

World Journal of *Gastrointestinal Surgery*

World J Gastrointest Surg 2024 July 27; 16(7): 1956-2364



Contents

Monthly Volume 16 Number 7 July 27, 2024

EDITORIAL

- 1956 Unveiling the potential of electrocautery-enhanced lumen-apposing metal stents in endoscopic ultrasound-guided biliary drainage
Chisthi MM
- 1960 Minimally invasive pelvic exenteration for primary or recurrent locally advanced rectal cancer: A glimpse into the future
Kehagias D, Lampropoulos C, Kehagias I
- 1965 Endoscopic submucosal dissection for early gastric cancer: A major challenge for the west
Schlottmann F
- 1969 Impact of immunotherapy on liver metastasis
Fu Z, Wang MW, Liu YH, Jiao Y
- 1973 Occurrence and prevention of incisional hernia following laparoscopic colorectal surgery
Wu XW, Yang DQ, Wang MW, Jiao Y
- 1981 Role of endoscopic-ultrasound-guided biliary drainage with electrocautery-enhanced lumen-apposing metal stent for palliation of malignant biliary obstruction
Deliwala SS, Qayed E

REVIEW

- 1986 Pancreatic pseudocyst: The past, the present, and the future
Koo JG, Liao MYQ, Kryvoruchko IA, Habeeb TA, Chia C, Shelat VG

ORIGINAL ARTICLE

Case Control Study

- 2003 Diagnostic significance of serum levels of serum amyloid A, procalcitonin, and high-mobility group box 1 in identifying necrotising enterocolitis in newborns
Guo LM, Jiang ZH, Liu HZ, Zhang L

Retrospective Cohort Study

- 2012 Clinical efficacy and safety of double-channel anastomosis and tubular gastroesophageal anastomosis in gastrectomy
Liu BY, Wu S, Xu Y
- 2023 Application of radioactive iodine-125 microparticles in hepatocellular carcinoma with portal vein embolus
Meng P, Ma JP, Huang XF, Zhang KL

Retrospective Study

- 2031** Reproducibility study of intravoxel incoherent motion and apparent diffusion coefficient parameters in normal pancreas
Liu X, Wang YF, Qi XH, Zhang ZL, Pan JY, Fan XL, Du Y, Zhai YM, Wang Q
- 2040** Weight regain after intragastric balloon for pre-surgical weight loss
Abbitt D, Choy K, Kovar A, Jones TS, Wikel KJ, Jones EL
- 2047** Retrospective analysis based on a clinical grading system for patients with hepatic hemangioma: A single center experience
Zhou CM, Cao J, Chen SK, Tuxun T, Apaer S, Wu J, Zhao JM, Wen H
- 2054** Spleen volume is associated with overt hepatic encephalopathy after transjugular intrahepatic portosystemic shunt in patients with portal hypertension
Zhao CJ, Ren C, Yuan Z, Bai GH, Li JY, Gao L, Li JH, Duan ZQ, Feng DP, Zhang H
- 2065** Evaluation of the clinical effects of atropine in combination with remifentanyl in children undergoing surgery for acute appendicitis
Li YJ, Chen YY, Lin XL, Zhang WZ
- 2073** The combined detection of carcinoembryonic antigen, carcinogenic antigen 125, and carcinogenic antigen 19-9 in colorectal cancer patients
Gong LZ, Wang QW, Zhu JW
- 2080** Clinical efficacy of laparoscopic cholecystectomy plus cholangioscopy for the treatment of cholecystolithiasis combined with choledocholithiasis
Liu CH, Chen ZW, Yu Z, Liu HY, Pan JS, Qiu SS
- 2088** Association between operative position and postoperative nausea and vomiting in patients undergoing laparoscopic sleeve gastrectomy
Li ZP, Song YC, Li YL, Guo D, Chen D, Li Y
- 2096** Preoperative albumin-bilirubin score predicts short-term outcomes and long-term prognosis in colorectal cancer patients undergoing radical surgery
Diao YH, Shu XP, Tan C, Wang LJ, Cheng Y
- 2106** Association of preoperative antiviral treatment with incidences of post-hepatectomy liver failure in hepatitis B virus-related hepatocellular carcinoma
Wang X, Lin ZY, Zhou Y, Zhong Q, Li ZR, Lin XX, Hu MG, He KL
- 2119** Effect of rapid rehabilitation nursing on improving clinical outcomes in postoperative patients with colorectal cancer
Song JY, Cao J, Mao J, Wang JL
- 2127** Interaction between the albumin-bilirubin score and nutritional risk index in the prediction of post-hepatectomy liver failure
Qin FF, Deng FL, Huang CT, Lin SL, Huang H, Nong JJ, Wei MJ

- 2135** Effectiveness of magnetic resonance imaging and spiral computed tomography in the staging and treatment prognosis of colorectal cancer
Bai LN, Zhang LX
- 2145** Correlation between abdominal computed tomography signs and postoperative prognosis for patients with colorectal cancer
Yang SM, Liu JM, Wen RP, Qian YD, He JB, Sun JS
- 2157** Study on the occurrence and influencing factors of gastrointestinal symptoms in hemodialysis patients with uremia
Yuan D, Wang XQ, Shao F, Zhou JJ, Li ZX
- 2167** "Hepatic hilum area priority, liver posterior first": An optimized strategy in laparoscopic resection for type III-IV hilar cholangiocarcinoma
Hu XS, Wang Y, Pan HT, Zhu C, Chen SL, Zhou S, Liu HC, Pang Q, Jin H
- 2175** Impact of nutritional support on immunity, nutrition, inflammation, and outcomes in elderly gastric cancer patients after surgery
Chen XW, Guo XC, Cheng F
- 2183** Therapeutic effects of Buzhong Yiqi decoction in patients with spleen and stomach qi deficiency after routine surgery and chemotherapy for colorectal cancer
Hu Q, Chen XP, Tang ZJ, Zhu XY, Liu C
- 2194** Influencing factors and risk prediction model for emergence agitation after general anesthesia for primary liver cancer
Song SS, Lin L, Li L, Han XD
- 2202** Potential applications of single-incision laparoscopic totally preperitoneal hernioplasty
Wang XJ, Fei T, Xiang XH, Wang Q, Zhou EC
- 2211** Clinical significance of preoperative nutritional status in elderly gastric cancer patients undergoing radical gastrectomy: A single-center retrospective study
Zhao XN, Lu J, He HY, Ge SJ
- 2221** Establishment and validation of a predictive model for peripherally inserted central catheter-related thrombosis in patients with liver cancer
Chen XF, Wu HJ, Li T, Liu JB, Zhou WJ, Guo Q
- Observational Study**
- 2232** Effect of information-motivation-behavioral skills model based perioperative nursing on pain in patients with gallstones
Ma L, Yu Y, Zhao BJ, Yu YN, Li Y
- 2242** Postoperative body weight change and its influencing factors in patients with gastric cancer
Li Y, Huang LH, Zhu HD, He P, Li BB, Wen LJ
- 2255** Cost burden following esophagectomy: A single centre observational study
Buchholz V, Lee DK, Liu DS, Aly A, Barnett SA, Hazard R, Le P, Kioussis B, Muralidharan V, Weinberg L

