Case #2

Clinical History
A 54 year old male presented with a chief complaint of intermittent abdominal discomfort and increasing abdominal fullness for a period of one year. Physical examination was significant for a mildly distended, non-tender abdomen. Imaging studies showed a large abdominal mass filling the entire peritoneal cavity. Surgical debulking of the abdominal tumor was subsequently performed.

Pathologic Findings
Gross examination revealed a multiloculated cystic mass measuring 40.0 cm in greatest dimension, involving the omentum and attached to the serosa of the right colon. The mass was comprised of numerous, translucent cysts ranging from 0.1 cm to 6.0 cm in diameter, filled with clear fluid. The cysts were thin walled and had uniformly smooth linings. No hemorrhage, necrosis, or solid areas were identified. Microscopic examination showed multiple cystic spaces lined by a single layer of flattened or cuboidal cells. Occasional lining cells also exhibited a hobnail type appearance. The cells were cytologically bland with no significant pleomorphism or mitotic activity identified. The cystic spaces were separated by an edematous, fibroblastic appearing stroma with scattered chronic inflammatory cells. Localized proliferations of cells embedded within the inflammatory stroma were observed focally. By immunohistochemistry, the cells lining the cysts expressed keratin, keratin 7, WT-1, and calretinin, and were negative for CD31 and CD34.

Diagnosis
Multicystic Mesothelioma

Multicystic mesothelioma is a well recognized, but uncommon lesion of the serosal membranes. [1-10] Other terms used to describe this particular entity include cystic mesothelioma, multilocular peritoneal inclusion cyst, peritoneal cystosis, postoperative peritoneal cysts, and multicystic mesothelial proliferation. Although this lesion has the potential to develop in all serosal cavities, it occurs most commonly in the peritoneal cavity, with only rare isolated cases reported in the pleura, [11] pericardium, [12] and tunica vaginalis. [13] Most cases occur in young to middle aged females. Presenting symptoms are nonspecific, and can include abdominal pain, distention, or a palpable mass.

The exact etiology and pathogenesis of multicystic mesothelioma is unknown, and controversy exists regarding the classification of the lesion as a reactive or neoplastic condition. In many patients, multicystic mesothelioma is associated with a history of previous abdominal surgery, pelvic inflammatory disease, or endometriosis, suggesting the lesion develops as a reactive inflammatory response to chronic serosal irritation. [6, 8-10] Evidence supporting a neoplastic nature of this entity includes progressive growth of the lesion if left untreated, the marked tendency of the lesion to recur following resection, and a rare documented case of malignant transformation of otherwise typical histologically benign appearing multicystic mesothelioma. [2, 7, 14]

Grossly, multicystic mesothelioma is characterized by numerous thin walled translucent cysts, which can range in size from a few millimeters to several centimeters in diameter. The cysts are often grouped together to form a confluent mass, but may also appear as isolated cysts studding the visceral and parietal serosal surfaces. The lesion can manifest as a discrete localized mass, or as multiple nodules diffusely involving the serosa. The cysts generally contain clear, watery fluid. The cyst linings are smooth, and lack areas of solid or papillary growth.
Histologically, multicystic mesothelioma is comprised of cystic spaces of variable size lined by a single layer of flattened to cuboidal mesothelial cells. Occasionally, the lining cells have a more prominent hobnail appearance. The constituent mesothelial cells are cytologically bland and lack significant pleomorphism. Rare mitotic figures may be observed, but are considered an unusual finding. The cysts are separated by connective tissue septa, which may have a variable appearance. The stroma between the cysts may be rather scant, consisting of mature collagen and thin walled capillaries, or alternatively, can appear more prominent and contain numerous fibroblasts as well as areas of fibrosis and hyalinization. Secondary inflammatory changes are not uncommon, characterized by an edematous, fibroblastic appearing stroma containing scattered inflammatory cells. In such cases, nodules of hyperplastic mesothelium entrapped within the inflammatory stroma may be seen (so called mural mesothelial proliferation). [6] The mesothelial cells in this setting can form glands, nests, and cords, and display cytologic atypia, imparting an appearance resembling infiltrating carcinoma or malignant mesothelioma. A subset of cases will display areas of adenomatoid change characterized by nested collections of vacuolated mesothelial cells similar to those seen in adenomatoid tumors, or squamous metaplasia of the lining mesothelium. Immunohistochemically, the cells lining the cysts express markers of mesothelial differentiation including calretinin, WT-1, and keratin 5/6. By electron microscopy, the cells also display ultrastructural features of mesothelial cells including prominent surface microvilli, tonofilaments, and desmosomal junctions.

