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PEMBROLIZUMAB IN COMBINATION WITH FOLFIRINOX FOR TREATMENT OF ADVANCED PANCREATIC ADENOCARCINOMA WITH MSI-H

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ABSTRACT

Pancreatic cancer is one of the four most common causes of cancer-related death in the United States. Our patient had metastatic pancreatic cancer with a high tumour burden. He was trialled on an unconventional treatment of combination immunotherapy and chemotherapy. It resulted in decreased cancer burden and decreased FDG activity on a PET scan. Further studies are needed for standard pancreatic cancer treatment.

KEYWORDS

MSI-H, pembrolizumab, pancreatic adenocarcinoma

LEARNING POINTS

- Very few patients survive pancreatic cancer, especially metastatic disease. Our patient is doing very well after a few years.
- There is little evidence for concurrent use of chemotherapy and immunotherapy. Our patient received it and has had no new lesions, and there has been an improvement on imaging.

INTRODUCTION

Pancreatic cancer is one of the leading causes of cancer-related deaths. Less than 20% of patients with this have resectable disease at presentation[1]; most patients have locally advanced or metastatic cancer. Here, we present a case of unresectable pancreatic cancer with a high tumour burden that showed excellent response to immunotherapy, using pembrolizumab in combination with chemotherapy.

CASE DESCRIPTION

A male patient in his 60s presented with 20 pounds of unintentional weight loss, poor appetite and abdominal pain in September 2021. A magnetic resonance imaging (MRI) in November 2021 showed a 7.6 cm pancreatic mass with splenic vein thrombosis and celiac axis encasement. An endoscopic ultrasound-guided biopsy showed a poorly differentiated adenocarcinoma with necrosis. FOLFIRINOX (oxaliplatin, irinotecan, 5-fluorouracil and leucovorin) was initiated in December 2021 but the tumour burden continued to increase, with worsening arterial and venous involvement in a repeat computed tomography (CT) scan. Due to the nature of the cancer, and the encasement of the celiac artery, the

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stage 3 pancreatic cancer was deemed unresectable. Further characterisation of the tumour showed microsatellite instability-high (MSI-H) and high tumour burden and the patient was started on pembrolizumab in combination with FOLFIRINOX in March 2022. He completed 12 cycles of the chemotherapy followed by immunotherapy every six weeks and reported improved symptoms after starting immunotherapy. Surveillance imaging obtained four months later showed decreased adenocarcinoma size from 6.3 × 4 cm to 4.2 × 3 cm and a PET scan showed decreased FDG avidity. In October 2023, a repeat CT scan showed a further decrease in adenocarcinoma pancreatic body mass to 3.2 × 1.6 cm. The most recent imaging from May 2024 showed a slight decrease to 2.9 × 1.6 cm. The patient continues to receive pembrolizumab every six weeks to this date and currently, he is doing very well and in an excellent health condition and continues to have a close follow-up with the Oncology clinic for immunotherapy.

DISCUSSION

In the USA, the five-year survival rate for pancreatic cancer is approximately 5%[2]. The National Comprehensive Cancer Network (NCCN) guidelines recommend chemotherapy using FOLFIRINOX as the mainstay of treatment for advanced cases[3]. Furthermore, no single second-line agent has been able to confer survival benefits for these patients. The concurrent use of chemotherapy and immunotherapy is currently under research, especially with pembrolizumab. Pembrolizumab is an immunoglobulin monoclonal antibody that triggers immune-mediated tumour destruction by binding with the immune checkpoint receptor programmed cell death protein 1 (PD-1)[4]. Immunotherapy has shown great success in many cancers; however, there remains little benefit in pancreatic cancers. Per NCCN guidelines, pembrolizumab can be used in pancreatic cancer for unresectable or metastatic tumours with MSI-H, which occurs due to mutations in the mismatch repair genes[3]. Such mutations are noted in cancers seen in Lynch syndrome and colon cancers, which are known to respond well to immune-based therapies compared to chemotherapy. However, chemotherapy continues to remain the initial therapy of choice in patients with pancreatic cancer, and pembrolizumab as the second-line therapy for patients testing positive for MSI-H mutations. In our patient, the combination of chemotherapy with pembrolizumab for high tumour burden resulted in an immune-responsive tumour and reduction of the pancreatic tumour. Our report shows that the combined use of FOLFIRINOX and pembrolizumab has the potential to be beneficial as a first-line agent in unresectable pancreatic cancer with MSI-H and not only those that are metastatic in nature. When treated with recommended first-line treatment chemotherapy, our patient experienced worsening of his disease. However, combination treatment with pembrolizumab and FOLFIRINOX showed marked improvement in his symptoms and decreased tumour burden on follow-up imaging. Since the literature review, there have been very few cases of unresectable pancreatic cancer with MSI-H mutation with subsequent resolution of the mass along with high survivorship for the patient, making this a unique case. Zhao et al. discussed similar findings with a resectable stage 3 pancreatic cancer patient who had a long-term outcome of deficient mismatch repair (dMMR) pancreatic cancer with pembrolizumab after initial chemoradiation and surgery showing a similar clinical benefit and stability as in our patient[5]. However, our report focuses on the initial application of concurrent use of chemotherapy and immunotherapy in a dMMR unresectable stage 3 pancreatic cancer patient. There continues to remain very little literature on unresectable pancreatic cancer with the simultaneous use of immunotherapy and chemotherapy. However, more research and clinical trials are needed before the combination of chemotherapy and immunotherapy can be recommended as initial guideline therapy.

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