Clinical case

21th BSCRS Post-Graduate Course

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“Colonic perforation after neoadjuvant immunotherapy for an MSI-high stage III colon cancer at the level of the splenic flexure”

31-01-2025

Case presentation

75-year old, ♀

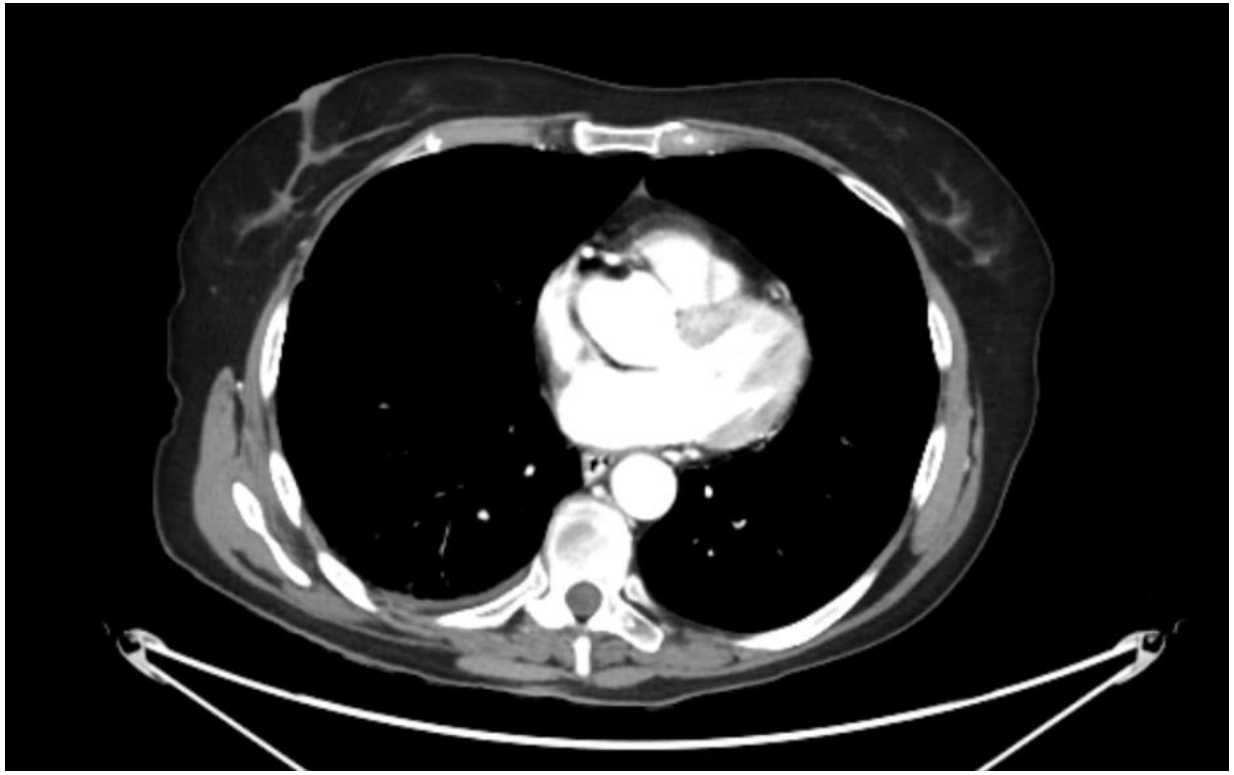
A/ Diffuse abdominal pain, N/V & absence of transit

C/ Tender left hemi-abdomen

L/ CRP 70 mg/L – WBC 18.1 – Hb 17.2 g/dL

ABG/ Lactate 2.12 mmol/L

Case presentation



→ **Urgent laparoscopy**

Case presentation

→ Urgent laparoscopy

1/ Small bowel obstruction caused by omental adhesion;
release of small bowel, no resection needed