Randomized Controlled Trial

- 2270** Effectiveness of colonoscopy, immune fecal occult blood testing, and risk-graded screening strategies in colorectal cancer screening
Xu M, Yang JY, Meng T

Clinical and Translational Research

- 2281** Construction of prognostic markers for gastric cancer and comprehensive analysis of pyroptosis-related long non-coding RNAs
Wang Y, Li D, Xun J, Wu Y, Wang HL

Basic Study

- 2296** Yangyin Huowei mixture alleviates chronic atrophic gastritis by inhibiting the IL-10/JAK1/STAT3 pathway
Xie SS, Zhi Y, Shao CM, Zeng BF
- 2308** Impacts of different pancreatic resection ranges on endocrine function in *Suncus murinus*
Li RJ, Yang T, Zeng YH, Natsuyama Y, Ren K, Li J, Nagakawa Y, Yi SQ

SYSTEMATIC REVIEWS

- 2319** Impact of frailty on postoperative outcomes after hepatectomy: A systematic review and meta-analysis
Lv YJ, Xu GX, Lan JR

CASE REPORT

- 2329** Multidisciplinary management of ulcerative colitis complicated by immune checkpoint inhibitor-associated colitis with life-threatening gastrointestinal hemorrhage: A case report
Hong N, Wang B, Zhou HC, Wu ZX, Fang HY, Song GQ, Yu Y
- 2337** Sequential bowel necrosis and large gastric ulcer in a patient with a ruptured femoral artery: A case report
Wang P, Wang TG, Yu AY
- 2343** Colon signet-ring cell carcinoma with chylous ascites caused by immunosuppressants following liver transplantation: A case report
Li Y, Tai Y, Wu H
- 2351** Misdiagnosis of hemangioma of left triangular ligament of the liver as gastric submucosal stromal tumor: Two case reports
Wang JJ, Zhang FM, Chen W, Zhu HT, Gui NL, Li AQ, Chen HT

LETTER TO THE EDITOR

- 2358** Revolutionizing palliative care: Electrocautery-enhanced lumen-apposing metal stents in endoscopic-ultrasound-guided biliary drainage for malignant obstructions
Onteddu NKR, Mareddy NSR, Vulasala SSR, Onteddu J, Virarkar M

- 2362** Preservation of superior rectal artery in laparoscopic colectomy: The best choice for slow transit constipation?

Liu YL, Liu WC

ABOUT COVER

Peer Reviewer of *World Journal of Gastrointestinal Surgery*, Hideki Aoki, MD, PhD, Chief Doctor, Surgeon, Department of Surgery, Iwakuni Clinical Center, Iwakuni 740-8510, Japan. aoki.hideki.hy@mail.hosp.go.jp

AIMS AND SCOPE

The primary aim of *World Journal of Gastrointestinal Surgery* (WJGS, *World J Gastrointest Surg*) is to provide scholars and readers from various fields of gastrointestinal surgery with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGS mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal surgery and covering a wide range of topics including biliary tract surgical procedures, biliopancreatic diversion, colectomy, esophagectomy, esophagostomy, pancreas transplantation, and pancreatectomy, *etc.*

INDEXING/ABSTRACTING

The WJGS is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Current Contents/Clinical Medicine, Journal Citation Reports/Science Edition, PubMed, PubMed Central, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2024 Edition of Journal Citation Reports® cites the 2023 journal impact factor (JIF) for WJGS as 1.8; JIF without journal self cites: 1.7; 5-year JIF: 1.9; JIF Rank: 123/290 in surgery; JIF Quartile: Q2; and 5-year JIF Quartile: Q3.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Zi-Hang Xu, Production Department Director: Xiang Li, Cover Editor: Jia-Ru Fan.

NAME OF JOURNAL

World Journal of Gastrointestinal Surgery

ISSN

ISSN 1948-9366 (online)

LAUNCH DATE

November 30, 2009

FREQUENCY

Monthly

EDITORS-IN-CHIEF

Peter Schemmer

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/1948-9366/editorialboard.htm>

PUBLICATION DATE

July 27, 2024

COPYRIGHT

© 2024 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/gerinfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/gerinfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/gerinfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



Multidisciplinary management of ulcerative colitis complicated by immune checkpoint inhibitor-associated colitis with life-threatening gastrointestinal hemorrhage: A case report

Na Hong, Bo Wang, Hang-Cheng Zhou, Zheng-Xiang Wu, Hua-Ying Fang, Geng-Qing Song, Yue Yu

Specialty type: Gastroenterology and hepatology

Provenance and peer review:

Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade C

Novelty: Grade C

Creativity or Innovation: Grade B

Scientific Significance: Grade B

P-Reviewer: Hassan SA

Received: February 24, 2024

Revised: May 26, 2024

Accepted: June 18, 2024

Published online: July 27, 2024

Processing time: 148 Days and 19.7 Hours



Na Hong, Bo Wang, Zheng-Xiang Wu, Hua-Ying Fang, Yue Yu, Department of Gastroenterology, The First Affiliated Hospital of University of Science and Technology of China, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei 230001, Anhui Province, China

Hang-Cheng Zhou, Department of Pathology, The First Affiliated Hospital of University of Science and Technology of China, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei 230036, Anhui Province, China

Hang-Cheng Zhou, Intelligent Pathology Institute, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei 230036, Anhui Province, China

Geng-Qing Song, Department of Gastroenterology and Hepatology, Metro Health Medical Center, Case Western Reserve University, Cleveland, OH 44109, United States

Co-first authors: Na Hong and Bo Wang.

