Case Report

Mesenteric Panniculitis as a Side Effect of Nivolumab in a Patient with Larnyngeal Cancer

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Abstract

Mesenteric panniculitis is rare, usually idiopathic, caused by inflammation of the fatty tissue of the mesentery, especially in the small intestine. The relation between cancer and mesenteric panniculitis is unclear. In some studies, mesenteric panniculitis precedes cancer diagnosis; on the other hand, some studies suggest no correlations. Immunotherapeutics have a wide range of side effects; virtually, every system and organ in the body can be affected. Herein, we presented a rare case of mesenteric panniculitis in a patient with larnyngeal cancer as a side effect of nivolumab treatment. The patient was presented with nausea and vomiting and diagnosed with intravenous contrast-enhanced computed tomography and fully recovered with corticosteroid treatment. The case report highlights the importance of noticing rarely seen side effects of immunotherapy which can be treated easily with immunosuppressive agents.

Keywords: *Laryngeal cancer, mesenteric panniculitis, nivolumab, side effect*

Introduction

Immunotherapy has changed the treatment landscape of many cancers including but not limited to melanoma, lung cancer, renal cell carcinoma, colon cancer, and head and neck cancer. Immune checkpoint (ICI) inhibitors were designed to block the negative regulatory pathway of the immune system, thus activating it against cancer.[1]

The relation between mesenteric panniculitis (MP) and cancer is not clearly defined. Even though MP is a rarely seen condition, it sometimes precedes cancer diagnosis. Herein, we report an unusual case of MP as a side effect of ICI in a patient with head and neck cancer.

Case Report

A 56-year-old male patient was diagnosed with laryngeal cancer. At the time of diagnosis, the disease was in the local stage, so he was treated with chemoradiotherapy. After one and a half years, the disease was recurred and he was treated with cetuximab, carboplatine, and paclitaxel chemotherapy. Unfortunately, chemotherapy treatment was ineffective and disease progressed. Afterward, nivolumab immunotherapy was initiated.

After two cycles of nivolumab, he complained of gradual worsening of vomiting and nausea; we admitted the patient to the hospital. Before admission to the hospital, a pulmonogist in another hospital ordered thorax computed tomography (CT) for another reason and the disease regressed in that graphy. His physical examination showed no tenderness and rebound sign. At the same time, his biochemical and hemogram parameters

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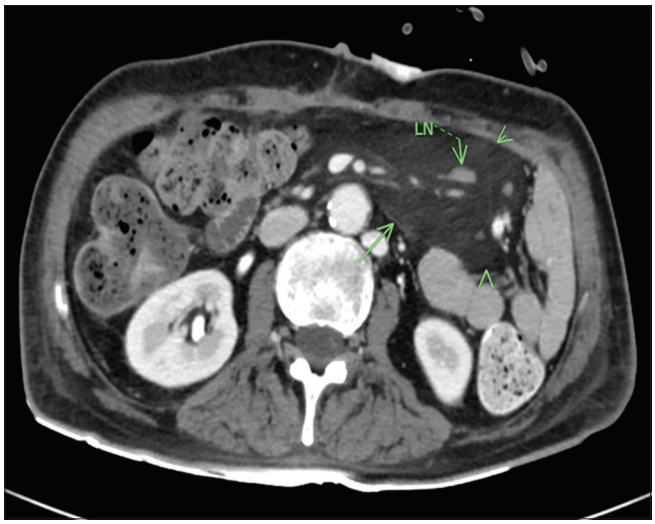

Figure 1: LN is lymph node; short green arrow is hyperattenuation; long green arrow is pseudocapsule

were in the normal range except for CRP, which was 230 mg/L (0–5). Plain abdominal X-ray showed no fluid level. The gastrointestinal surgeon examined the patient and recommended discontinuation of enteral nutrition via PEG (percutaneous endoscopic gastrostomy). According to the suggestion, enteral feeding was stopped, and metoclopramide and granisetron were started. The patient's nausea and vomiting worsened; repeated physical examination showed no defense rebounds and tenderness. Transdermal fentanyl patch was removed to eliminate opioid-induced nausea and vomiting. Additionally, to exclude cranial metastasis, cranial MRI was performed and no metastasis was detected.

