Clinical Oncology: Case Reports

Case Reports A SCITECHNOL JOURNAL

Case Report of Radiographic Pseudoprogression in a Localized dMMR Rectal Cancer Patient Following Treatment with Neoadjuvant PD1-Based Immunotherapy

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Abstract

PD-1 based immunotherapy has shown significant efficacy in Deficient Mismatch Repair (dMMR) metastatic Colo Rectal Cancer (CRC), leading to FDA approval of several immunotherapeutic agents. Clinical trials have explored the use of immunotherapy in localized dMMR CRC, with promising results. This case report presents a challenging case of a patient with localized dMMR rectal cancer treated with a novel bispecific antibody (XmAb20717; vudalimab) targeting of PD1 and CTLA4. The patient initially experienced radiographic pseudoprogression but achieved a complete radiographic response after six months of therapy. The occurrence of pseudoprogression in localized dMMR rectal cancer is of relevance given the curative- intent setting and challenges it creates for treatment decision-making. In this case, endoscopic evaluation played a vital role in determining the presence of pseudoprogression, guiding treatment continuation, and enabling non-operative management. A multidisciplinary approach is needed for the management of locally advanced dMMR rectal adenocarcinoma treated with PD-1 based therapy to guide the appropriate treatment decision.

Keywords: Pseudoprogression; dMMR Rectal cancer; PD-1 therapy

Background

PD-1 based immunotherapy has demonstrated dramatic activity for dMMR CRC, which has led to the FDA approval of nivolumab, pembrolizumab, dostarlimab, and nivolumab/ipilimumab. The recent KEYNOTE 177 clinica trial demonstrated the superiority of pembrolizumab compared to chemotherapy in the first- line metastatic setting for dMMR CRC [1]. Based on this high level of activity a number of phase II trials have explored the use of immunotherapy in patients with localized dMMR[2-4]. In particular, the report by Cercek et al onin 18 dMMR rectal adenocarcinomas demonstrated complete radiographic and endoscopic responses in all patients resulting in a non-surgical, watchful waiting approach in all patients. In part, this data ledlead to the National Comprehensive Cancer Network (NCCN) guidelines recent April 2023 incorporation of nivolumab, dostarlimab, or pembrolizumab as treatment options for localized dMMR rectal cancer.

This rapid incorporation into the management of localized rectal cancer, however, has provided limited guidance regarding the optimal disease assessments, potential pattern of treatment responses, and duration of therapy [5]. In this report, we present a challenging case of a novel immunotherapy for a localized dMMR rectal cancer, in which the primary tumor demonstrated radiographic pseudoprogression.

Case Presentation

We present the case of a patient in their 50s who presented with intermittent constipation, hematochezia, rectal pressure, and tenesmus. Colonoscopy revealed a fungating, infiltrative, and ulcerated non-obstructing mass at 4 cm from the anal verge. Biopsies revealed a moderately differentiated adenocarcinoma with loss of MLH1 and PMS2 immunohistochemistry expression consistent with a deficiency in mismatch repair. MLH1 methylation testing revealed no methylation and germline genetic panel found no alterations. Further next-generation sequencing was not possible due to insufficient tumor tissue.

Radiographic imaging with Computed Tomography (CT) of the chest abdomen and pelvis and Magnetic Resonance Imaging (MRI) of the pelvis revealed no metastatic disease and a T3b, N+ rectal tumor located 2.7 cm from the anal verge, Figure 1A. The mass abutted and involved the top of the internal anal sphincter. The serum Carcino Embryonic Antigen (CEA) was normal.

