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Case Report

Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in the management of recurrent uterine leiomyosarcoma with peritoneal sarcomatosis: A case report and review of the literature

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Abstract

Uterine leiomyosarcoma (ULMS) is a rare uterine malignancy that is aggressive and typically spreads to the lungs and liver hematogenously. However, it may recur with seeding to the peritoneal surfaces, of which the prognosis is historically dismal. ULMS with peritoneal dissemination has limited treatment options. We report a case of uterine leiomyosarcoma in which the patient underwent previous debulking surgery but developed recurrence with peritoneal sarcomatosis 7 months later. She underwent cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) with cisplatin 16mg (0.32mg/kg) but had tumour recurrence 5 months later. This report presents a case of CRS and HIPEC performed for a patient with recurrent ULMS with peritoneal dissemination and a review of the literature on CRS and HIPEC for ULMS with peritoneal sarcomatosis.

Key Words:

Uterus, leiomyosarcoma, cytoreductive surgery (CRS), hyperthermic intraperitoneal chemotherapy (HIPEC)

Introduction

Uterine leiomyosarcoma (ULMS) is a rare uterine malignancy that represents 1% to 2% of uterine malignancies. Compared with other types of uterine cancers, ULMS is known to be aggressive, has a high risk of recurrence ranging from 53-71%, and poor prognosis with 5- year survival rate of 18.8% to 65% [1-3]. Primary treatment of ULMS is surgical and includes a total abdominal hysterectomy and tumour debulking. It typically spreads hematogenously to lungs and liver. It may also recur by seeding to nearby peritoneal surfaces, the prognosis of which is historically dismal, highlighting the need for better treatment options for peritoneal metastases [1-3]. Limited medical data has been published with regards to management of ULMS with peritoneal dissemination. Conversely, there is a plethora of literature on the treatment of peritoneal dissemination of cancer arising from the appendix or mesothelioma, with cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). Retrospective studies and a randomised controlled trial [2,3] have suggested improved survival outcomes in patients with peritoneal dissemination from colon, ovarian, primary peritoneal malignancies after CRS/HIPEC [4-7]. This procedure consists of complete resection of all visible disease from the abdominal cavity, including affected viscera (CRS), followed by administration of hyperthermic intraperitoneal chemotherapy (HIPEC). National Cancer Centre Singapore (NCCS) remains the single largest cancer centre in South East Asia performing CRS and HIPEC for colorectal, ovarian, appendiceal, and primary peritoneal neoplasms. We previously reviewed our institutional experience with our first 100 consecutive patients and showed that CRS and HIPEC can be safely carried out in Asian patients with peritoneal carcinomatosis [8]. This report presents a case of CRS and

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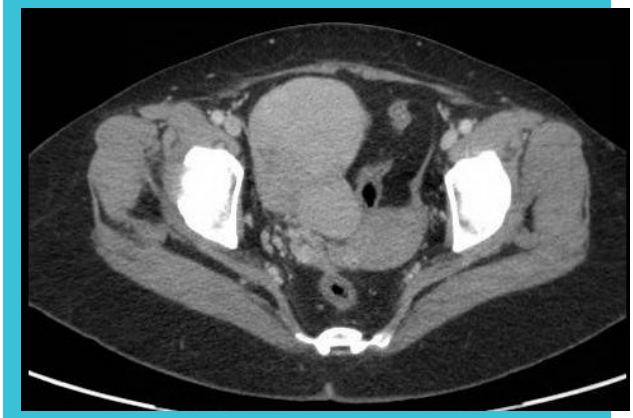
HIPEC performed for a patient with recurrent ULMS with peritoneal dissemination and a review of the literature on CRS and HIPEC for ULMS with peritoneal sarcomatosis.

Figure 1.