Co-corresponding authors: Geng-Qing Song and Yue Yu.

Corresponding author: Yue Yu, MD, PhD, Chief Doctor, Chief Physician, Professor, Department of Gastroenterology, The First Affiliated Hospital of University of Science and Technology of China, Division of Life Sciences and Medicine, University of Science and Technology of China, No. 17 Lujiang Road, Hefei 230001, Anhui Province, China.

yuyuemd@163.com

Abstract

BACKGROUND

Programmed cell death 1 (PD-1) inhibitors are immune checkpoint inhibitors (ICI) that have demonstrated significant efficacy in treating various advanced malignant tumors. While most patients tolerate treatment well, several adverse drug reactions, such as fatigue, myelosuppression, and ICI-associated colitis, have been reported.

CASE SUMMARY

This case involved a 57-year-old male patient with ulcerative colitis complicated by hepatocarcinoma who underwent treatment with tirelizumab (a PD-1 inhibitor) for six months. The treatment led to repeated life-threatening lower

gastrointestinal hemorrhage. The patient received infliximab, vedolizumab, and other salvage procedures but ultimately required subtotal colectomy due to uncontrollable massive lower gastrointestinal bleeding. Currently, postoperative gastrointestinal bleeding has stopped, the patient's stool has turned yellow, and his full blood cell count has returned to normal.

CONCLUSION

This case highlights the necessity of early identification, timely and adequate treatment of ICI-related colitis, and rapid escalation to achieve the goal of improving prognosis.

Key Words: Ulcerative colitis; Hepatocarcinoma; Immune checkpoint inhibitor-associated colitis; Colectomy; Case report

©The Author(s) 2024. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: Immune checkpoint inhibitors (ICIs), such as ICI-associated colitis, have demonstrated significant efficacy in treating various advanced malignant tumors, but several immune-related adverse drug reactions, such as ICI-associated colitis, have attracted increasing attention. In this article, we present a case of a patient with hepatocarcinoma and ulcerative colitis with ICI-related colitis in which repeated life-threatening lower gastrointestinal hemorrhage occurred during the disease course. Despite comprehensive salvage treatments through multidisciplinary management, the patient eventually required surgical intervention due to persistent gastrointestinal bleeding. This case highlights the necessity of early identification, timely and adequate treatment of ICI-related colitis and rapid escalation to improve patient prognosis.

Citation: Hong N, Wang B, Zhou HC, Wu ZX, Fang HY, Song GQ, Yu Y. Multidisciplinary management of ulcerative colitis complicated by immune checkpoint inhibitor-associated colitis with life-threatening gastrointestinal hemorrhage: A case report. *World J Gastrointest Surg* 2024; 16(7): 2329-2336

URL: <https://www.wjgnet.com/1948-9366/full/v16/i7/2329.htm>

DOI: <https://dx.doi.org/10.4240/wjgs.v16.i7.2329>

INTRODUCTION

Programmed cell death 1 (PD-1) inhibitors are immune checkpoint inhibitors (ICIs) that bind to the PD-1 receptor on the surface of T cells, blocking the tumor immune escape pathway[1]. It has demonstrated significant efficacy in treating various advanced malignant tumors[2,3]. However, ICIs can induce immune-related adverse events (irAEs), among which gastrointestinal adverse events are the most common. This process mainly involves the colon and is called ICI-associated colitis. The small intestine and upper digestive tract were also involved. Diarrhea is the most common clinical symptom. It is also characterized by abdominal pain, hematochezia, fever, and intestinal perforation[4,5]. Because ICI-related colitis often resembles symptoms of inflammatory bowel disease (IBD), especially ulcerative colitis (UC)[6,7], the diagnosis of ICI-associated colitis is challenging. In this report, we present the case of a patient with UC complicated with liver cancer. After secondary ICI-associated colitis, rare fatal massive hemorrhage in the lower digestive tract occurred repeatedly, and multidisciplinary treatment was successful.

CASE PRESENTATION

Chief complaints

A 57-year-old male patient with UC developed significant abdominal pain and mucopurulent bloody stools after taking a PD-1 inhibitor.

History of present illness

The patient had 5-6 episodes of bloody diarrhea daily approximately 2 months after the use of PD-1 without abdominal pain and underwent right hepatectomy on August 10, 2022. On the ninth day following hepatectomy, his condition worsened, marked by an increase to more than 10 episodes of bloody diarrhea daily, along with new-onset periumbilical and lower abdominal pain, bloating, and nausea, though without vomiting or fever.

History of past illness

He was diagnosed with UC 5 years ago, which was well controlled with both oral and rectal mesalazine. In March 2022, a pathological biopsy in the Department of Liver Surgery confirmed a diagnosis of hepatocellular carcinoma. In preparation for liver surgery, he received comprehensive targeted anticancer therapy for five months, including intravenous tirlezumab (200 mg, administered five times) and daily oral lenvatinib (12 mg).

Personal and family history

He had no family history of tumors, autoimmune diseases or genetic disorders.

Physical examination

His temperature was 36.2 °C, his pulse was 84 breaths/minute, his respiration rate was 19 breaths/minute, and his blood pressure was 95/56 mmHg. His abdomen was soft with mild tenderness, no rebound pain, and active bowel sounds at approximately 8 breaths/minute. The bilateral lower limbs showed moderate edema. The surgical incision on the right side of the abdomen appeared dry and clean, with intact stitches. A small amount of yellow fluid was observed in the drainage bag on the right side of the abdomen.

