Malignant peritoneal mesothelioma (MPM) who responded to rechallenge with cisplatin and pemetrexed with current literature review

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SUMMARY

Peritoneal mesothelioma is an aggressive malignancy which is indeed very rare. Due to rarity, experience among many physicians surrounding the treatment of peritoneal mesothelioma is limited. Recently, we have received a patient who was initially treated palliatively with a combination of pemetrexed and cisplatin showing good response. On progression of his disease, he was again treated with the same drugs. This is not the strategy commonly used. We consider rechallenging cisplatin and pemetrexed to such patients who respond for the first time.

BACKGROUND

Our patient responded well not only to initial treatment but also on rechallenging the cisplatin and pemetrexed on progression of his peritoneal malignant mesothelioma. This triggered us to write this case report to share our experience with the medical community. This strategy may be an option for some patients who show response initially.

CASE PRESENTATION

A 57-year-old gentleman presented with a history of abdominal pain, nausea and vomiting for 9 months suggestive of partial bowel obstruction (figure 1).

Figure 1 Plain abdominal x-ray showing dilated bowel loops suggestive of partial intestinal obstruction.

INVESTIGATIONS

CT scan of the abdomen revealed 8 cm small bowel mass causing proximal dilation along with scattered lymphadenopathy but no evidence of pleural disease (figure 2).

Laparotomy findings showed multiple, dense adhesions without obvious intestinal obstruction. Biopsies from the mass and peritoneum revealed a neoplasm with epithelioid cells arranged in a tubulo-papillary pattern. Neoplastic cells were infiltrating fibro-collagenous stroma and adipose tissue (figure 3A). Immunohistochemistry showed a strong expression of the neoplastic cells with positive mesothelial markers like Calretinin and CK5/6 and 7 (figure 3B) but negative for typical epithelial cell markers—Ber-Ep4 and CEA (monoclonal carcino-embryonic antigen). The histo-morphology and immune-profile of the neoplasm were consistent with diagnosis of malignant mesothelioma.

TREATMENT

Radical surgery was not possible due to extensive disease, hence palliative chemotherapy using six cycles of combination of pemetrexed (500 mg/m²) and cisplatin (75 mg/m²) day 1 were repeated 3 weekly along with folic acid and Vit B2 supplementations. He developed grade 2/3 palmo-planter erythema and grade 3 pancytopenia requiring dose reduction and supportive treatment. Post-treatment CT scan showed good partial response (figure 4).

OUTCOME AND FOLLOW-UP

He remained symptom free for 8 months and had an episode of sub-acute bowel obstruction but CT

Figure 2 CT scan of abdomen at the time of diagnosis: huge mass measuring almost 8 cm attached to the bowel loops is clearly visible.

To cite: Gilani SN, Gridley R, Searle G, et al. *BMJ Case Reports* Published online: [please include Day Month Year] doi:10.1136/bcr-2012-007786

Figure 3 (A) Neoplastic cells arranged in tubulo-papillary fashion infiltrating into adipose tissue (magnification $\times 100$), (B) immunohistochemical staining showed strong positivity of Calretinin and CK5/6 but negative for typical epithelial cell markers—Ber-Ep4 and monoclonal carcino-embryonic antigen.

scan showed only non-specific mesenteric lymph nodes. He was followed up for another 8 months when a further CT scan confirmed incomplete intestinal obstruction due to disease progression with an appearance of several serosal deposits throughout small and large bowel. At that time he was not fit for cytoreductive surgery (CRS), hence a plan to rechallenge with same chemotherapy was proposed. He was again offered palliative chemotherapy using pemetrexed and cisplatin as a special case.

After receiving this chemotherapy again, he developed significant thrombocytopenia resulting in the termination of treatment after only one cycle. In spite of haematological toxicity, his intestinal symptoms improved significantly with reduction in disease volume on CT scan indicating partial response. This provided an indirect evidence to support re-using PC in similar patients with peritoneal mesothelioma who respond first time but are not fit to undergo cytoreductive surgery. Subsequently, cisplatin was dropped due to impairment of renal functions. He continued to receive single agent pemetrexed maintaining tumour response. Even after many months, his disease remains stable on repeat CT scans.

DISCUSSION

MPM is rare and aggressive neoplasm. It comprises 30% of all malignant mesotheliomas.¹ Majority of patients have a history of asbestos exposure. Overall incidence of peritoneal mesothelioma is 2–3 cases per million per year² which provides orphan status to this disease. It has poor prognosis with overall survival of

6 months without treatment. Mesothelioma is not curable but is often treated with a combination of surgery, chemotherapy and radiotherapy. Over the last decade, treatment and prognosis of this disease have dramatically changed especially with the introduction of chemotherapy regimen with an antimetabolite (pemetrexed and raltitrexed) together with a platinum-based agent (cisplatin) providing a median survival of about 1 year.³ From year 2000 to 2002, pemetrexed was evaluated in phases I, II and III trials with encouraging results in pleural mesothelioma.⁴ In an open-label study, Janne *et al*⁵ showed a disease control rate of 71.2% in peritoneal mesothelioma treated with pemetrexed in combination with cisplatin. However, most of the experience was inferred from the treatment of pleural mesothelioma. Direct experience with peritoneal mesothelioma is indeed very limited.^{6,7}

Peritoneal mesothelioma remains almost localised exclusively to abdominal cavity without distant metastasis. A loco-regional approach with CRS and intraperitoneal chemotherapy using cisplatin and doxorubicin has been tried. It has shown some promising results in recent years with overall 5-year survival rate of 29–63%.¹ Patients not fit for CRS or loco-regional radical treatments are often left with palliative chemotherapy comprising pemetrexed and cisplatin.⁸ However, these drugs can be rechallenged again on recurrence of disease but usually the outcome remains uncertain. Whether we should offer rechallenge to all such patients is unknown. One can only guess by applying knowledge gained from the treatment of pleural mesothelioma.⁹ Few institutions recommend using gemcitabine (GEM) and cisplatin/carboplatin (CDDP/CBDCA) instead as second-line drugs.^{3,10} But our experience suggests that reusing PC again may be a reasonable possible option for diffuse peritoneal malignant mesothelioma for patients who show response for the first time.

Figure 4 Post-treatment CT scan showing radiological disappearance of mass suggestive of good clinical response.

Learning point

Reusing cisplatin and pemetrexed for a second time may be a possible palliative option for diffuse peritoneal malignant mesothelioma for patients who exhibit response to the same drugs for the first time.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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