CASE REPORT

Peritoneal Metastases From Prostate Adenocarcinoma – A Case Report

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ABSTRACT

Metastatic spread of prostate cancer to the peritoneum is rare but may be either due to an iatrogenic cause or a sign of a more aggressive disease. We present a patient with peritoneal carcinomatosis who survived prostate and colon cancer. A 72-year-old male presented with abdominal pain, weight loss, and abdominal distension. He was treated surgically for prostate cancer and colon cancer in the past. Investigations revealed liver and peritoneal metastases, and the liver biopsy suggested that the lesions were of colorectal origin. The patient had a good response after 18 cycles of systemic chemotherapy, allowing cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) to be performed. Pathological examination of tissues removed during surgery revealed the prostatic origin of the peritoneal nodules. The final diagnosis altered his adjuvant treatment and may have implications for his post-operative monitoring. CRS and HIPEC could improve survival but there is no established regime for prostatic peritoneal metastases. However, the use of regimes applied to other primaries has been reported. Personalisation of treatment using novel technologies could potentiate treatment benefits.
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Keywords: Cytoreductive surgery, Prostate cancer, Peritoneal metastases, Hyperthermic intraperitoneal chemotherapy, CRS & HIPEC

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INTRODUCTION

Metastases of prostate cancer only affect about a third of patients, and spread to the peritoneum is rare(1). Treatment by cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) in this condition is limited to several case reports, and no specific regime has been investigated for efficacy(1,2). However, peritoneal metastases from colorectal cancer are more common(3). There are also numerous clinical series and randomised trials investigating the utilisation of HIPEC in colorectal peritoneal metastases(3). We present a patient who presented with peritoneal carcinomatosis, having been treated for both prostate and colorectal cancer. The management of this patient evokes the saying, "between Scylla and Charybdis" – choosing the lesser of two evils. This case report follows the CARE Guidelines (available at doi: 10.1016/jclinepi.2017.04.026).

CASE REPORT

A 72-year-old male presented with abdominal distension and weight loss in January 2021. He also had a generalised dull pain throughout his abdomen. The symptoms were gradually worsening over three months prior to presentation. His appetite has been poor, and his weight has reduced by five kilograms since October 2020.

The patient had an emergency Hartmann's procedure in October 2020 for obstipation due to a sigmoid adenocarcinoma. It was noted that he had liver and peritoneal metastases during the surgery. He had four cycles of chemotherapy (FOLFOX plus Bevacizumab) after the surgery. The patient also underwent an open radical prostatectomy in August 2015 for a Stage IVa

prostatic adenocarcinoma (Gleason score 9, T3bN1M0). There was no significant family history of medical conditions. He was an ex-smoker and did not consume alcohol.

Clinical examination revealed a mildly distended abdomen and mild generalised tenderness. There were no masses or lymph nodes palpable, nor was there any organomegaly. He was not jaundiced, and there was no clinical evidence of cachexia.

His complete blood count, renal profile, and liver function tests were within the normal range. His serum tumour markers test results were as followed; CEA: 9.3 ng/ml, CA 19-9: 43.3 U/ml, CA 125: 21 U/ml, and PSA: 4 ng/ml. A PET-CT scan showed increased pathological FDG uptake in both lobes of the liver, abdominal wall, small bowel mesentery, and para-caecal region (Fig. 1). A biopsy from the liver nodule suggested that it had a colonic adenocarcinoma origin. The biomolecular test results are summarised in Table I.

The patient was started on palliative chemotherapy, consisting of the FOLFIRI regime plus Cetuximab. A scan after twelve cycles showed complete regression of the liver lesions, with multiple peritoneal lesions still present. The patient completed 18 cycles of the FOLFIRI plus Cetuximab regime in December 2021. The post-chemotherapy scan showed significant disease regression compared to pre-chemotherapy scans, with only peritoneal lesions remaining (Fig. 1). A discussion within the hospital's multidisciplinary tumour board concluded that as the patient was physically fit (ECOG 1) and complete clearance was obtainable, he would benefit from CRS.