Besides all these actions, nausea and vomiting persisted, so intravenous contrast-enhaced abdominal CT was ordered. Abdominal CT showed hyperattenuation of mesenteric fat, psuedocapsule, and lymph node in mesenteric fat [Figure 1].

The patient was diagnosed with MP. Methylprednisolone 1 mg per kg was started. After 3 days, nausea and vomiting subsided; his CRP value decreased from 230 mg/L to 107 mg/L. After 1 week, methylprednisolone dose was reduced by one quarter, and after 2 weeks of the treatment, the CRP value was decreased to 11 mg/L. In the third week of the treatment, methylprednisolone dose was 0.5 mg per kilogram. His complaints were totally disappeared. After 4 weeks, methylprednisolone dose was 8 mg and nivolumab was restarted again. After a week, methylprednisolone was reduced to 4 mg, and after that, it was stopped. At that time, intravenous contrast-enhanced abdominal CT showed resolution of all signs including hyperattenuation of mesenteric fat, pseudocapsule, and lymph node in mesenteric fat [Figure 2].

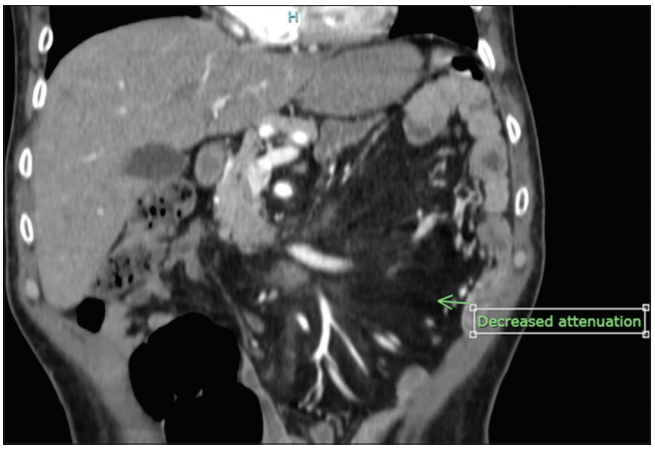

Figure 2: Hyperattenuation resolution

After four cycles of nivolumab treatment, neck MRI showed disease progression, the patient's dyspnea worsened, and he was followed up in the intensive care unit and passed away 1 week later.

Discussion

MP is a rare, usually idiopathic inflammation of the fatty tissue of the mesentery, especially in the small intestine. Some suggested etiological factors include abdominal surgery, inflammatory disorders, granulomatous diseases, malignancy, and pancreatitis.[2]

The relation between cancer and MP is unclear. While there are many studies suggesting the existence of correlation, some studies suggest that there is no correlation between malignancy and MP.[3] Although predominantly lymphoma, other cancers such as breast cancer, lung cancer, gastrointestinal cancers, gynecological cancers, hepatocellular carcinoma, and prostate adenocarcinoma have also been implicated.[4]

The ICI approval is rapidly expanding in many solid cancers including head and neck cancer. Nivolumab, anti PD-1 inhibitor, has shown a survival advantage after the first-line chemotherapy in the head and neck cancer.[5] Unlike conventional chemotherapy, ICI has unique side effects. Almost every system in human body can be affected, but the skin, endocrine system, and gastrointestinal system are most commonly affected.[6] Herein, we presented a case of MP caused by nivolumab treatment.