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Received: November 20, 2023; Manuscript No: COCR-23-121395 **Editor Assigned:** November 25, 2023; PreQC Id: COCR-23-121395 (PQ) **Reviewed:** December 08, 2023; QC No: COCR-23-121395 (Q) Revised: December 16, 2023; Manuscript No: COCR-23-121395 (R) **Published:** December 25, 2023; DOI: 10.4172/cocr.6(11).320

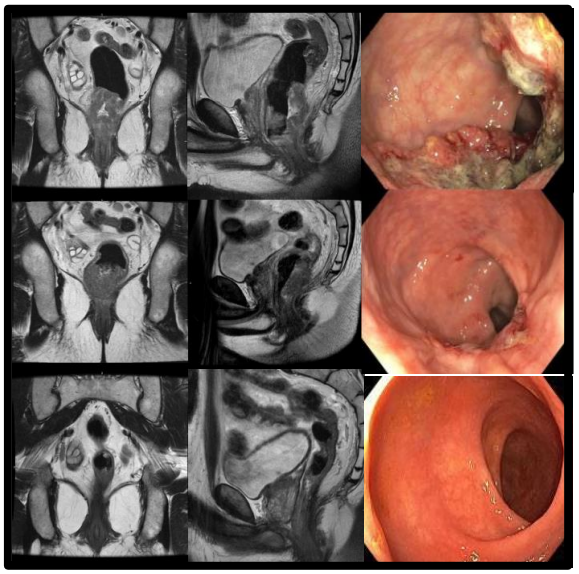

Figure 1. Sagittal, coronal T2 weighted Magnetic Resonance Images, and endoscopic tumor assessment from (1A) baseline showing a low rectal annular tumor; (1B) 8 weeks post treatment showing interval increase in the tumor, especially with regard to the posterior wall and on the left, with increased involvement of adjacent structures but endoscopic response and (1C) 16 weeks post treatment showing interval decrease in the rectal tumor and 6-month endoscopy showing complete endoscopic tumor response.

Systemic treatment was initiated on a clinical trial with vudalimab a novel bispecific antibody designed to simultaneously engage both programmed cell-death protein 1 (PD1) and Cytotoxic T-Lymphocyte associated protein-4 (CTLA4). Following four doses given every two weeks (8 weeks) the patient underwent a restaging MRI pelvis that revealed progressive disease with new involvement of the left levator muscle consistent with T4b, and a tumor regression grade of 3, Figure 1B. CT of the chest, abdomen, and pelvis revealed progressive disease with the superior portion of the rectal tumor measuring 2.0 x 4.5 cm compared to the prior2.2 x 3.2 cm. In addition, increased lymph nodes in the retroperitoneum, axillary, mediastinal, and bilateral lung hilum were present.

Bronchoscopy with endobronchial ultrasound was conducted and fine needle aspiration of multiple lymph nodes revealed no metastatic carcinoma. A Sigmoidoscopy was performed revealing improvement in the rectal tumor. The endoscopic improvement, negative lymph node biopsies, and patient's improved rectal discomfort were determined to be most consistent with radiographic pseudoprogression, and the patient was continued on a clinical trial with vudalimab.

Following an additional 4 cycles repeat MRI pelvis demonstrated a near complete resolution of the rectal tumor, tumor regression grade 1, Figure 1C. CT chest abdomen and pelvis revealed improvement in all prior enlarged lymph nodes. Subsequent MRI pelvis at 6 months post the start of therapy demonstrated a complete radiographic response, tumor regression grade of 0 and endoscopic assessment at 8 months demonstrated an endoscopic complete response.

Discussion

In this case we report the use of a novel bispecific PD1 and CTLA4 antibody in a localized dMMR rectal adenocarcinoma that resulted in a complete radiographic response following six months of therapy. However, the finding of greatest interest is the occurrence of pseudoprogression in a patient with localized dMMR rectal cancer.

The presence of pseudoprogression in localized disease is of much greater concern than in the metastatic disease setting, as surgery with or without radiation therapy represents the standard curative treatment option. Thus, the recognition that radiographic pseudoprogression of both lymph nodes and the primary tumor can occur in the management of localized dMMR rectal cancer is of critical importance to treating physicians.

Pseudoprogression has been well described in metastatic patients treated with PD1 based therapy with one retrospective study of 123 metastatic dMMR CRC patients reporting a rate of pseudoprogression of 10% [6]. The rate in localized dMMR cancers is not known though one prior report described cases of lymph node based pseudoprogression in 3 dMMR rectal cancer patients [7].