The surgery was performed in January 2022. The intraoperative findings were as follows; subcapsular segment V liver lesion infiltrating the right diaphragm, nodule on the antimesenteric surface of the small bowel at 50 cm, 70 cm, and 170cm from the Treitz ligament, nodules on the small bowel mesentery at 100 cm and 130 cm from Treitz ligament, multiple omental nodules, para-caecal and right paracolic peritoneal nodules, and pelvic peritoneal nodules. The PCI score was 12. Segmental small bowel resection was performed, along with wedge resection of the small bowel closer to the duodenum and terminal ileum. A non-anatomical segment V liver resection along of right diaphragmatic peritonectomy was completed to remove the liver lesion. Total omentectomy, and selective peritonectomy to the pelvis and right parietal peritoneum complete the cytoreductive surgery. Complete cytoreduction (CC-0 score) was achieved.

Table I: Summary of immunohistochemistry staining tests

Biomolecular test	January 2021 (Liver biopsy)	January 2022 (Post CRS)
MLH 1	Nuclear (+)	Nuclear (+)
PMS 2	Nuclear (+)	Nuclear (+)
MSH 2	Nuclear (+)	Nuclear (+)
MSH 6	Nuclear (+)	Nuclear (+)
Cerb B2	10% (2+)	Not tested
BRAF/NRAS/KRAS	Not detected	Not tested
CK 20	Not tested	Negative
CK 7	Not tested	Negative
PSA	Not tested	Positive

Bidirectional intraoperative chemotherapy (BIC) regime was chosen after discussion within the multidisciplinary tumour board. A closed HIPEC was applied immediately after the completion of surgery. The chemotherapy agent used was Oxaliplatin 460 mg/m2, with temperature maintained at 42°C, and peritoneal infusion was carried out for 90 minutes. 400mg/m2 5-Flurouracil (5-FU) was utilised for the intravenous component.

The final histopathology report for the peritoneal and small bowel nodules was surprising as the adenocarcinoma was deemed to be of prostate origin. The liver lesion only contained granulation tissue. The immunohistochemistry staining results are summarised

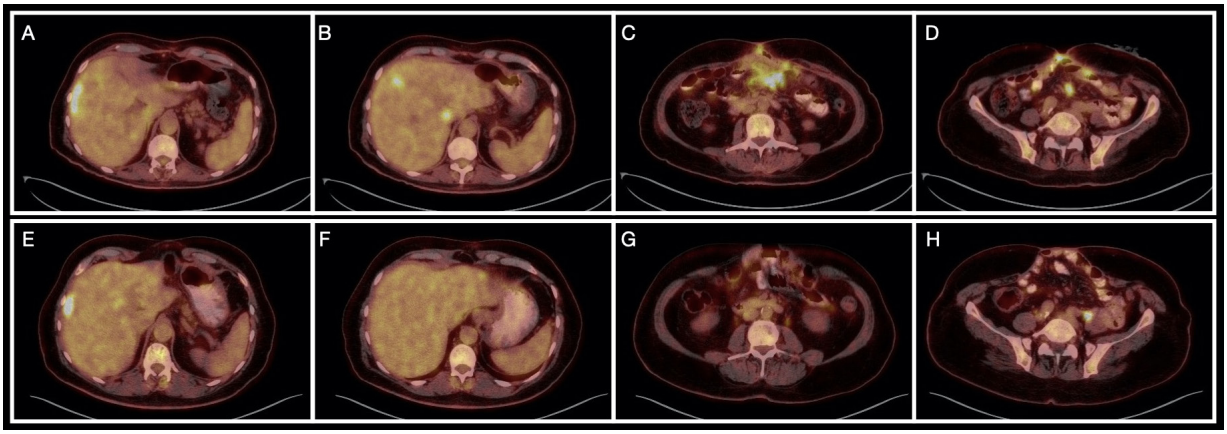

Figure 1: PET-CT scan images between two distinct periods of the patient's management. Pictures A, B, C, and D, were taken from PET-CT scan done prior to starting chemotherapy. The scan showed pathological lesions in the liver, small bowel mesentery, and peritoneum. Pictures E, F, G, and H, were taken from PET-CT scans done after 18 cycles of FOLFIRI plus cetuximab, before CRS/HIPEC. The images showed the degree of response to the chemotherapy