Laboratory examinations

The white blood cell count was $9.37 \times 10^9/L$ (normal range: $3.5-9.5 \times 10^9/L$), the neutrophil ratio was 71.1% (normal range: 40%-75%), the red blood cell count was $2.71 \times 10^{12}/L$ (normal range: $4.3-5.8 \times 10^{12}/L$), the hemoglobin level was 83 g/L (normal range: 120-160 g/L), the platelet count was $63 \times 10^9/L$ (normal range: $125-350 \times 10^9/L$), the albumin concentration was 26.7 g/L (normal range: 35-55 g/L), the C-reactive protein concentration was 14.2 mg/L (normal range: 0-8 mg/L), the prothrombin time concentration was 18.50 seconds (normal range: 10.5-16 seconds), the D-dimer concentration was 5.13 mg/L (normal range: 0-0.5 mg/L), and the stool routine parameters included white blood cells (+++), red blood cells (++), and a few pus balls; ELISA detection of *Mycobacterium tuberculosis* revealed reactive pore A20 and pore B13. TBNK cell subsets were detected as follows: CD3-CD16+56+ 2.8% (normal range: 5.6%-30.9%); decreased levels of immunoglobulin complement C3, C4, and IgM; and Th1/2/17 cytokine levels of 170.26 pg/mL (normal range: 0-5.3 pg/mL) and 41.51 pg/mL (normal range: 0-4.91 pg/mL) for interleukin (IL)-6 and IL-10, respectively. Blood tests for cytomegalovirus (CMV) PCR and Epstein-Barr virus PCR were negative, and CMV immunohistochemistry was negative. Parasite ova and *Plasmodium* were not detected in multiple fecal or blood samples. Blood culture and stool *C. difficile* culture were negative, and the erythrocyte sedimentation rate and procalcitonin level were within the normal ranges. There was no significant change in fecal calprotectin level before and after treatment.

Imaging examinations

Full abdominal pelvic spiral computed tomography plain scan on August 20, 2022. **Figure 1** shows bilateral pleural effusion with adjacent lung tissue atelectasis and pericardial effusion with postoperative liver changes. The walls of the ascending colon, transverse colon, and descending colon were slightly thickened and exhibited uniform edema, while the surrounding fat space was slightly blurred, with evidence of moderately enlarged lymph nodes scattered throughout the region. There was no obvious lesion in the small intestine.

MULTIDISCIPLINARY EXPERT CONSULTATION

Considering the patient's medical history, endoscopy and pathology, the final diagnosis was UC accompanied by ICI-associated colitis.

FINAL DIAGNOSIS

UC accompanied by ICI-associated colitis.

TREATMENT

Postoperative management with broad-spectrum antibiotics (cefoperazone sodium and sulbactam sodium, 2 g IV daily) and corticosteroids (methylprednisolone 40 mg IV daily) did not improve the patient's condition; instead, the frequency of bloody diarrhea intensified to 20 episodes per day. Given the complexity of his condition, he was transferred to the Department of Gastroenterology. Upon transfer, the dose of methylprednisolone was increased to 60 mg IV daily, and somatostatin was administered intravenously with a micropump of 6 mg daily. Despite these treatment adjustments, the bloody diarrhea persisted. To evaluate intestinal inflammation, the first sigmoidoscopy was performed and revealed extensive mucosal exfoliation of the sigmoid colon (**Figure 2**). Biopsy and pathological examination confirmed the presence of colitis, characterized by surface inflammatory exudation and the loss of mucosal glands (**Figure 3**).

On August 26, 2022, the patient suddenly experienced massive lower gastrointestinal tract bleeding, resulting in a loss of approximately 4950 mL of blood. Moreover, on August 28, 2022, hematochezia of approximately 2000 mL occurred. Subsequently, the patient's condition deteriorated significantly. The surgical team recommended immediate surgery for hypotension (80/50 mmHg) due to massive bleeding. However, the patient resolutely refused colectomy because of a recent history of right liver surgery. In the critical state (8.26-30), he underwent a massive blood transfusion [B, RH- (+), red blood cell 19 U, fresh plasma 2025 mL, and cryoprecipitate coagulation Factor 18 U] to save his life. To address severe UC accompanied by immune-related colitis induced by a PD-1 inhibitor, the medical team, including American experts who consulted online and multiple disciplines within the hospital, discussed the case of intermittent improvement of

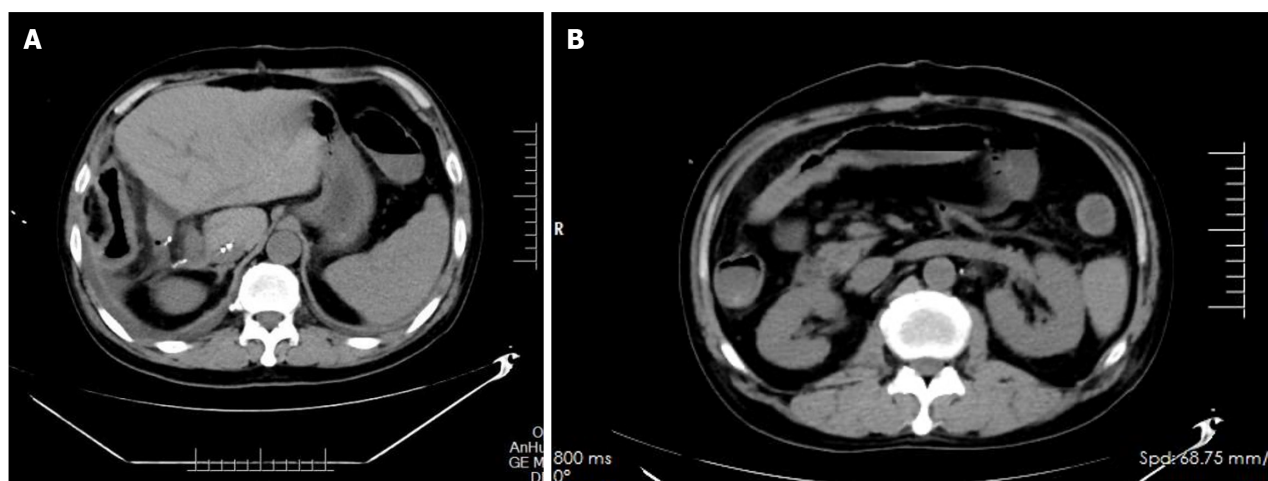


Figure 1 Full abdominal pelvic spiral computed tomography plain scan on August 20, 2022. A: The wall of the ascending colon was slightly thickened and showed uniform edema, while the surrounding fat space was slightly blurred; B: The wall of the transverse colon was slightly thickened, and moderate lymph nodes were scattered. There was no obvious lesion in the small intestine.

