Immune Checkpoint Inhibitors (Nivolumab)-Induced Enterocolitis Demonstrated on ^{18}Fluorine-Fluorodeoxyglucose Positron Emission Tomography-Computed Tomography

Abstract

Nivolumab, an immune checkpoint inhibitor, is a humanized anti-programmed death-1 monoclonal antibody that is used for the treatment of various cancers after second-line chemotherapy. We report a 23-year-old male with relapsed Hodgkin's lymphoma Stage IV treated with nivolumab. After 3 months of treatment, he developed watery diarrhea and cramping abdominal pain. Follow-up positron emission tomography-computed tomography scan showed complete metabolic resolution of the disease; however, there is bowel wall thickening and colonic distension with corresponding increased fluorodeoxyglucose uptake. These findings are related to immune-related adverse event associated with nivolumab treatment, i.e., secondary enterocolitis. These adverse events can be successfully treated if timely and appropriately diagnosed.

Keywords: *^{18}Fluorine-fluorodeoxyglucose positron emission tomography-computed tomography, anti-programmed death-1 monoclonal antibody, enterocolitis, nivolumab*

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A 23-year-old male has relapsed Hodgkin's lymphoma Stage IV receiving an immune checkpoint inhibitor (ICI) therapy (nivolumab). After 3 months of treatment, the patient developed watery diarrhea and cramping pain. ^{18}Fluorine-fluorodeoxyglucose positron emission tomography-computed tomography (^{18}F-FDG PET-CT) is performed for restaging. ^{18}F-FDG PET-CT images showed bowel wall thickening and colonic distension with corresponding increased tracer uptake [Figure 1]. Although compare to prior study, there is complete metabolic resolution of prior hypermetabolic lesions are noted. Baseline and follow-up scans after nivolumab therapy are shown in Figure 2. In the current study, the findings in the bowel are likely related to side effects of immunotherapy inducing secondary enterocolitis. Other causes like drug (e.g., metformin)-induced nonspecific uptake in the bowel is excluded.

Nivolumab is an ICI, is a humanized anti-programmed death-1 (PD-1) monoclonal antibody that is used as second-line therapy in various types of cancer such as melanoma, non-small cell lung cancer, renal cancer, Hodgkin's lymphoma, urothelial cancer, and head and neck cancers.[1,2] Recently, nivolumab has demonstrated high (64%–87%) response rates in relapsed or refractory Hodgkin's lymphoma.[3] Nivolumab may activate T cells to develop antitumor effects, but this immune activation sometimes causes immune-related adverse events, such as pneumonitis, hepatitis, and enterocolitis.[4] Sometimes, these adverse events are serious and life-threatening, which require timely patient management and adequate therapeutic decisions.

ICIs, nivolumab is associated with many immune-regulated adverse events including nausea, abdominal pain, and diarrhea. Diarrhea is observed in about one-third of patients. It usually occurs in the 3rd month of therapy. Diarrhea may be infectious or autoimmunological. About 8%–22% of patients receiving immunotherapy develop autoimmunological enterocolitis.[5] Clinical symptoms of enterocolitis include mixed watery and bloody diarrhea and cramping pain.[6] Enterocolitis can be managed with cessation of nivolumab and administration of intravenous corticosteroid therapy or infliximab therapy in severe cases,

