

A case of enteritis induced by ipilimumab and nivolumab combination therapy

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Case

A 65-year-old man with a history of left renal cell carcinoma 25 years ago underwent left nephrectomy and was regularly followed up. Last year, positron emission tomography showed mediastinal lymph node enlargement. Bronchoscopic biopsy revealed cancer recurrence and metastasis. We administered ipilimumab (1 mg/kg) and nivolumab (4 mg/kg) combination therapy. A week later, he developed diarrhea and abdominal pain. Colonoscopy revealed a reddish edematous mucosa with erosions and ulcers from the terminal ileum to the ileocecal valve (Figure 1A, B). Terminal ileum biopsy revealed lamina propria by inflammatory cell infiltration; however, no crypt abscess or apoptotic bodies were observed. The colon and esophagogastroduodenoscopy findings were normal (Figure 1C, D). Small intestinal capsule endoscopy revealed redness and edema in the jejunum (Figure 2 upper). From the deep jejunum to the ileum, and further into the ileum, common villi, erosions, and ulcers became apparent (Figure 2 lower). Tests for stool bacteria, cytomegalovirus, and other viruses were negative. Therefore, his condition was diagnosed with immune-related enteritis. His symptoms did not improve after stopping ipilimumab and nivolumab. Treatment with prednisolone 40 mg/day immediately improved his symptoms.

Combining nivolumab and ipilimumab (Immune checkpoint inhibitors) is more effective than monotherapy; however, it increases diarrhea and colitis incidence more than nivolumab monotherapy and even more than ipilimumab monotherapy [1,2] While there exist reports of enteritis due to combination therapy, involvement of entire small intestine has not been confirmed [3]. This is the first report explaining the side effects of this combination therapy on the entire gastrointestinal tract, and interestingly, with only enteritis. In addition, small intestinal mucosal damage appeared as different findings on the jejunal and ileal sides. Enteritis can manifest as multiple presentations during combination therapy, and capsule endoscopy may help in its diagnosis.

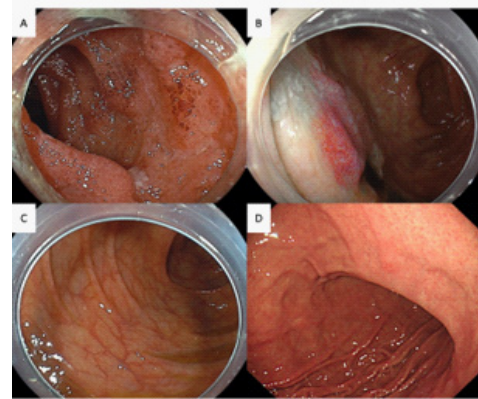


Figure 1: Colonoscopy (EC-L600ZW7; Fuji) revealed a reddish edematous mucosa with erosions and small ulcers in the terminal ileum (A). Linked-color imaging revealed a reddish ileocecal valve with continuous purulent mucus adhesion from the small intestine, clearly bordering the normal colonic mucosa (B). The mucous membranes of the large intestine (C; in colonoscopy) and stomach (D; in esophagogastroduodenoscopy) were normal.

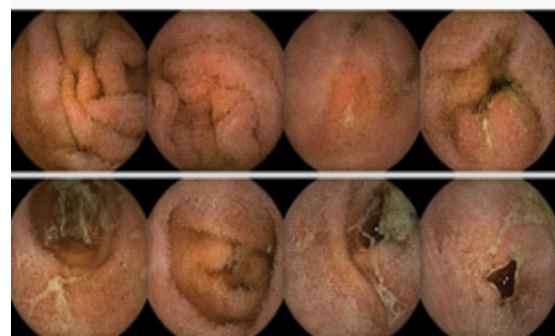


Figure 2: Small bowel capsule endoscopy shows redness and edema in the jejunum (upper), erosions and ulcers in the ileum (lower).

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