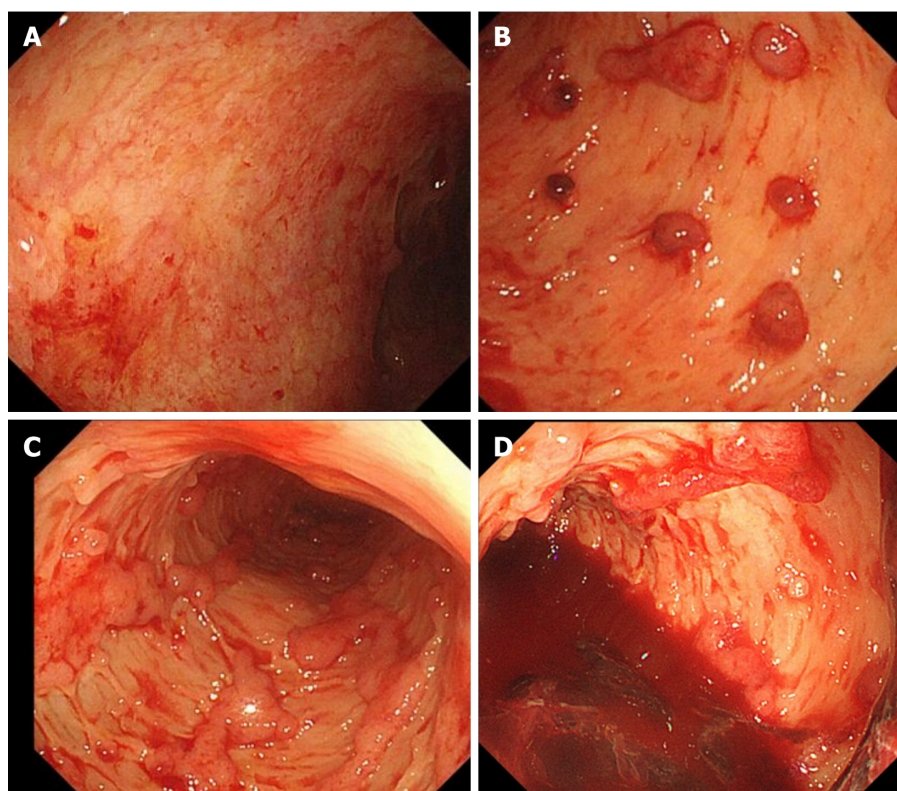


Figure 2 Sigmoidoscopy examination. A: The lesions in the rectum, which were less than 5 cm, appeared to be relatively mild; B and C: Extensive mucosal exfoliation was observed below 30 cm in the sigmoid colon, along with scattered, small, dotted mucous membranes; D: A significant presence of blood and clots was found in the sigmoid colon.

hormones in this patient and implemented salvage therapy *via* 0.5 g (10 mg/kg) intravenous infusion of infliximab. Bloody stools turned into yellow pasty feces, occurring 7 to 8 times per day, and he had a few bloody stools occasionally.

Due to a combination of latent tuberculosis infection and decreased leukocyte and neutropenia, the patient received 300 mg of vedolizumab two weeks and one month after infliximab, respectively, resulting in further improvement, with yellow pasty stool and occasional formed stool approximately 4-5 times a day. Subsequent endoscopic reexamination revealed that the terminal ileum was normal, without blood staining, that the sigmoid lesions were significantly reduced, that the rectal mucosa was hyperemic and edematous, and that no obvious ulcers were observed. However, the ileocecal region, the ascending colon, transverse colon and descending colon exhibited continuous extensive hyperemia, edema, erosion, polypoid hyperplasia, and irregular deep perforated and geographic ulcers, especially in the right half of the colon (Figure 4).

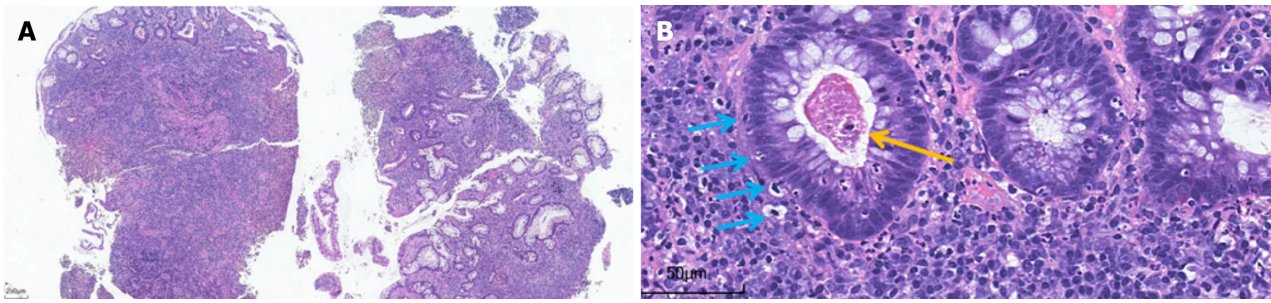


Figure 3 Pathology of the sigmoidoscopic biopsy specimen. A: Ulcer formation: Surface inflammatory exudation necrosis, underlying granulation tissue hyperplasia, interstitial "transmural" hybrid inflammatory cell infiltration, hematoxylin and eosin (HE) staining $\times 40$; B: Cryptitis, crypt abscesses (yellow arrow), and significantly increased numbers of apoptotic cells (blue arrows), HE $\times 400$.