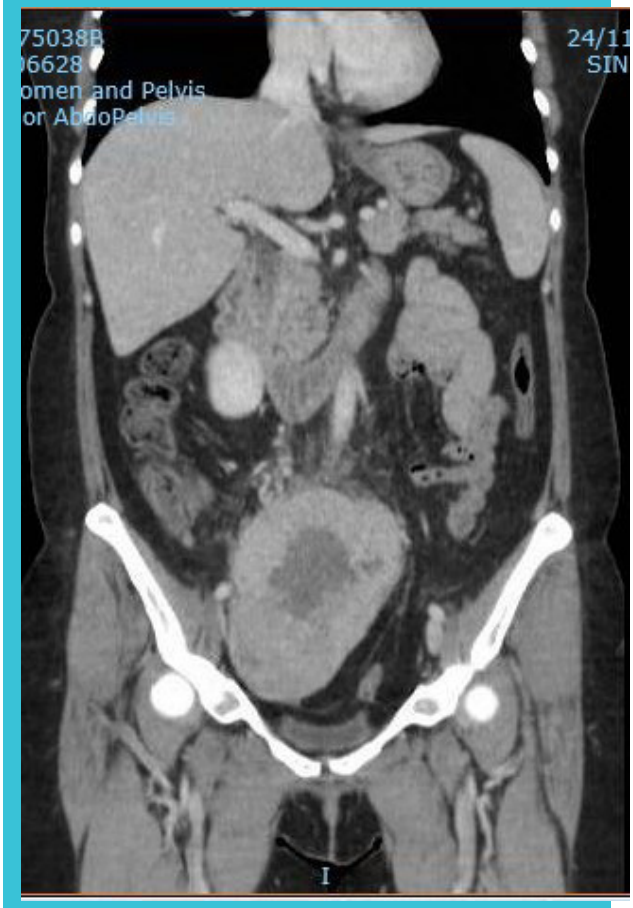


Axial view of the abdomen and pelvis on computerized tomography (CT) showing the pelvic mass before the first surgery

Case Presentation

A 56-year-old Chinese female with past medical history of hyperlipidemia presented with colicky right iliac fossa pain of 1 year in November 2013. A Computed tomography (CT) scan of the abdomen and pelvis showed a large lobulated heterogeneously enhancing solid pelvic neoplasm measuring 12.3 x 11.5 x 8.1 cm arising from the right adnexa, intimately associated with right ovarian pedicle and right lateral wall of uterus (Figures 1, 2). The serum Ca-125 was normal at 8.5 u/ml (0 to 35 u/ml). A CT scan of the thorax showed no pulmonary metastases. She underwent planned debulking surgery by gynae-oncologist on 30 December 2013.The intraoperative finding was that of a large 16 cm ovarian mass adherent to small bowel mesentery and right ureter and pelvic lymphadenopathy. There were no liver metastases and no evidence of peritoneal dissemination. A total abdominal hysterectomy, bilateral salpingooophrectomy, infracolic omentectomy, bilateral pelvic lymph node dissection was performed, with no documented intra-operative spillage. She suffered an inadvertent right ureteric transection that was managed with a primary ureteric anastomosis and a right double-J ureteric stent insertion. She recovered well and discharged on postoperative day (POD) 5. Histology returned as uterine leiomyosarcoma and all 22 lymph nodes and omentum were negative for metastasis. There was no adjuvant chemotherapy or radiotherapy administered.

Figure 2.

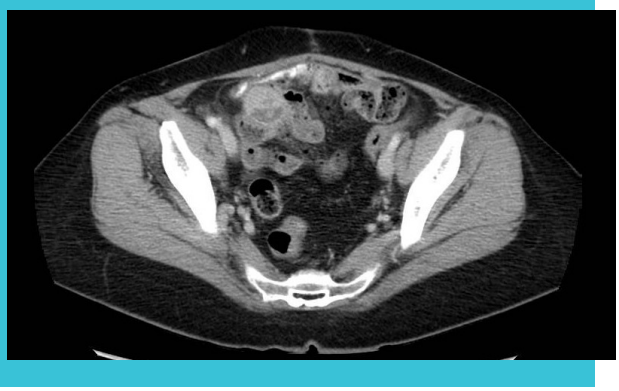


Coronal view of the abdomen and pelvis on CT showing the pelvic mass before the first surgery

She remained well on follow-up but a surveillance scan performed on 11 August 2014 (7 months after her surgery) showed an heterogeneously enhancing mass in the right hemipelvis measuring 2.6 x 2.9cm (Figure 3) and another heterogeneously enhancing mass measuring 2.7 x 3.2 cm, closely related to small bowel (Figure 4), both suspicious for tumour recurrence. The serum Ca-125 was once again normal (5.3 u/ml). There were no distant metastases detected and the case was discussed at the multi-disciplinary

