Sarcomatous malignant peritoneal mesothelioma with large bowel involvement

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Abstract

Sarcomatous malignant peritoneal mesothelioma developing in the abdominal cavity is very rare, and little is known about its behavior. A 72-year-old woman was referred to our hospital with anemia and weight loss. Tumor marker levels were within normal limits. Abdominal computed tomography showed an 11×7 cm tumor in the pelvis, with possible invasion of the large bowel. Colonoscopy revealed a tumor protruding into the cecal lumen with an ulceration of the cecal wall. Although malignancy was suspected, the histological type was not identified in the biopsy specimens. Right hemicolectomy and ileocolic anastomosis were performed as a treatment. A postoperative histopathological examination confirmed the initial diagnosis of malignant mesothelioma. Finally, immunohistochemical examination revealed a localized sarcomatous malignant peritoneal mesothelioma with regional lymph node metastases. The patient followed up postoperatively as an outpatient, and local recurrence was detected in the abdominal cavity 11 months after surgery. In conclusion, localized malignant peritoneal mesothelioma, especially the sarcomatous type, with large bowel involvement is very rare. We should carefully consider the diagnosis and select adequate therapy, because little is known about the behavior of this disease.

Introduction

Malignant peritoneal mesothelioma (MPM) is an uncommon tumor of the serous membrane lining the abdominal cavity. Little is known about the disease behavior of MPM. We experienced a case of localized MPM with large bowel involvement and with a sarcomatous histological appearance. Here we report this case of sarcomatous MPM because such cases are very rare in the literature.

Case Report

A 72-year-old woman was referred to our hospital for evaluation of anemia and weight loss. She had no history of serious illness, surgery, or hospitalization. Her brother had died of rectal carcinoma. Laboratory data at the outpatient department showed anemia (Hb, 6.4 g/dL) and hypalbuminemia (serum albumin, 1.8 g/dL). The tumor marker levels of carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9) were within normal limits. On palpation, there was an ill-defined, firm, mobile tumor in the right lower abdomen. Abdominal computed tomography (CT) showed an 11×7-cm tumor in the pelvis (Figure 1). The tumor seemed to invade the large bowel directly. A colonoscopy revealed a tumor protruding into the cecal lumen with an ulceration of the cecal wall (Figure 2). A histological examination of biopsy specimens taken from the ulcer margin revealed a non-epithelial malignant tumor. However, it was impossible to identify the histological type.

The patient underwent surgery to remove the tumor in April 2000. On exposure of the peritoneal cavity, two small nodules were seen; one each in the greater omentum and the small intestinal mesentery. However, the peritoneal surface appeared intact, and ascites cytology was negative for tumor cells. An ill-defined hard mass (15×11 cm) was identified near the cecum, and it involved both the cecum and ascending colon. Regional lymph nodes were enlarged on palpation and were suspected to be metastases of the tumor. A right hemicolectomy and ileocolic anastomosis were performed as a radical treatment.

A postoperative histopathological examination confirmed the initial diagnosis of malignant mesothelioma. The tumor showed an expansive growth and was well-demarcated from the surrounding connective tissue (Figure 3). Histological examination revealed that the tumor was composed of three types of tumor cells: large polygonal tumor cells with eosinophilic cytoplasm, spindle tumor cells in an intertwined pattern, and tumor cells in a trabecular and/or glandular pattern. The majority of the tumor consisted of large polygonal/spindle tumor cells. These tumor cells showed pleomorphism as well as anisokaryosis, hyperchromatic nuclei, and prominent nucleoli. Sections of the tumor tissue showed degeneration, necrosis, and lymphoplasmacytic infiltration along with infiltration of histiocytes and multinucleated foreign-body giant cells (Figure 4).

Immunohistochemical examination revealed large polygonal/spindle tumor cells that were positive for mesenchymal markers, as well as tumor cells in a trabecular/glandular pattern that were positive for epithelial markers as follows: CEA (-), epithelial membrane antigen (EMA) (+), mesothelioma antibody HBMA-1 (+), thrombomodulin (+), cytokeratin (+), vimentin (+), and calretinin (+). Less than 10% of the tumor in area showed tumor cells in a trabecular/glandular pattern. Based on the histopathological finding and result of phenotypical expression analysis by immunohistochemical examination, the tumor was diagnosed as a sarcomatous type of malignant mesothelioma. A large body of the dissected lymph nodes showed metastasis of the tumor deposits (Figure 5).