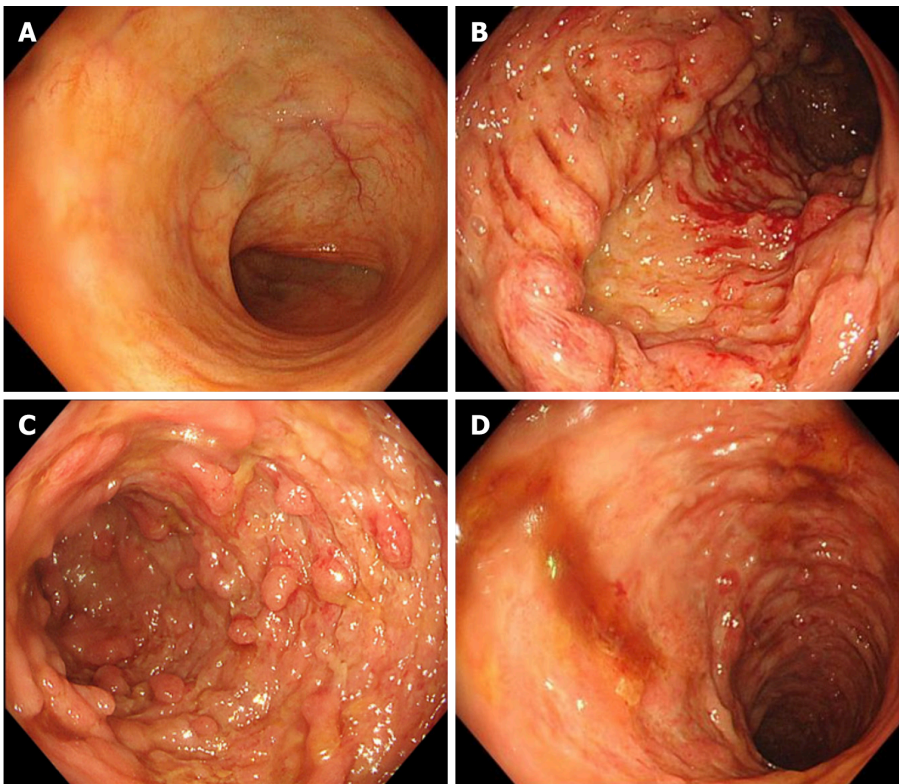


Figure 4 Colonoscopy examination. A: The mucosa of the terminal ileum is normal; B and C: Extensive and continuous hyperemia, edema, erosion, polypoid hyperplasia, irregular deep chisel and geoglyphic ulcers; D: The ulcers and erosion of the sigmoid colon were significantly improved.

On September 23, 2022, a routine blood test revealed a significant reduction in all three blood cell types (white blood cells $1.66 \times 10^9/L$ (normal range: $3.5-9.5 \times 10^9/L$), red blood cells $2.25 \times 10^{12}/L$ (normal range: $4.3-5.8 \times 10^{12}/L$), and platelets $45 \times 10^9/L$ (normal range: $125-350 \times 10^9/L$)). After excluding patients with malignant hematological diseases through bone marrow aspiration and pathological analysis, immune pancytopenia was considered. The patient received a 300-UG subcutaneous injection of human granulocyte stimulating factor to promote white blood cells and a 12 million U subcutaneous injection of recombinant human IL-11 to promote platelet recovery, along with component transfusion. However, despite a brief increase in white blood cells and platelets, they continued to decline, and the patient experienced hematochezia again, with approximately 100-200 mL each time.

The recurrence and deterioration of the disease prompted the patient to decide to transfer to a hospital in Nanjing for surgery involving subtotal resection of the colon + ileostomy + intestinal adhesion release. Intraoperative exploration of the small intestine revealed no abnormalities, and the whole colon showed chronic inflammatory changes. Postoperative pathology revealed extensive erosion with superficial ulcers and a large number of acute and chronic inflammatory cells infiltrating the mucosal layer and submucosa, including neutrophil or eosinophilic infiltration, cryptinitis, crypt microabscesses, and increased apoptosis, which tends to be UC accompanied by ICI-associated colitis (Figure 5 and Supplementary material).

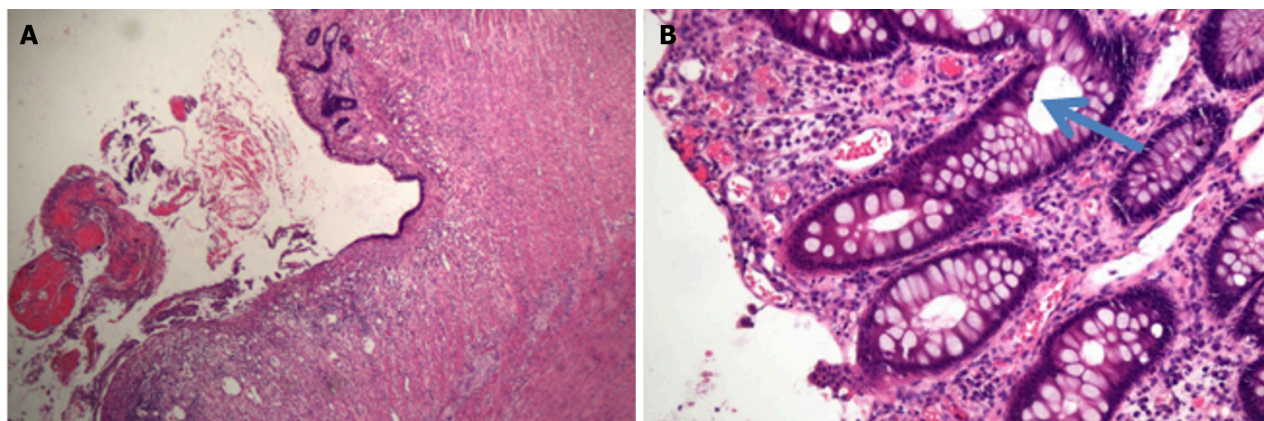


Figure 5 Postoperative pathology. A: Ulcer formation, surface bleeding with inflammatory exudation, necrosis, mucous membrane accompanied by hemorrhagic changes. Hematoxylin and eosin (HE) staining $\times 40$; B: Apoptotic cells were found in the crypt (blue arrow). HE $\times 400$.

