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Pembrolizumab Efficacy in Metastatic Colon Cancer: Case Report

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Abstract

Colorectal cancer is the third most commonly diagnosed cancer and second leading cause of cancer-related death in the world. Chemotherapy has been shown to be a more effective treatment for colorectal cancer over the past two decades and additionally survival rates have begun to increase further with the introduction of targeted monoclonal antibodies. Immunotherapies are more effective than chemotherapy in the subset (15%) of patients with metastatic colorectal cancer, whose tumors are mismatch-repair-protein deficient (i.e. microsatellite unstable). We presented a case of colorectal adenocarcinoma who was progressed under conventional chemotherapy but after immunotherapy with pembrolizumab, according to her molecular study, she showed complete response in PET scan.

Keywords: Metastatic colon cancer; Immunotherapy; Pembrolizumab.

Introduction

According to GLOBOCAN 2020 data, colorectal cancer is the third most commonly diagnosed cancer and second leading cause of cancer-related death in the world. Total resection of the tumor is the optimal treatment in the setting of colorectal malignant lesion [1]. Reliance on the patients TNM stage, their individual performance and treatment with chemotherapy and irradiation are the proceeding courses of treatment. Chemotherapy has been shown to be a more effective treatment for colorectal cancer over the past two decades, and additionally survival rates have begun to increase further with the introduction of targeted monoclonal antibodies [2]. Immunotherapy has changed cancer treatment in recent years, and since its initial approval for the treatment of melanoma, it has become the standard of care for numerous other malignancies including colorectal cancer [3]. Emerging data suggest that the use of checkpoint inhibitors (i.e., PD-1 and PD-2) as immunotherapies is more effective than chemotherapy in the subset (15%) of patients with metastatic colorectal cancer, whose tumors are mismatch-repair-protein deficient (i.e. microsatellite unstable).

Case presentation

A 67-year-old female patient with the initial symptoms of iron deficiency anemia, severe non-bloody diarrhea, severe nausea and vomiting was under investigation and symptomatic treatment since 2018, until a colonoscopy was performed at the end of 2018. This showed multiple and small left side colonic polyps and large proximal transverse colonic mass.

The pathology of the mass was reported as an adenocarcinoma, which showed to be moderately differentiated and mucin producing. The doctor performed a total colectomy surgery in March 2018 and starts the patient on chemotherapy in April 2019. During the treatment, the patient developed fever and pancytopenia, which was due to 5FU toxicity as a result of the TYMS heterozygous mutation.

A small hypodense lesion was reported in the right lobe of the liver in the follow-up CT scan during treatment in June 2020. The patient's chemotherapy was then continued until October 2020. The following CT scan taken the next month reported the following:

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Two hypodense nodes measuring 6 x 4.6 mm and 9.2 x 6.2 mm are seen in posterior -inferior segment of right liver lobe probably due to a liver cyst. A small calcified spot with diameter 3 mm is detected in the right liver lobe that is highly suggestive for an old granuloma. A small node with D=10 mm is seen within the mesenteric fat adjacent of the lower pole of spleen. Another attenuated node (cystic lesion) with 27 x 24 mm is seen at LUQ Of cavity posterior aspect of left kidney.

In the follow-up colonoscopy in the same time period, there were polyps detected in the rectosigmoid. A polypectomy was performed, and its pathology showed a tubular adenoma with focal surface high grade dysplasia. The patient's ostomy return surgery was performed on December 2020. In January 2020, the patient became a candidate for immunotherapy, and was subjected to molecular and PET examination. Her PET report showed an FDG avid lesion in the high rectum region, compatible with malignancy. The study is consistent with metastatic disease: A mildly FDG-avid right lower lobe pulmonary nodule, multiple FDG-avid peritoneal/soft tissue lesions (seeding) and several FDG-avid abdominopelvic lymph nodes. A tiny right middle lobe pulmonary nodule is beyond the resolution of PET.

Molecular study reported wild type BRAFF oncogene, Kras mutant wild type Nras oncogene, MSI - H negative, PDL-1 positive, HER2 1+.