The differential diagnosis of multicystic mesothelioma includes several other cystic lesions of the peritoneum. Multicystic mesothelioma is most often confused with intraabdominal cystic lymphangioma. Cystic lymphangiomas occur most frequently in the head and neck or axilla; intraabdominal lymphangiomas, in contrast, are quite rare, comprising less than 5% of all lymphangiomas. The tumor is observed primarily in the pediatric population, with presentation in adulthood considered a rare occurrence. Similar to multicystic mesothelioma, lymphangioma is composed of variably sized cystic spaces lined by a single layer of cytologically bland epithelium. The cysts comprising lymphangioma are lined by flat, attenuated endothelial cells that lack the more plump cuboidal appearance of the mesothelial cells seen in multicystic mesothelioma. Lymphangioma can also be distinguished histologically from multicystic mesothelioma by the frequent presence of lymphoid aggregates and poorly developed fascicles of smooth muscle in the cyst walls. In diagnostically difficult cases, immunohistochemistry can assist in separating these two entities as lymphangioma positively expresses endothelial markers such as CD31, CD34, and factor VIII related antigen, and is negative for keratin, while the opposite is true of multicystic mesothelioma. Differentiation between multicystic mesothelioma and lymphangioma is important from a clinical standpoint as the latter rarely recurs following surgical excision.

Solitary mesothelial inclusion cysts are not infrequent incidental findings at the time of abdominal surgery. They are generally observed attached to the mesentery or omentum. Solitary mesothelial inclusion cysts differ from multicystic mesothelioma in that grossly they are small, unilocular, localized lesions that do not produce clinical symptoms. Histologically, the unilocular mesothelial cyst is lined by a single layer of flattened mesothelial cells, identical in appearance to those of multicystic mesothelioma. Thus, distinction between the two lesions is based primarily on differences in macroscopic appearance.

Other considerations in the differential diagnosis of multicystic mesothelioma include more uncommon entities such as mullerian cyst of the retroperitoneum [15, 16] and florid cystic endosalpingiosis. [17] Retroperitoneal cysts with mullerian type differentiation are extremely rare. Hypotheses regarding the origin of these cysts include derivation from mullerian duct remnants, specialized cells of the urogenital ridge, metaplasia of the coelomic
epithelium lining the peritoneum, and ectopic ovarian tissue. Mullerian cysts typically manifest as a large localized abdominal mass involving the retroperitoneum, unattached to any pelvic or abdominal viscera. The cyst may be uni- or multilocular, and has a smooth lining. Histologically, the cyst lining is most often composed of ciliated cuboidal to columnar cells. Tubal and mucinous type lining epithelium has also been reported. Smooth muscle bundles are also often seen beneath the lining epithelium. These features serve to distinguish mullerian cyst of the retroperitoneum from multicystic mesothelioma, which lacks ciliated and mucinous cells and smooth muscle in the cyst walls. Although endosalpingiosis is almost always an incidental microscopic finding, rare unusual cases of cystic endosalpingiosis involving the peritoneum which presented as grossly apparent masses have been reported. [17] These cases have manifested as multiple cysts involving the peritoneum and serosal surfaces of abdominal and pelvic organs, simulating the macroscopic appearance of multicystic mesothelioma. The distinction between cystic endosalpingiosis and multicystic mesothelioma is readily made on microscopic examination; the former is lined by simple columnar epithelium displaying tubal type differentiation comprised of ciliated cells, secretory cells, and peg cells, while the latter is lined exclusively by flattened to cuboidal mesothelial cells.

Multicystic mesothelioma should not be confused with malignant mesothelioma. This differential diagnosis is rarely a problem as the two entities exhibit marked differences in macroscopic appearance. Unlike multicystic mesothelioma, malignant mesothelioma grossly manifests as solid plaques or nodules and never displays a predominantly cystic appearance. As discussed above, some multicystic mesotheliomas with inflammatory changes may be associated with a proliferation of mesothelial cells within the walls of the cysts. This reactive mesothelial hyperplasia, which can appear worrisome histologically, should not be interpreted as evidence of malignant mesothelioma.

The prognosis of multicystic mesothelioma is considered excellent, although recurrence of disease is frequently observed, with a local recurrence rate of approximately 50% following therapy. There has only been one reported case of death attributed directly to disease, which occurred in a patient who refused treatment. [7] Transformation of multicystic mesothelioma to diffuse malignant mesothelioma has also been observed in one patient following multiple recurrences over a period of ten years. [14] No clinical or histopathologic factors predictive of recurrence have been identified. Surgical resection remains the mainstay of treatment for multicystic mesothelioma. This generally involves complete surgical excision of localized lesions or debulking procedures for more extensive disease. Adjuvant systemic chemotherapy and/or radiation therapy are generally not indicated, though cytoreductive surgery combined with intraperitoneal chemotherapy to eradicate microscopic residual disease has been shown to be effective in a small series of patients. [18]

References