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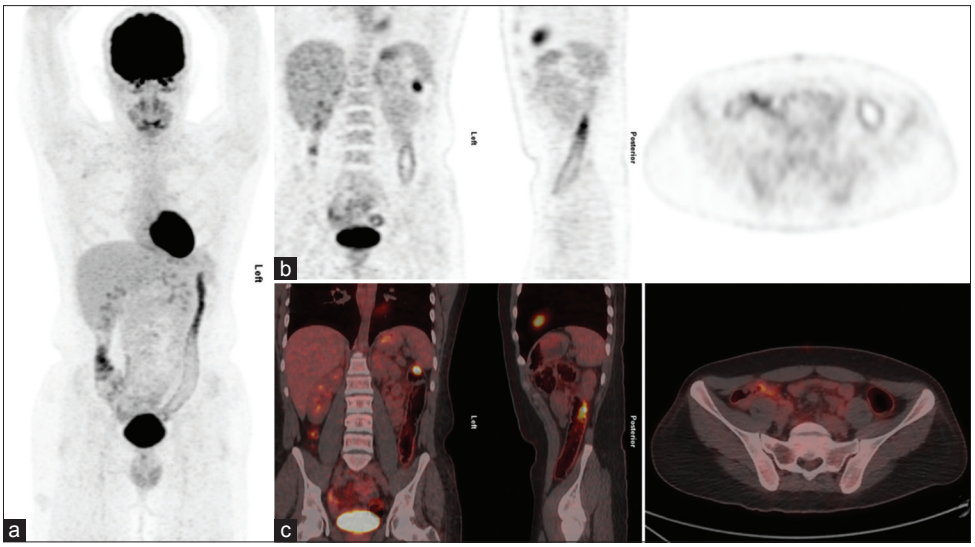

Figure 1: ^{18}Fluorine-fluorodeoxyglucose positron emission tomography-computed tomography is performed for restaging. (a) Maximum intensity projection fluorodeoxyglucose (b) coronal, sagittal, and transaxial images show increased tracer uptake in the ascending and descending colon. (c) Fused positron emission tomography-computed tomography images showed bowel wall thickening and colonic distension with corresponding increased tracer uptake. These findings are likely related to side effects of immunotherapy inducing secondary enterocolitis

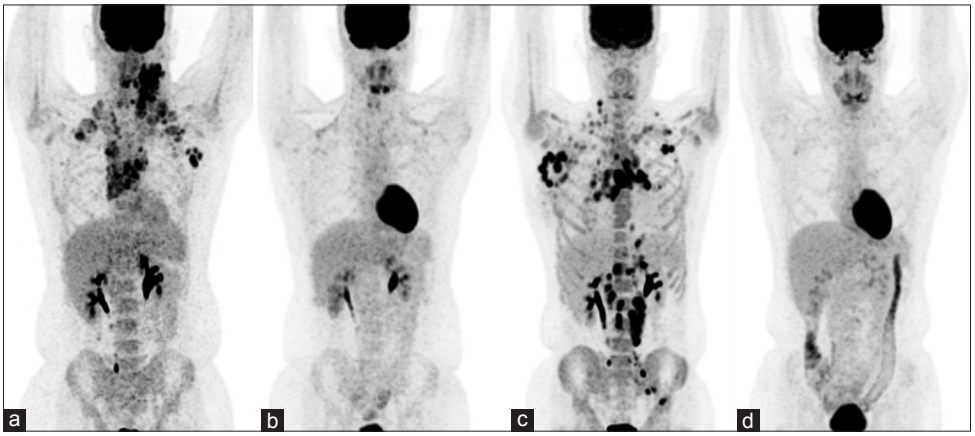

Figure 2: (a) Baseline ^{18}fluorine-fluorodeoxyglucose positron emission tomography-computed tomography (b) after 6 cycles of adriamycin, bleomycin, vinblastine, and dacarbazine showed complete remission (c) follow-up ^{18}fluorine-fluorodeoxyglucose positron emission tomography-computed tomography after 2 years demonstrate disease relapsed in nodal, pulmonary, adrenals, and bones (Stage IV). (d) After 3 months of nivolumab therapy, scan showed complete metabolic resolution

like in our case.[7] ^{18}F-FDG PET-CT is standard of care for the staging, monitoring of response to therapy, and detection of disease recurrence for Hodgkin's disease and non-Hodgkin's lymphomas.[8,9] ^{18}F-FDG PET-CT can be used to identify regions of active inflammation in ulcerative colitis.[10] ICI is a potentially important therapeutic agent for refractory and relapsed Hodgkin's lymphomas.[11] As the use of ICIs in cancer therapy increases, therefore immune-related adverse events are frequently identified on ^{18}F-FDG PET-CT, which may lead to early diagnosis, close clinical follow-up, and appropriate clinical management of immune-related adverse events.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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