A critical finding from this case is the use of endoscopic evaluation to help determine the presence or absence of pseudoprogression [8]. The endoscopic response along with clinical symptom improvement supported the determination of radiographic pseudoprogression and were the key factors that resulted in continued therapy. This decision resulted in a complete radiographic response and plan for non-operative management, which enabled this patient to avoid an perineal resection and resulting permanent colostomy.

This report also provides a single case example of the potential activity of novel immunotherapy approaches for localized dMMR rectal cancer with a complete radiographic

response from the bispecific antibody, vudalimab. Enrollment to this clinical trial is ongoing, NCT05337735.

Conclusions

This case highlights the importance of a multidisciplinary approach, including endoscopic assessment, in managing immune therapy for locally advanced dMMR rectal adenocarcinoma. As illustrated by this case, PD1 based therapy can result in radiographic pseudoprogression in both lymph nodes and primary tumor. The use of endoscopic assessment should be utilized to help guide management in such cases. Continued research and clinical trials are necessary to optimize the management of locally advanced dMMR colorectal adenocarcinoma in the era of immunotherapy.

Abbreviations

Colorectal cancer (CRC), deficient mismatch repair (dMMR), National Comprehensive Cancer Network (NCCN), computed tomography (CT), magnetic resonance imaging (MRI), carcinoembryonic antigen (CEA), programmed cell-death protein 1 (PD1), and cytotoxic T-lymphocyte associated protein-4 (CTLA4)

Declarations

Ethics approval and consent to participate: This case report was approved by the MD Anderson Institutional Review Board.

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analysedanalyzed during the current study.

Competing Interests

AD receives research funding support from Xencor.

Authors' Contributions

IO and MO conceived of the idea and performed major contributions to writing. CV perfromedperformed radiology interpretation and manuscript review. BB, AD HM, BJ provided manuscript review. All authors reviewed the manuscript.

Acknowledgements

The authors would like to thank the patient of this case, who participated in this Xencor sponsored clinical trials. not applicable

References

1. Andre T, Shiu KK, Kim TW, Jensen BV, Jensen LH, et al. (2020). Pembrolizumab in microsatellite-instability–high advanced colorectal cancer. N Engl J Med, 383(23), 2207-2218.
2. Cercek A, Lumish M, Sinopoli J, Weiss J, Shia J, et al. (2022). PD-1 blockade in mismatch repair–deficient, locally advanced rectal cancer. N Engl J Med, 386(25), 2363-2376.
3. Ludford K, Ho WJ, Thomas JV, Raghav KP, Murphy MB, et al. (2023). Neoadjuvant pembrolizumab in localized microsatellite instability high/deficient mismatch repair solid tumors. J Clin Oncol, 41(12), 2181-2190.
4. Chalabi M, Fanchi LF, Dijkstra KK, Van den Berg JG, Aalbers AG, et al. (2020). Neoadjuvant immunotherapy leads to pathological responses in MMR-proficient and MMR-deficient early-stage colon cancers. Nat med, 26(4), 566-576.
5. Zhang X, Wu T, Cai X, Dong J, Xia C, et al. (2022). Neoadjuvant immunotherapy for MSI-H/dMMR locally advanced colorectal cancer: New strategies and unveiled opportunities. Front immunol, 13, 795972.
6. Colle R, Radzik A, Cohen R, Pellat A, Lopez Tabada D, et al. (2021). Pseudoprogression in patients treated with immune checkpoint inhibitors for microsatellite instability-high/mismatch repair-deficient metastatic colorectal cancer. Eur J Cancer, 144, 9-16.
7. Xie Y, Lin J, Zhang N, Wang X, Wang P, et al. (2023). Prevalent pseudoprogression and pseudoresidue in patients with rectal cancer treated with neoadjuvant immune checkpoint inhibitors. J Natl Compr Cancer Netw, 21(2), 133-142.
8. Fox DA, Bhamidipati D, Konishi T, Kaur H, You N, et al. (2023). Endoscopic and imaging outcomes of PD-1 therapy in localised dMMR colorectal cancer. Eur J Cancer, 194, 113356.

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