Our patient was treated with nivolumab after definitive chemoradiotherapy and anti-EGFR-containing chemotherapy regime. Nausea and vomiting are ordinary side effects of conventional chemotherapy, but as an immune-related side effect, they often presented with other symptoms such as colitis and hepatitis. Isolated nausea and vomiting are rarely seen as a side effect of immunotherapy.[6]

In our patient, the cancerous lesions were regressed after two cycles of nivolumab, but gradually, worsening of vomiting and nausea developed. To exclude metabolic disorders, especially hypercalcemia and hyponatremia, we investigated biochemical parameters, both of which were within the normal range. Intestinal obstruction, mechanical or pseudo-obstruction, is frequently seen in cancer patients,[7] so we consult the patient with a gastrointestinal surgeon, and the absence of defense and rebound together with the absence of fluid level on plain X-ray of the abdomen excludes this possibility.

Drugs are the usual suspects of nausea and vomiting. Chemotherapeutics such as antiseizure drugs, antibiotics, digitalis, nonsteriod anti-inflammatory drugs, and opioids can cause nausea and vomiting. Our patients use fentanyl transdermal patch; we removed it for excluding opioid-induced vomiting and nausea.

In addition to all these interventions, the patient continued to have nausea and vomiting, and although he had no neurological symptoms, we requested a cranial MRI to rule out metastasis and no metastasis was detected on MRI. Eventually, we performed abdominal CT with intravenous contrast to detect peritoneal pathology and vascular pathology causing vomiting and nausea. MP was detected.

Abdominal CT with an intravenous contrast agent is the best modality for diagnosis of MP. The five cardinal radiological findings of MP are pseudocapsule, hyperattenuation in mesenteric fat, millimetric lymph nodes in fatty mass, halo sign, and fatty mass lesion in the mesentery.[2] In our case, pseudocapsule, hyperattenuation of mesenteric fat, and millimetric lymph nodes in fatty mass were detected.

The association of MP and cancer is complex; sometimes, it may precede the diagnosis of cancer; in our case, it occurred long after the diagnosis. MP may be part of a paraneoplastic syndrome, but in our patient, the disease regressed during MP, which made it unlikely.

The treatment of MP is not uniform standard treatment. Most incidental MP is asymptomatic and does not require treatment. A minority of patients have symptoms, and the most common symptom is abdominal pain seen in more than half of the patients. Vomiting is seen in 18% of patients and nausea in 5%.[8] Isolated nausea and vomiting are rarely seen indeed, which occur in our patient.

Generally, gastrointestinal side effects start within 2 to 14 weeks after initiation of ICI. In our case, vomiting and nausea started nearly 4 weeks after treatment initiation. There are erythema nodosum-like skin panniculitis related to ICI use in the literature.[9] To the best of our knowledge, this is the first case of nivolumab-related MP in the literature.

The treatment of irAE usually starts with corticosteroid. In general, after 48–72 hours, symptoms begin to resolve; if not, other immunosuppressive drugs such as anti-TNF agents, methotrexate, and azathiopirin should be administered. In our patient, vomiting and nausea start after 4 weeks from nivolumab initiation. He had grade 3 nausea and vomiting; we suspended nivolumab treatment and began methylprednisolone. In 48–72 hours, his symptoms began to resolve, and gradually, we decreased dosage and in 4 weeks, we stopped treatment and began nivolumab again.

In conclusion, ICI has a wide range of indications in cancer treatment and has unique side effects. MP is a rare disease often presented with abdominal pain, nausea, and vomiting. Isolated nausea and vomiting can be signs of serious medical conditions. All clinicians should remember that ICI can cause inflammation anywhere in body including isolated mesenteric inflammation.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

Written informed consent was obtained from the patient's family for the publication of this case report.

Author contributions

OK was involved in the identification and selection of patient case as well as in writing, editing of case. YS was involved in writing, investigation of literature and supervision, SI was involved in writing, conceptualisation and investigagtion of literature, ST was involved in writing, formal analysis and software. All authors contributed to the article and approved the submitted version.

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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