Sarcoma Tumour Board that recommended a consideration of CRS and HIPEC. After a detailed discussion of available options with the patient, she underwent surgery on 9 September 2014. Intra- operative findings were that of a 3x3cm tumour nodule adherent to 2 regions of ileum and multiple small bowel implants of 3-5mm adherent to peritoneal surface on abdominal wall and small bowel mesentery. The peritoneal carcinomatosis index (PCI) was 9. She underwent segmental resection of small bowel in which tumour nodule was adherent to, resection of small bowel nodules off the small bowel mesentery and completion omentectomy. Complete cytoreduction (CC-0) was achieved with minimal blood loss and without any intra-operative complications. In view of the peritoneal dissemination, HIPEC was administered using cisplatin 16mg (0.32 mg/kg). Her post-operative course was uncomplicated and she was discharged home well on POD 8. She was reviewed in the Specialist Outpatient Clinic two weeks and again at two months after discharge and found to have recuperated well. She was offered adjuvant chemotherapy but opted instead for observation, understanding that the risk of relapse was high. At 5 months follow-up, a surveillance CT scan showed multiple pelvic nodules suggestive of recurrence. She was started on palliative chemotherapy with gemcitabine and taxotere. At 7 months follow-up and after 3 cycles of palliative chemotherapy, repeat CT scan showed that multiple pelvic nodules have become smaller in size.

Figure 3.

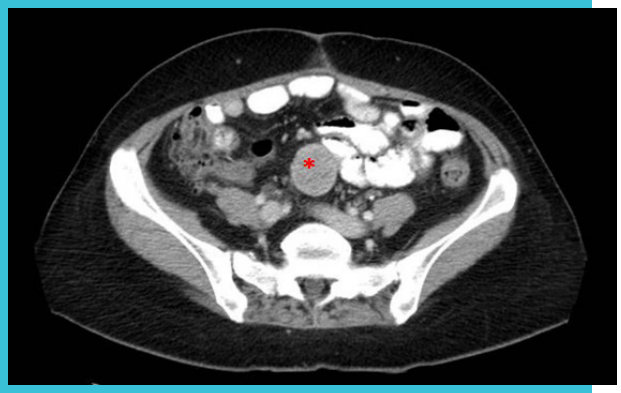


*Axial view of the abdomen and pelvis on CT showing a site of tumour recurrence involving small bowel**

Discussion

Nearly all patients with ULMS and extra-uterine disease at initial diagnosis will eventually recur. ULMS most commonly metastasizes to the lungs, liver, abdomen, pelvis and pelvic or para-aortic lymph nodes [9]. Median survival of advanced or unresectable recurrent disease is less than 1 year [10, 11]. The literature on imaging features of peritoneal sarcomatosis due to leiomyosarcoma is also limited. It is reported that it usually manifests as bulky masses or peritoneal thickening. The large masses are usually heterogeneously enhancing and may demonstrate calcifications. There is usually no ascites and nodal involvement [20, 21]. As compared to peritoneal carcinomatosis, sarcomatosis is more frequently associated with discrete nodules >2cm in size, less frequently associated with pleural effusion, ascites, peritoneal thickening, omental caking, serosal disease, lymphadenopathy [22]. In our patient, only 2 nodules were identified on CT scan, the rest of the peritoneal nodules discovered intra-operatively were otherwise not identified on pre-operative imaging.

Figure 4.



*Axial view of the abdomen and pelvis on CT showing another site of tumour recurrence involving small bowel**