2/ Observation of hard tumoral colonic mass at splenic flexure

→ Colonoscopy

Totally circumferential tumoral mass, at 65cm

→ APO

Invasive adenocarcinoma, dMMR → MSI-high

→ Staging

cT3N1M0

Case presentation

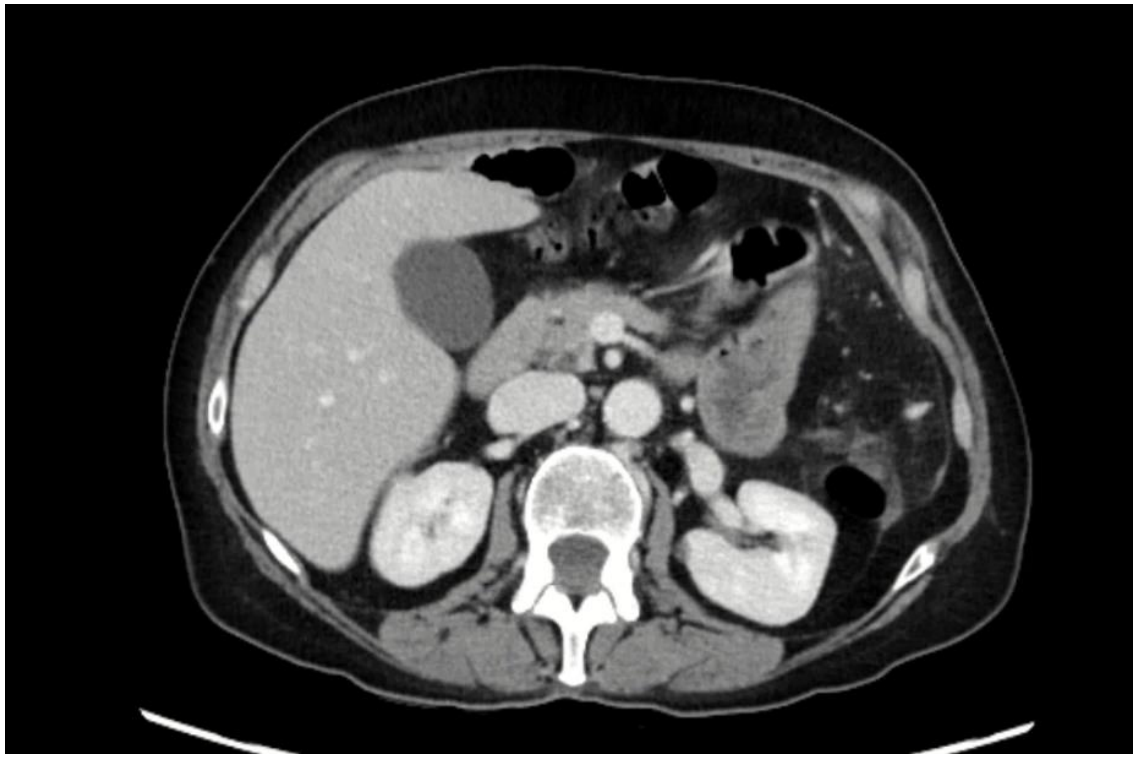
IMP arm of AZUR-2 protocol
Dostarlimab pre- and postoperatively versus surgery + SOC

Dostarlimab 500mg IV q3w x4 → surgery → 1000mg IV q6W x6

- One week after 1st cycle
  → vomiting, fever, tender LUQ and CRP of 324 mg/L

- CT abdomen
  Covered colonic perforation with adjacent collection at the tumor site

