alone. To achieve a correct diagnosis, a panel of immunohistochemical stains should be used. This panel should include some of the positive markers such as calretinin, HBME-1, WT-1, cytokeratin 5/6 and D2-40 in combination with some of the negative markers such as CEA, BerEP4, MOC-31, B72.3, and BG-8 (12-14). Generally, a differential diagnosis of MM is broad and has been discussed in detail elsewhere (4).

Regarding diffuse MM with myxoid change, this tumor should be included in the differential diagnosis of other myxoid lesions of the peritoneum, particularly pseudomyxoma peritonei, or metastases of mucinous adenocarcinoma (6). In a limited sample, other myxoid tumors, including soft tissue lesions, should be considered in the differential diagnosis as well.

The prognosis of MM is generally poor. Diffuse MM is an almost universally fatal tumor resistant to all treatment modalities for reasons that are still unknown (9,15-17). However, according to some authors, the behavior of peritoneal mesotheliomas is not always aggressive, but there are no universally accepted morphological features which can be reliably correlated with the behavior. Some studies suggest that a small nuclear size is the only good independent prognostic determinant (1). Others consider the Ki-67 labeling index to be a useful prognostic indicator for MM of the peritoneum (15). According to reported cases, the survival rate of patients with myxoid MM appears to be better than that of epitheloid MM in general (5). The tumor cells of myxoid MM were always epitheloid, without significant atypia, and mitoses were not common, just like in our case (2). No dominant therapeutic guidelines for MM currently exist: surgery and chemotherapy have been used with relative success, and the median survival rate is usually less than 1 year from the date of diagnosis.

In conclusion, we have described an additional case of a primary myxoid epitheloid MM occurring in the peritoneum. Because of varying prognosis and therapeutical approaches, this tumor should be included, despite its rarity, in the differential diagnosis of the more common myxoid peritoneal lesions, particularly pseudomyxoma peritonei.

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