Initial attempts at surgical treatment of peritoneal sarcomatosis, centred on maximal debulking without the addition of intraperitoneal chemotherapy, have resulted in prolonged survival in some, but 35 to 82% will inadvertently recur again [18, 19]. Karakousis et al. reported debulking in 72 patients with disseminated intraperitoneal sarcoma and found that patients with resectable disease had an improved median survival of 23 months compared with 9 months for those found to be unresectable [12]. Similar studies reported that cytoreduction improves outcome. However, it is clear that cytoreduction alone does not eliminate microscopic disease and results in high peritoneal failure of up to 72%, hence the rationale for addition of HIPEC to maximal cytoreduction [13]. Due to the small number of cases and heterogeneity in histopathologic features of peritoneal sarcomatosis, there are few studies that review the role of CRS and HIPEC in the management of ULMS with peritoneal sarcomatosis. Jimenez et al. reported their experience with applying CRS and HIPEC in 3 patients with uterine sarcoma with peritoneal dissemination. Among the 3 patients, 2 were leiomyosarcomas and 1 was an adenosarcoma, and the follow-up ranged from 34 to 140 months. The first patient with leiomyosarcoma presented with a large pelvic mass, was found to have peritoneal disease with a PCI of 16 and underwent CRS and HIPEC (doxorubicin, cisplatin). This patient recurred in the liver at 20 months, the lung at 115 months and the left breast at 118 months. All recurrences were resected when they presented and the patient was disease-free at 143 months since the CRS and HIPEC, and 25 months after her last surgery. The second patient had total hysterectomy and bilateral salpingo-oophrectomy for high grade ULMS with adjuvant chemotherapy (Gemicitabine, docetaxel). She developed a pelvic recurrence 7 months later and underwent cytoreductive surgery. She developed another recurrence 2 months later and underwent CRS and HIPEC with melphalan, and has remained disease-free for 26 months after CRS and HIPEC. This case series suggests that CRS and HIPEC as a treatment for high grade ULMS with peritoneal sarcomatosis is feasible treatment option [17]. In the absence of improved outcomes with previous treatment options for ULMS with peritoneal sarcomatosis, CRS and HIPEC may be an acceptable approach with possibly better overall and recurrence-free survival. Rossi et al. analysed 60 patients with abdominal sarcomas, of which 12 were uterine sarcomas (8 leiomyosarcoma and 4 endometrial stroma sarcoma), who underwent CRS and HIPEC with doxorubicin and cisplatin. After a median follow-up of 28 months, 32 patients (53%) died of disease, 12 (20%) were alive with disease and 16 (27%) were alive without any evidence of disease. Estimated overall survival was 36 months and median time to local disease recurrence was 24 months. Type of histology of the abdominal sarcoma did not influence overall and local progression free survival [14]. Baumgartner et al. reviewed 15 patients who underwent CRS and HIPEC for recurrent sarcomatosis. There were 3 leiomyosarcomas among the 15 patients. Chemoperfusion drug was mitomycin C, cisplatin or doxorubicin. Median intra-abdominal disease-free and overall survival after CRS and HIPEC was 17.2 and 22.6 months respectively. There was a trend towards delayed recurrence after combined CRS and HIPEC than after prior CRS alone (17.2 months vs 10.7 months respectively). Median overall survival was 38.5 months for leiomyosarcomas which had the best survival as compared to other histological types of sarcomas [16]. These studies though limited by the small number of cases, suggest that there is improved survival for leiomyosarcomas after CRS and HIPEC. The value of systemic chemotherapy in uterine leiomyosarcoma with peritonei sarcomatosis is not well known. However, combination treatment with gemcitabine and docetaxel has the highest reported response rate of 36% [24]. Studies have suggested that gemcitabine and docetaxel are also effective as second-line therapy. Gemcitabine and docetaxel achieved an overall response rate of 27% among 51 patients who had progression after first-line treatment and 52% were disease-free at 6 months [25]. With regards to the role of CRS and HIPEC, combined together with systemic chemotherapy, in patients with uterine leiomyosarcoma and peritoneal sarcomatosis is also not well established. Baratti et al. reviewed a prospective database of 37 patients with peritoneal sarcomatosis who underwent CRS and HIPEC with cisplatin, doxorubicin or mitomycin-C. After median follow-up of 104 months, peritoneal disease progression occurred among 16 patients, distant metastases in 5 and both peritoneal and distant sites in 13. There were 8 patients with GIST, 11 with ULMS, 13 with retroperitoneal liposarcoma (RPLP) and 5 with other types of sarcomas. RPLP had the best overall survival (34 months) but 100% peritoneal relapse. Patients with GIST had dismal overall, local-regional free and distant free survival. Patients with ULMS had the highest proportion of long term survivors and best local-regional free survival. 5 of the 11 ULMS patients were alive at 4 -10 years after combined treatment (CRS and HIPEC with systemic che-

motherapy – docetaxel and gemcitabine). This supports a possible role for combined treatment approach for patient with recurrent ULMS and peritoneal sarcomatosis [15]. The current case shows that it is feasible to perform CRS and HIPEC for ULMS with peritoneal sarcomatosis but patient selection is crucial if prolonged survival is to be attained. A combination of CRS, HIPEC and systemic chemotherapy may yield the best clinical outcomes but further studies are required to determine which patients would most benefit from this approach.

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Declaration of Interest
None

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