in Table I.

The patient had a smooth recovery and was discharged six days after the procedure. He was started on Abiraterone acetate given the histopathological findings and had been tolerating the treatment well. A follow-up PET-CT scan four months after the CRS did not reveal any evidence of recurrence, and his tumour markers were within the normal range at seven months post-surgery. He is scheduled for regular PET-CT scan and serial tumour markers testing for 2 years post-surgery.

DISCUSSION

Peritoneal spread of prostate adenocarcinoma has been documented but rare. It makes up less than 7% of prostate cancer metastases(2). The increased reporting of peritoneal metastases, along with the higher application of laparoscopic and robotic radical prostatectomy birthed the idea of an iatrogenic cause(1,2). However, more undifferentiated, and aggressive tumour histology were commonly found in reported cases. High-grade Gleason scores (≥8), such as in our case, neuroendocrine differentiation, and multiple germline mutations (i.e. BRCA 1 and BRCA 2) are associated with the peritoneal spread of prostate cancer(1,2). Hence, peritoneal metastases may be part of the natural history of the more aggressive prostate diseases.

HIPEC allows high concentration of chemotherapy agents to be delivered intraperitoneally. Hyperthermia synergises with the anti-cancer agents and increases tissue penetration(3). These factors increase the drug concentration in cancer tissues, making it more effective compared to systemic therapy when treating intraperitoneal lesions. The combination of complete CRS and HIPEC has been shown to increase survival(1,3,4). However, the ideal regime is still being debated.

Even though the final diagnosis was a surprise, the patient's perioperative management would not have differed much. A multidisciplinary team decision was made to aggressively tackle the disease with CRS and HIPEC due to the patient's reasonable response to systemic chemotherapy and the absence of extra-peritoneal metastases. However, our centre is a tertiary referral centre with high-volume experience in CRS. The limit of what is considered resectable may be more stretched than the average. There is no consensus on the ideal regime for peritoneal metastases from prostate adenocarcinoma. The BIC regime chosen has been shown to produce good results in diseases from other primaries (3). However, the patient had a history of receiving Oxaliplatin as a systemic treatment, which may result in his peritoneal metastases acquiring resistance to the agent (3). Using novel techniques such as predicting tumour response using patient-derived tumour organoids could help in identifying the optimum agent and regime to be used (4).

1% of patients with metastatic prostate cancer, like our patient, will have low PSA levels (1). Conventional PET-CT scan using FDG tracer lack the sensitivity and may lead to detection of recurrences at a later stage (5). The use of other tumour markers may help, as almost half of metastatic prostate cancer patients show elevated CEA, CA 19-9, and CA 125 (1). Coupling prostate-specific radioactive tracers with a PET-CT scan could improve detection. However, these tracers such as 11C-Choline, 18F-Fluciclovine, and Gallium68- Prostate-Specific Membrane Antigen (^{68}Ga-PSMA) are new, expensive, and may currently be licensed for investigative use only (5).

CONCLUSION

This patient was initially treated for metastatic colorectal cancer but was discovered to have prostate-cancer derived peritoneal metastases. Complete CRS and the use of HIPEC could improve the patient's survival, however, the evidence of benefit in metastatic prostate cancer is still scarce. Personalisation of HIPEC treatment using patient-derived tumour organoids could increase the potential benefit of the treatment.

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