There were no peri-operational complications. Adjuvant therapy was not administered because the patient did not want further therapy, and she was followed up as an outpatient. Local recurrence in the abdominal cavity occurred 11 months after surgery.

Discussion

MPMs arising from the serous membranes of the abdominal cavity are known to be invasive tumors with a poor prognosis.

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Approximately 2500 cases of diffuse peritoneal mesothelioma were diagnosed per year, and diffuse MPM accounts for 10-20% of all forms of malignant mesothelioma diagnosed in the United States.1

Morphological and histological type of malignant peritoneal mesothelioma

MPM is generally classified into two main morphological types: a diffuse type and a localized type. Localized MPM is very rare compared to the diffuse type. Some authors have reported cases of localized malignant mesothelioma. Allen et al.2 reported the full details of localized malignant mesothelioma including MPM. Localized MPM arising from the peritoneum occurred in only two (4%) of 23 cases, and the purely sarcomatous type occurred in only one. The characteristics of recurrent localized malignant mesothelioma are different from those of diffuse malignant mesothelioma. Allen et al.3 concluded that these two types can be distinguished because the former has a localized presentation, contrasting biologic behavior, and improved prognosis. Regarding the microscopic appearance, the histological type of malignant mesothelioma is usually classified into four main categories: epithelial, sarcomatous, biphasic (mixed), and undifferentiated type, by immunohistochemical tests using epithelial membrane antigen (EMA), Wilms’ tumor 1 antigen (WT-1), cytokeratin 5/6, human mesothelial cell 1 (HBME-1), mesothelin and negative staining for CEA, B72.3, MOC-31, TTF-1, and Ber-EP4. The sarcomatous component is observed in 25% of MPM but a pure sarcomatous type is very rare.3,4 Bridda et al.5 noted only 32 cases had been reported in the literature up until 2006. In another study, Yan et al.6 noted that there was no sarcomatous type in 62 cases, whereas 92% were epithelial and 8% were mixed type. Recent reports of sarcomatous malignant mesothelioma are presented in Table 1.

Diagnosis

Early diagnosis of MPM is difficult when based on clinical symptoms and laboratory tests. Although patients with MPM complain of various symptoms such as distention and a sense of fullness, abdominal pain, abdominal mass, and anorexia, these are not characteristic of MPM. The CA 125 level is elevated in the majority of patients with diffuse MPM, while levels of CEA and CA 19-9 are normal. However, these indicate that CA 125 elevation is not a valid criterion to exclude diffuse MPM from the diagnosis.7 Serum mesothelin-related protein (SMRP) has recently been considered as a potentially useful serum marker for diagnosis and follow-up, because it is elevated in more than 84% of patients with mesotheliomas and has a sensitivity of 60%.8-10 A biopsy is very useful for the diagnosis of MPM, and if appropriate tumor tissue samples are obtained, the MPM diagnosis rate may be as high as 80%.11 Laparoscopic biopsy rather than surgical exploration is recommended because it is minimally invasive, and can be used for disease staging and selection of surgical candidates. The experts stated that a preoperative CT scan is useful to evaluate tumor extent, while there was no significant consensus about the role of colonoscopy, endogastroduodenoscopy, and positron emission tomography scans.12 It is important to evaluate the disease distribution, especially when making a distinction between the localized and diffuse types. Sugarbaker et al.13 noted that there are three types of CT scan appearances. A “dry-painful” type is the most common, in which a CT scan...
reveals one large mass or multiple small peritoneal masses in one quadrant, with no sign of ascites. The “wet” type is associated with intestinal distension and ascites, widespread small nodules and plaques, but no solid masses. In addition, there is the “mixed” type. Preoperative CT scan findings of a tumor size of >5 cm or loss of normal small bowel architecture and its mesentery are important for adequate cytoreduction.\(^4\) In our patient, the angiography and colonoscopy were performed for diagnosis. A superior mesenteric artery angiography showed that the tumor had a feeding artery from the ileocecal artery, and a colonoscopy revealed a tumor protruding into the cecal lumen with an ulceration of the cecal wall. Invasive MPM protruding into the intestinal lumen is very rare, and the invasion into the mucosal membrane has been identified histologically in only four cases.\(^5\) We suspected a gastrointestinal malignancy in our patient from these findings, but we could not diagnose MPM. Our case is only the second reported in the literature as being identified during a colonoscopy.\(^6\)