A course of immunotherapy with Kytruda was started from January 2020 and continued until December 2021. During the treatment in July and February 2020, a PET scan was scheduled for the patient, which reported the following:

The current study is compatible with near complete metabolic response to therapy (with faintly FDG-avid peritonea/residual lesions) due to interval resolution. Near complete resolution of previously seen FDG-avid peritoneal soft tissue lesions and abdominopelvic, lymph nodes/soft tissue nodules, resolution of previously seen FDG-avid lesion in rectum (surgically removed), and significant decrease in size and resolution of FDG uptake of the previously seen right lower lobe pulmonary nodule were all reported.

The current study is compatible with excellent complete metabolic response to therapy due to interval resolution of FOG uptake of the previously seen peritoneal soft tissue lesions and abdominopelvic lymph nodes/soft tissue nodules.

Discussion

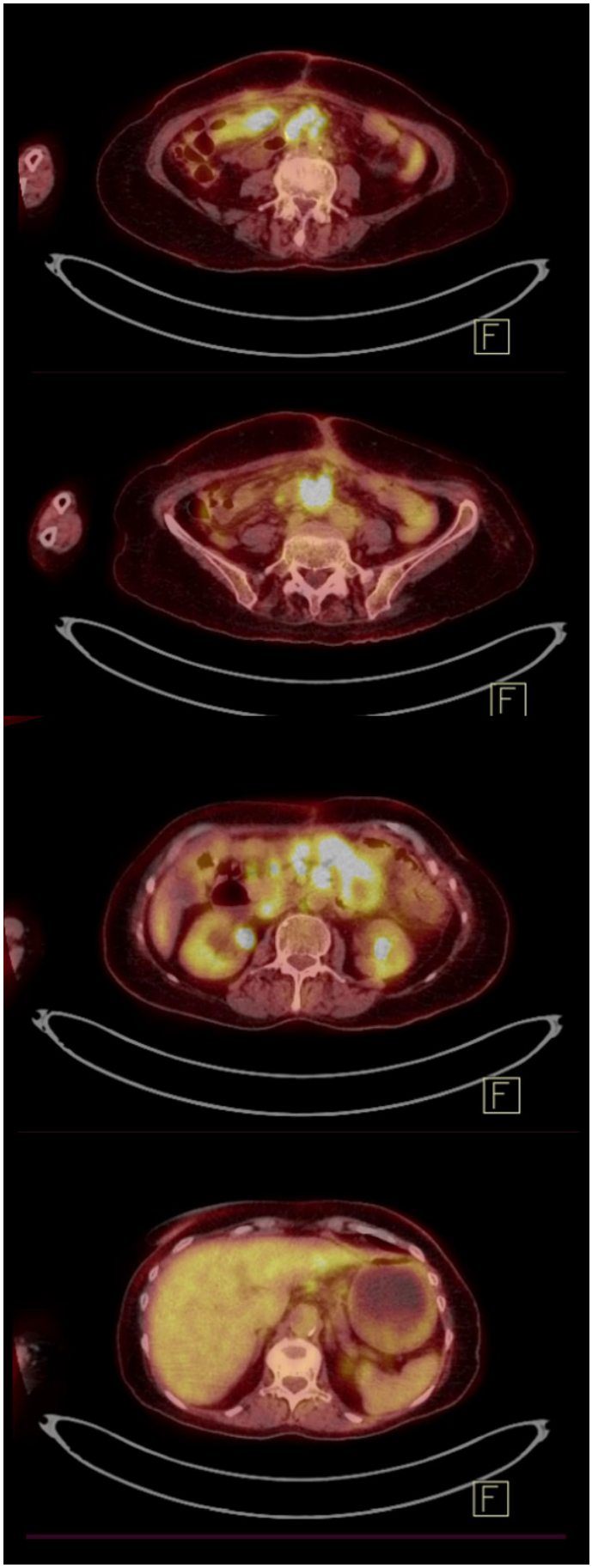
In the 21th century targeted therapy was introduced and accepted and as a viable cancer treatment. Monoclonal antibodies and immune check point inhibitors were approved in a subset of mCRC patients.

According to promising role of ICI in metastatic disease, clinical trials are studying ICI in dMMR/MSI-H in the adjuvant and neoadjuvant setting in colorectal cancer [4].

