Characteristics, treatment, and outcome of patients with bowel perforation after immune checkpoint inhibitor exposure

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Introduction

- Exposure to immune checkpoint inhibitors (ICI) can predispose to immune-related adverse events (irAE) involving the gastrointestinal tract such as, colitis, diverticulitis etc.
- The association between ICI and bowel perforation has yet to be elucidated. We aim to describe the clinical course, complications, treatment and outcomes of patients with bowel perforation on ICI therapy.

Methods

- A retrospective chart review was conducted on cancer patients who were exposed to ICIs between January 2010 and April 2021.
- Patients were divided into two groups: those with complicated (sepsis, fistula, abscess, expired on the same admission) and those with non complicated bowel perforation.
- Diagnosis of bowel perforation was made by abdominal imaging.
- Patient's clinical characters, treatment, and outcomes were compared between the two groups.

Results

- Among 13,991 cancer patients with a exposure of ICI in the study window, 90 eligible patients were included in our final analysis.
- Overall incidence of bowel perforation in our cohort was 0.6%; much lower than comparing other cancer therapies.
- From the 90 patients included in our study, a total of 46 patients had a complication derived from the perforation itself; mortality rate was 15.5%.
- Onset of perforation typically occurred after a median of 4 ICI treatment cycles. The presentation was the typical manifestations of acute abdomen with abdominal pain in 95.5%.
- It was found that 28 patients (31%) had evidence of inflammation in the GI tract such as enterocolitis, diverticulitis and appendicitis.
- Colon was the most common place of perforation in at least 37.7%, other rare cases of perforation such as in the stomach were seen (figure).
- As for treatment, 95% of our sample received antibiotics and with 38% had surgery or interventional radiology procedure, most of the patients evaluated by surgery were not candidate for intervention.

Conclusion

Bowel perforation can occur after ICI therapy at very low incidence (0.6%). Its clinical presentation is similar to traditional perforation; but associated with higher complication rates requiring surgical intervention and impairing lower overall survival.

Table. Baseline demographic characteristics of patients with post-ICI bowel perforation (n=90).

Characteristic	No. of patients (%) or median (IQR)
Median age at time of diverticulitis diagnosis, (IQR)	64 (54-70)
Male sex, no. (%)	49 (54.4)
Cancer types	
Melanoma	21 (23.3)
Gastrointestinal	15 (16.6)
Time from ICI initiation to perforation diagnosis, median (IQR), months	3 (1-6)
Overall duration of ICI treatment before perforation, median (IQR), cycles	4 (2-7)
Concurrent GI conditions	
Immune-related colitis	7 (7.7)
Diverticulitis	??
Appendicitis	??
Symptom: Abdominal pain	86 (95.5)
Complication of perforation, no. (%)	
Fistula	3 (3.3)
Abscess	10 (11.1)
Free air	15 (16.6)
Sepsis	35 (38.8)
Death during the same admission, no. (%)	14 (15.5)