

# Impressive remission of locally advanced malignant peritoneal mesothelioma treated with combination of radiotherapy and intraperitoneal paclitaxel

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## Summary

**Background:** The results of treatment of malignant peritoneal mesothelioma are quite unsatisfactory, especially in the later stages of the disease, regardless of the treatment modality employed.

**Case:** We report a case of locally advanced malignant peritoneal mesothelioma, in which the combination of radiotherapy and intraperitoneal paclitaxel was beneficial for long-term disease stabilization. A 71-year-old woman presented with abdominal pain. Abdominal ultrasound and magnetic resonance imaging confirmed the presence of a mass with both cystic and solid components with moderate ascites. Serum CA-125 concentration was 727 IU/ml. At exploratory laparotomy, a large mass originating from the pouch of Douglas was found. A total abdominal hysterectomy and bilateral salpingo-oophorectomy was performed with partial excision of the mass and involved the peritoneum of the pouch of Douglas. The histologic study showed malignant peritoneal mesothelioma. One year and five months after surgery, significant progression of the residual tumor with increasing ascites was noted. Radiotherapy to the whole pelvis with 45 Gy in 25 fractions was given over five weeks together with intraperitoneal paclitaxel (60 mg/m<sup>2</sup>) instillation, which was repeated every three weeks. The patient received eight cycles of paclitaxel instillation over seven months. The compliance of the patient was excellent under therapy and her general condition improved significantly one and half year with a marked regression of the tumor masses after this treatment.

**Conclusion:** The combination of radiotherapy and intraperitoneal paclitaxel seems suitable in palliative settings primarily aimed at improving the quality of life.

**Key words:** Malignant peritoneal mesothelioma; Radiotherapy; Intraperitoneal paclitaxel.

## Introduction

Malignant peritoneal mesothelioma is an aggressive malignancy with very poor prognosis regardless of the treatment modality employed. This tumor is particularly rare in women in whom the most common malignant peritoneal neoplasm is extraovarian papillary serous carcinoma. The current lack of curative approaches underlines the importance of efficient palliative therapies. In this article, we report a case of locally advanced malignant peritoneal mesothelioma, in which the combination of radiotherapy and intraperitoneal paclitaxel was beneficial for long-term disease stabilization.

## Case report

A 71-year-old woman presented, at another hospital, with a 4-month history of lower abdominal pain and increased abdominal girth, which had deteriorated over the last six weeks before her admission. A prior exposure to asbestos could not be demonstrated. Gynecologic examination was suggestive of the presence of a large, immobile, pelvic-abdominal mass. Subsequent abdominal ultrasound and magnetic resonance imaging confirmed the presence of a mass with both cystic and solid components with moderate peritoneal effusion. The liver, spleen and kidneys all appeared normal. No enlarged pelvic or aortic

nodes were found. Routine blood tests showed slight anemia. Liver function tests were normal. Tumor markers were measured; CA-125 was 727 IU/ml, CEA was 3 ng/ml, CA19-9 was 0.4 IU/ml, and alpha-fetoprotein was 4.7 ng/ml. Chest X-rays, gastroscopy, large bowel radiology series, and mammography were all negative.

At exploratory laparotomy, a large mass of 15 x 15 x 10 cm originating from the pouch of Douglas was found. It involved the anterior surface of the rectosigmoid colon. Both ovaries and tubes were of normal size but their surfaces presented with multiple implants. There was moderate ascites. The pelvic peritoneum where uninvolved from the above tumor, appeared thick and inflamed. The omentum, subdiaphragmatic spaces, liver, pancreas, stomach, and spleen had no evidence of a primary or metastatic neoplasm. Total abdominal hysterectomy and bilateral salpingo-oophorectomy were then performed with partial excision of the mass and the involved peritoneum of the pouch of Douglas. The histological study confirmed the diagnosis of malignant mesothelioma of the epithelial subtype. Immunohistochemically the tumor cells were strongly positive for calretinin and podoplanin (D2-40), and did not stain for EMA and Ber-EP4.

Chemotherapy of oral fluoropyrimidine anticancer drug TS-1 was administered at a dose of 100 mg/day. One year and five months after surgery, the patient was referred to our institute because of deteriorating abdominal distension due to increasing ascites. Because the patient refused surgical excision by posterior exenteration, we started radiotherapy to the whole pelvis with 45 Gy in 25 fractions given over five weeks and ultrasound needle-guided aspiration of the ascites (3500 ml) followed by

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60 mg/m<sup>2</sup> paclitaxel instillation to the peritoneal cavity. Instillation was repeated every three weeks. The patient received ten cycles of paclitaxel instillation over seven months. In the fourth week after the beginning of treatment, abdominal distension apparently improved and ultrasound exhibited a marked regression of the tumor masses. The compliance of the patient was excellent and abdominal pain was not observed. Two years after the radiotherapy and intraperitoneal paclitaxel, the general condition of the patient stabilized and abdominal distension improved significantly.

## Discussion

Peritoneal mesothelioma is generally a rapid fatal primary peritoneal surface malignancy with a median survival time of less than one year [1], mainly because of lack of an optimal treatment regimen in the operative and postoperative management, due to their rarity. Recently, efficacy of an intensive local-regional treatment strategy that included surgical removal of large disease deposits combined with perioperative intraperitoneal chemotherapy was reported in selected cases [2]. However, in most cases the extent of tumor spread precludes complete surgical resection. Limited surgery only to obtain biopsy material or cytoreductive surgery followed by radiotherapy or intraperitoneal or systemic chemotherapy after surgery, have all been used in the treatment of patients with peritoneal mesothelioma with no obvious efficacy [3, 4].

The role of radiotherapy alone in the treatment of mesothelioma has been studied mainly in pleural mesothelioma and, overall, the results have been largely disappointing; the exception is for local postsurgical radiotherapy of pleural mesothelioma, which is effective in the prevention of seeding of tumor cells in the wound site [5]. Although the efficacy of radiotherapy has been shown in the literatures, in terms of a reduction in the gross tumor volume and palliation of symptoms in the later stages of the disease, the effect is often brief [6, 7]. No chemotherapy regimen for mesothelioma has proven curative, but several regimens reported to demonstrate response in peritoneal mesothelioma include systemic paclitaxel plus cisplatin [8] and intraperitoneal cisplatin [9] or paclitaxel-based [10] regimens, although most articles are clinicopathological retrospective reviews or case reports compiling disparate therapeutic experiences.

This report describes the efficacy of the combination of radiotherapy and intraperitoneal paclitaxel in peritoneal mesothelioma. The rationale for intraperitoneal paclitaxel is based on the facts that paclitaxel was demonstrated to inhibit the growth of all three mesothelioma cell lines grown in the subcutaneous tissue of nude mice [11], and that pharmacologic studies of the intraperitoneal and plasma concentrations of paclitaxel after intraperitoneal administration at 20 mg/m<sup>2</sup> showed 2,000 times the drug concentration in the peritoneal cavity compared to the serum levels [3]. Feldman *et al.* [10] reported that surgical resection and single postoperative intraperitoneal dwell of fluorouracil and paclitaxel for 49 patients with

peritoneal mesothelioma resulted in durable progression-free and overall survival. Sugarbaker *et al.* [3] studied 49 cases of peritoneal mesotheliomas and reported the efficacy of intraperitoneal cisplatin, doxorubicin and paclitaxel, combined with cytoreductive surgery.

Against the background of the current unsatisfactory therapeutic situation in advanced peritoneal mesothelioma, the combination of radiotherapy and intraperitoneal paclitaxel seems suitable in palliative settings primarily aimed at improving the quality of life.

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