Recently, pembrolizumab was approved by the U.S Food and Drug Administration as a first-line treatment for patients with dMMR/MSI-H mCRC.

According to NCCN guidelines (version 2021) colorectal cancer patients, for whom intensive therapy was not deemed appropriate, can be treated with nivolumab or pembrolizumab (preferred), in settings of dMMR/MSI-H only.

Before



We also used pembrolizumab (under brand name Kytruda) in our patient who was deemed an appropriate candidate based on her molecular study.

Andre et al. (2021) in a phase III, randomized open-label KEYNOTE-177 study, showed that pembrolizumab, as opposed to chemotherapy, provided superior progression-free survival at second interim analysis in patients with MSI-H/dMMR mCRC [5].

The NICHE study showed pathological responses in all 20 dMMR/MSI-H patients who received ipilimumab + nivolumab, with 12 pCRs [6].

In our case, clinical and radiological response to Kytruda was established in PET scans.

Despite advances in ICI therapies in CRC treatment, >50% of patients with dMMR/MSI-H mCRC do not respond [7]. Meanwhile, multiple studies explore novel therapeutic approaches with immunotherapy, including combinations with radiation therapy, chemotherapy, targeted therapy and treatment for early-stage CRC in the neoadjuvant and adjuvant settings.

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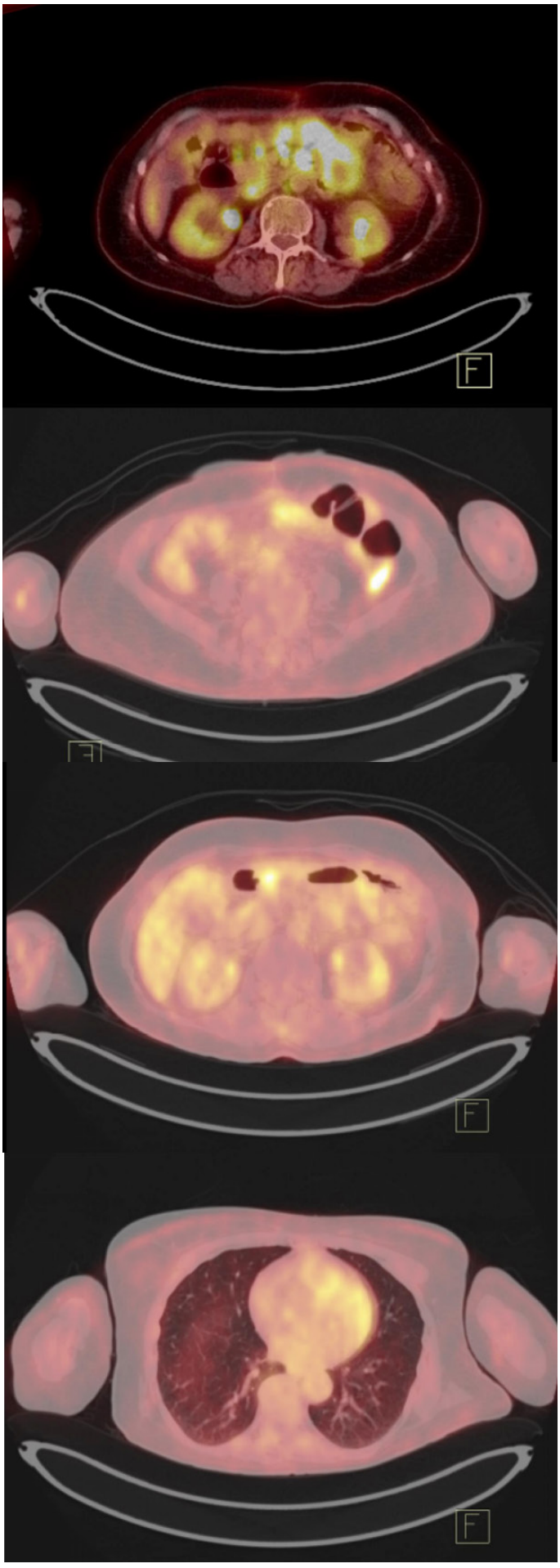
After



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