OUTCOME AND FOLLOW-UP

Currently, postoperative gastrointestinal bleeding has stopped, the patient's stool has turned yellow, and his full blood cell count has returned to normal.

DISCUSSION

The use of ICIs has led to significant advancements in cancer treatment, but it has also led to immune-related adverse reactions, with the digestive system being the most commonly affected[8]. ICI-associated colitis typically occurs 6 to 7 weeks after the first use of ICIs and usually achieves remission within 4 months or more after stopping PD-1 inhibitor treatment. Colitis and diarrhea are the main manifestations of ICI-related colitis. The severity of ICI-related colitis is classified into five grades according to the National Cancer Institute (NCI) adverse event evaluation criteria[9]. According to the literature[10], the incidence of colitis caused by PD-1 was 1.4% (95%CI: 1.1%-1.8%), and the incidence of grade 3-4 colitis was 0.9% (95%CI: 0.7%-1.3%). A multicenter retrospective study of IBD patients treated with ICIs showed that cancer patients with IBD had significantly greater rates of gastrointestinal irAEs (41% *vs* 11%, $P < 0.01$) and higher grades of diarrhea and colitis than cancer patients without IBD[11]. In this case, the patient had grade 4 colitis according to the NCI grading criteria.

The diagnosis of ICI-associated colitis can be challenging because its clinical symptoms, endoscopic manifestations, and histological features are similar to those of IBD[6,7]. Endoscopic features usually include mucosal edema, erythematous lesions, erosion, ulcers, and other changes in the colon[12]. Endoscopic biopsy has been considered the gold standard criterion for the diagnosis of ICI-related colitis[13]. Microscopic changes in ICI-associated colitis may include increased apoptosis, neutrophil infiltration, crypt microabscesses, erosion, or ulcer formation[14,15]. In this patient, similar changes were observed in postoperative pathology (Figure 5).

Treatment of ICI-associated colitis typically involves glucocorticoids as the first-line therapy for moderate to severe cases. If glucocorticoid therapy is ineffective, infliximab or vedolizumab should be considered, especially for patients with severe endoscopic manifestations or high endoscopic disease activity scores[16]. In this patient, infliximab and vedolizumab were added to the treatment regimen when sufficient hormone therapy failed, resulting in partial improvement of colitis symptoms. However, due to the development of immune pancytopenia and recurrent lower gastrointestinal bleeding, surgery was ultimately performed as a last resort. ICIS-associated colitis may deteriorate to colonic perforation, and colectomy is considered to be the most effective therapy, although the estimated incidence is 1% to 1.5%[17]. In fact, because patients often have extensive colonic lesions, subtotal colectomy is the preferred surgical option[13].

The association between ICI-associated colitis outcome and survival is still unclear[13]. In line with Abu-Sbeih *et al*[11], we found that patients tend to have more aggressive disease and worsen earlier when the two diseases (UC and ICI-associated colitis) are combined. Although most patients can achieve remission with conservative medical treatment, some patients may require prompt surgery due to serious complications. The experience gained from this case highlights the importance of early diagnosis and prompt surgery to improve clinical outcomes.

Above all, the precise diagnosis and treatment of CIC requires multidisciplinary management and persistent monitoring, and timely adjustment of treatment regimens based on guidelines is essential for effectively managing ICI-associated colitis.

CONCLUSION

This case highlights the necessity of early identification, timely and adequate treatment of ICI-related colitis, and rapid escalation to improve prognosis. Multidisciplinary management and persistent monitoring are essential for identifying and managing irAEs effectively.

ACKNOWLEDGEMENTS

We thank the patient and his wife for their consent to publish their case and everyone involved in the diagnosis and treatment of the patient for their hard work.

FOOTNOTES

Author contributions: Hong N conceived the study, analyzed and interpreted the data, drafted the article, and revised it critically for important intellectual content; Wang B and Zhou HC helped acquire the data and drafted the article; Wu ZX and Fang HY helped collect and analyze the data; Both Song GQ and Yu Y have played important and indispensable roles in the study design, data interpretation and manuscript preparation as the co-corresponding authors. Song GQ was responsible for data re-analysis and re-interpretation, literature search, the early revised version of the manuscript. Yu Y searched comprehensive literature and revised it critically for important intellectual content, approved the version to be submitted. This collaboration between Song GQ and Yu Y is crucial for the publication of this manuscript and other manuscripts still in preparation. All the authors have read and approved the final manuscript.

Supported by the National Natural Science Foundation of China, No. 31870993.

Informed consent statement: The patient and his wife for their consent to publish their case.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

CARE Checklist (2016) statement: The authors have read CARE Checklist (2016), and the manuscript was prepared and revised according to CARE Checklist (2016).

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

Country of origin: China

ORCID number: Na Hong 0009-0000-1940-5997; Geng-Qing Song 0000-0001-5551-1818; Yue Yu 0000-0002-3617-2037.