Case presentation

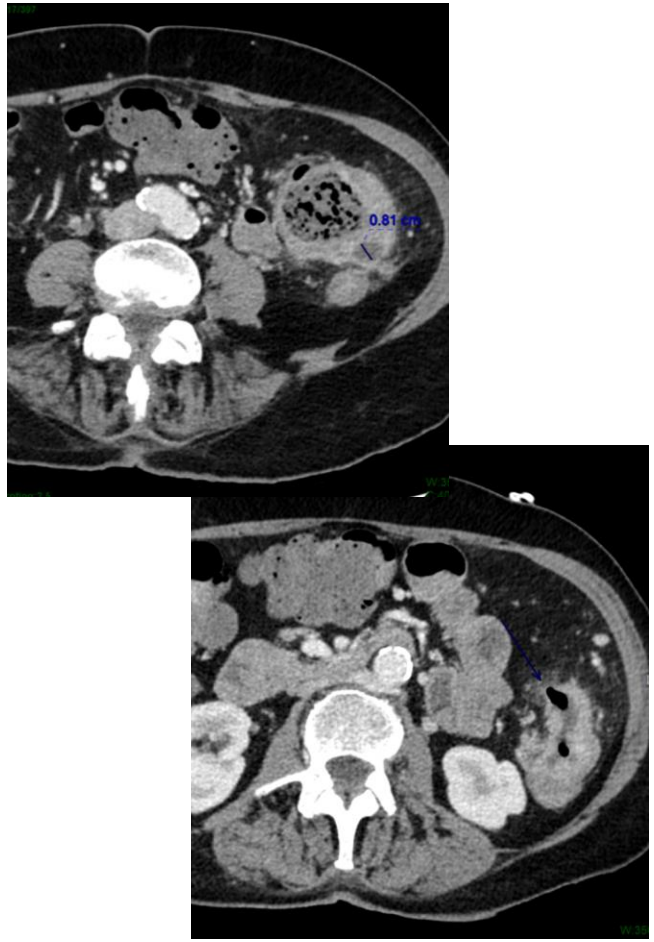


→ Oncological department; conservative treatment

Case presentation

After 7 days of Piperacillin-Tazobactam: CT-abdomen

- ↓ collection volume
- ↓ edematous wall thickening of the distal transverse colon
- ↓ peritoneal enhancement in the left flank
- Resolution of the free fluid in the pelvis
- **Persistent perforation of bowel wall**



→ "Urgent" robot assisted left hemicolectomy

APO = MSI high, invasive adenocarcinoma

→ ypT3 N0 L0 V0 Pn0 R0

→ Completion of adjuvant Dostarlimab

Immunotherapy in CRC

- Mismatch repair-deficient (dMMR) tumors → 10-15% of non-metastatic colon cancer

- Efficacy of chemotherapy = limited
  - **But still treated similarly as pMMR!**

- SOC of stage III dMMR = surgery → adjuvant chemotherapy
  - Recent data (FoxTROT): use of neo-adjuvant CT in patients with locally advanced colon cancer
  - **Pathological response in dMMR: 7%**

Immunotherapy in CRC

Immune checkpoint blockade = highly effective in patient with metastatic dMMR & dMMR locally advanced rectal cancer

↓

Recent data strongly supports the use of neo-adjuvant immunotherapy in non-metastatic dMMR

Promising efficacy → high proportions of clinical & pathological response

AZUR-2 protocol

Dostarlimab = anti-programmed cell death protein 1 (PD-1)

Global, multicenter, randomized, open label phase III study

711 patients

Inclusion criteria
Min. 18 years, no prior therapy, ECOG PS 0-1 and no symptomatic bowel obstruction

AZUR-2 protocol

Stratified by TN-staging, randomised 2:1

Dostarlimab pre- and postoperatively versus surgery + SOC

Dostarlimab 500mg IV q3w x4 → surgery → 1000mg IV q6W x6

Primary endpoint
→ event free survival

Secondary endpoint
→ pathological response, OS, safety

Side-effects of immunotherapy in CRC

→ Enhancing the immune system's ability to attack cancer cells

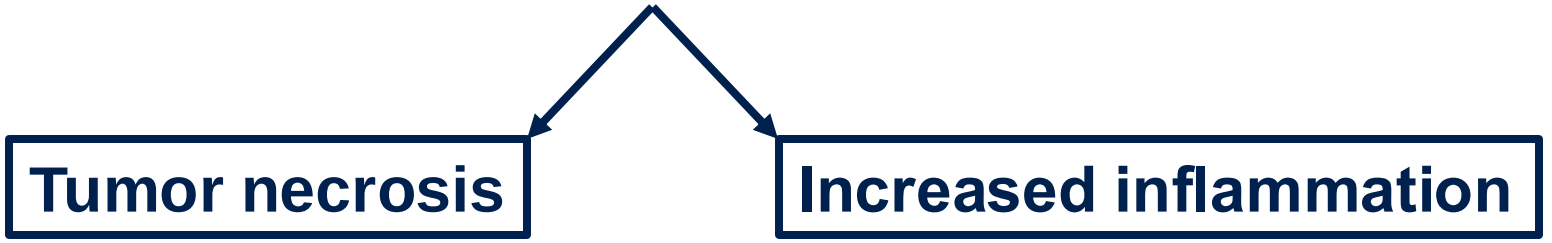
Common (manageable) side effects	Immune related side effects
• Fatigue • Nausea • Diarrhea • Decreased appetite • Constipation • Rash • Myalgia, arthralgia • Fever	• Endocrine disorders • **GI-issues (colitis and perforation)** • Hepatitis due to liver toxicity • Pneumonitis • Severe skin reactions • Renal toxicity • Rare: myocarditis or neurologic conditions

Attacking healthy tissue

Tumor perforation after immunotherapy for CRC

Based on case reports

Tumor perforation = rare and serious
→ Based on tumor biology and immune response



- **Advanced disease; large tumor, deep in bowel wall**
- **Pre-existing bowel bowel wall fragility; prior treatments and condition**

Key (discussion) points

Immunotherapy in dMMR CRC → very promising efficacy

Perforation = life-threatening medical emergency

What about neo-adjuvant immunotherapy in bulky tumors that are initially resectable?

References

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