Immunohistochemical panels are integral to diagnosis of malignant mesothelioma. In peritoneal mesothelioma, the frequently positive mesothelial markers are assessed in comparison with those for gastric, pancreatic, colon, and ovarian carcinoma, and less often for lobular breast carcinoma.\(^7\) For differentiating malignant mesothelioma from nongynecologic adenocarcinoma, calretinin and Wilms’ tumor 1 antigen (WT-1) are known to be very useful positive markers; D2-40 is considered a potentially useful positive marker; and CEA, MOC-31, BG8, and B72.3 are considered useful negative markers.\(^8\) A combination of positive cytokertatin expression and calretinin seems to be highly characteristic of sarcomatoid malignant mesothelioma;\(^9\) however, cytokertatin and calretinin immunohistochemistry does not always discriminate between malignant mesotheliomsa versus synovial sarcomas and spindle cell carcinoma.\(^10\) Therefore, it is necessary to consider age and tumor location (diffuse or localized).

In our case, less than 10% of the tumor in area showed tumor cells in a trabecular/glandular pattern: CEA (-), EMA (+), HBMA-1 (+), thrombomodulin (+), cytokertatin (+), calretinin (+), and vimentin (+). The diagnosis of a sarcomatous type of malignant mesothelioma was based on the histopathological finding and result of phenotypical expression analysis by immunohistochemical examination.

**Therapy and prognosis**

Independent predictors of adverse prognosis included no prior debulking, deep tissue invasion, Eastern Cooperative Oncology Group performance status of >6, and a mitotic index of >5/50 high power fields, correlated with prognosis-free survival.\(^11\) Male gender, incomplete surgical resection, and aggressive histological invasion are factors related to reduced overall survival. Cytoreduction surgery and chemotherapy, including hyperthermic intraperitoneal chemotherapy and immunotherapy, have been reported as therapies for diffuse MPM with poor prognosis.\(^12\) In our case, the patient had a good survival rate of five years and 11 months from the prior surgery until death owing to this disease, although she also developed a local recurrence 11 months after surgery.

From a histological point of view, patients might have a poorer prognosis because of the sarcomatous type of the most aggressive histological type as well as lymph node involvement.\(^13\) As Deraco et al.\(^14\) and Nonaka et al.\(^15\) noted, complete cytoreduction surgery for our patient's localized MPM might be useful for good survival, although it is unclear why our case had a better prognosis. Allen et al.\(^16\) noted that the histological subtype did not correlate with survival in 23 cases of localized MPM, because the patients with localized MPM have a good prognosis compared to those with diffuse MPM, and good survival was obtained with surgical excision alone. Although the useful prognostic factors have been reported by some authors, there is controversy, and which are the most important factors for the prognosis of MPM have not been clarified.

**Conclusion**

We report a very rare case of the sarcomatous type of localized MPM with large bowel involvement. We should consider the diagnosis carefully and select appropriate therapy because little is known about the behavior of this disease.

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**Table 1. Published cases of sarcomatous malignant peritoneal mesothelioma.**

| Author No. of sarcomatous-type malignant peritoneal mesothelioma |
|---------------------------------------------------------------|
| Author No. of sarcomatous-type malignant peritoneal mesothelioma |
| Our case 2010 | 1 |
| Klebe et al.\(^17\) 2010 | 7 |
| Griniatios et al.\(^18\) 2009 | 1 |
| Baratti et al.\(^19\) 2009 | 1 |
| Kusama et al.\(^20\) 2009 | 1 |
| Klebe et al.\(^21\) 2008 | 2 |
| Hesdorffer et al.\(^22\) 2008 | 4 |
| Zhang and Hao\(^23\) 2003 | 11 |
| Feldman et al.\(^24\) 2003 | 1 |
| Deraco et al.\(^25\) 2003 | 1 |
| Sebag et al.\(^26\) 2000 | 2 |
| Neumann et al.\(^27\) 1999 | 1 |
| Ros et al.\(^28\) 1991 | 2 |
| Naka and Naka\(^29\) 1984 | 11 |

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**Figure 5. Immunohistochemical examination (magnification, 400X).** Only the epidermal type is positive in epithelial membrane antigen (a, b, c). All types are positive for calretinin (d, e, f) and vimentin (g, h, i).
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