S-Editor: Li L

L-Editor: A

P-Editor: Zhang XD

REFERENCES

- 1 **Tang Q**, Chen Y, Li X, Long S, Shi Y, Yu Y, Wu W, Han L, Wang S. The role of PD-1/PD-L1 and application of immune-checkpoint inhibitors in human cancers. *Front Immunol* 2022; **13**: 964442 [PMID: 36177034 DOI: 10.3389/fimmu.2022.964442]
- 2 **Sabbatino F**, Liguori L, Pepe S, Ferrone S. Immune checkpoint inhibitors for the treatment of melanoma. *Expert Opin Biol Ther* 2022; **22**: 563-576 [PMID: 35130816 DOI: 10.1080/14712598.2022.2038132]
- 3 **DeCarli K**, Strosberg J, Almhanna K. Immune Checkpoint Inhibitors for Gastrointestinal Malignancies: An Update. *Cancers (Basel)* 2022; **14** [PMID: 36077740 DOI: 10.3390/cancers14174201]
- 4 **Marthey L**, Mateus C, Mussini C, Nachury M, Nancey S, Grange F, Zallot C, Peyrin-Biroulet L, Rahier JF, Bourdier de Beauregard M, Mortier L, Coutzac C, Soularue E, Lanoy E, Kapel N, Planchard D, Chaput N, Robert C, Carbonnel F. Cancer Immunotherapy with Anti-CTLA-4 Monoclonal Antibodies Induces an Inflammatory Bowel Disease. *J Crohns Colitis* 2016; **10**: 395-401 [PMID: 26783344 DOI: 10.1093/ecco-jcc/jjv227]
- 5 **Martins F**, Sofiya L, Sykietis GP, Lamine F, Maillard M, Fraga M, Shabafrouz K, Ribi C, Cairoli A, Guex-Crosier Y, Kuntzer T, Michielin O, Peters S, Coukos G, Spertini F, Thompson JA, Obeid M. Adverse effects of immune-checkpoint inhibitors: epidemiology, management and surveillance. *Nat Rev Clin Oncol* 2019; **16**: 563-580 [PMID: 31092901 DOI: 10.1038/s41571-019-0218-0]
- 6 **Wang Y**, Abu-Sbeih H, Mao E, Ali N, Ali FS, Qiao W, Lum P, Raju G, Shuttlesworth G, Strohlein J, Diab A. Immune-checkpoint inhibitor-induced diarrhea and colitis in patients with advanced malignancies: retrospective review at MD Anderson. *J Immunother Cancer* 2018; **6**: 37 [PMID: 29747688 DOI: 10.1186/s40425-018-0346-6]
- 7 **Wang Y**, Abu-Sbeih H, Mao E, Ali N, Qiao W, Trinh VA, Zobniw C, Johnson DH, Samdani R, Lum P, Shuttlesworth G, Blechacz B, Bresalier R, Miller E, Thirumurthi S, Richards D, Raju G, Strohlein J, Diab A. Endoscopic and Histologic Features of Immune Checkpoint

- Inhibitor-Related Colitis. *Inflamm Bowel Dis* 2018; **24**: 1695-1705 [PMID: 29718308 DOI: 10.1093/ibd/izy104]
- 8 **Samaan MA**, Pavlidis P, Papa S, Powell N, Irving PM. Gastrointestinal toxicity of immune checkpoint inhibitors: from mechanisms to management. *Nat Rev Gastroenterol Hepatol* 2018; **15**: 222-234 [PMID: 29512649 DOI: 10.1038/nrgastro.2018.14]
- 9 **Lui RN**, Chan SL. Management of Gastrointestinal Side Effects of Immune Checkpoint Inhibitors. *Clin Gastroenterol Hepatol* 2021; **19**: 2262-2265 [PMID: 34324843 DOI: 10.1016/j.cgh.2021.06.038]
- 10 **Wang DY**, Ye F, Zhao S, Johnson DB. Incidence of immune checkpoint inhibitor-related colitis in solid tumor patients: A systematic review and meta-analysis. *Oncoimmunology* 2017; **6**: e1344805 [PMID: 29123955 DOI: 10.1080/2162402X.2017.1344805]
- 11 **Abu-Sbeih H**, Faleck DM, Ricciuti B, Mendelsohn RB, Naqash AR, Cohen JV, Sellers MC, Balaji A, Ben-Betzalel G, Hajir I, Zhang J, Awad MM, Leonardi GC, Johnson DB, Pinato DJ, Owen DH, Weiss SA, Lamberti G, Lythgoe MP, Manuzzi L, Arnold C, Qiao W, Naidoo J, Markel G, Powell N, Yeung SJ, Sharon E, Dougan M, Wang Y. Immune Checkpoint Inhibitor Therapy in Patients With Preexisting Inflammatory Bowel Disease. *J Clin Oncol* 2020; **38**: 576-583 [PMID: 31800340 DOI: 10.1200/JCO.19.01674]
- 12 **Soularue E**, Lepage P, Colombel JF, Coutzac C, Faleck D, Marthey L, Collins M, Chaput N, Robert C, Carbonnel F. Enterocolitis due to immune checkpoint inhibitors: a systematic review. *Gut* 2018; **67**: 2056-2067 [PMID: 30131322 DOI: 10.1136/gutjnl-2018-316948]
- 13 **Tang L**, Wang J, Lin N, Zhou Y, He W, Liu J, Ma X. Immune Checkpoint Inhibitor-Associated Colitis: From Mechanism to Management. *Front Immunol* 2021; **12**: 800879 [PMID: 34992611 DOI: 10.3389/fimmu.2021.800879]
- 14 **Karamchandani DM**, Chetty R. Immune checkpoint inhibitor-induced gastrointestinal and hepatic injury: pathologists' perspective. *J Clin Pathol* 2018; **71**: 665-671 [PMID: 29703758 DOI: 10.1136/jclinpath-2018-205143]
- 15 **Star KV**, Ho VT, Wang HH, Odze RD. Histologic features in colon biopsies can discriminate mycophenolate from GVHD-induced colitis. *Am J Surg Pathol* 2013; **37**: 1319-1328 [PMID: 24076772 DOI: 10.1097/PAS.0b013e31829ab1ef]
- 16 **Thompson JA**, Schneider BJ, Brahmer J, Andrews S, Armand P, Bhatia S, Budde LE, Costa L, Davies M, Dunnington D, Ernstoff MS, Frigault M, Kaffenberger BH, Lunning M, McGettigan S, McPherson J, Mohindra NA, Naidoo J, Olszanski AJ, Oluwole O, Patel SP, Pennell N, Reddy S, Ryder M, Santomaso B, Shofer S, Sosman JA, Wang Y, Weight RM, Johnson-Chilla A, Zuccarino-Catania G, Engh A. NCCN Guidelines Insights: Management of Immunotherapy-Related Toxicities, Version 1.2020. *J Natl Compr Canc Netw* 2020; **18**: 230-241 [PMID: 32135517 DOI: 10.6004/jnccn.2020.0012]
- 17 **Haanen JBAG**, Carbonnel F, Robert C, Kerr KM, Peters S, Larkin J, Jordan K; ESMO Guidelines Committee. Management of toxicities from immunotherapy: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2017; **28**: iv119-iv142 [PMID: 28881921 DOI: 10.1093/annonc/mdx225]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-3991568

E-mail: office@baishideng.com

Help Desk: <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

