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## Contents

Monthly Volume 15 Number 10 October 27, 2023

## MINIREVIEWS

- 2098 Minimally invasive surgery for post cholecystectomy biliary stricture: current evidence and future perspectives  
*Kalayarasan R, Sai Krishna P*
- 2108 From basic to clinical: Anatomy of Denonvilliers' fascia and its application in laparoscopic radical resection of rectal cancer  
*Chen Z, Zhang XJ, Chang HD, Chen XQ, Liu SS, Wang W, Chen ZH, Ma YB, Wang L*

## ORIGINAL ARTICLE

## Basic Study

- 2115 Effects of thrombopoietin pre-treatment on peri-liver transplantation thrombocytopenia in a mouse model of cirrhosis with hypersplenism  
*Liu ZR, Zhang YM, Cui ZL, Tong W*

## Retrospective Cohort Study

- 2123 Effect of low anterior resection syndrome on quality of life in colorectal cancer patients: A retrospective observational study  
*Jin DA, Gu FP, Meng TL, Zhang XX*
- 2133 Stent fracture after transjugular intrahepatic portosystemic shunt placement using the bare metal stent/stent-graft combination technique  
*Liu QJ, Cao XF, Pei Y, Li X, Dong GX, Wang CM*

## Retrospective Study

- 2142 Robotic natural orifice specimen extraction surgery I-type F method *vs* conventional robotic resection for lower rectal cancer  
*Tao F, Liu DN, He PH, Luo X, Xu CY, Li TY, Duan JY*
- 2154 Gene polymorphisms associated with sudden decreases in heart rate during extensive peritoneal lavage with distilled water after gastrectomy  
*Yao S, Yuan Y, Zhang J, Yu Y, Luo GH*
- 2171 Analgesic effect of ultrasound-guided bilateral transversus abdominis plane block in laparoscopic gastric cancer  
*Wang YY, Fu HJ*
- 2179 Effects of an Omaha System-based follow-up regimen on self-care and quality of life in gastrointestinal surgery patients  
*Li YD, Qu N, Yang J, Lv CY, Tang Y, Li P*

- 2191** Optimizing surgical outcomes for elderly gallstone patients with a high body mass index using enhanced recovery after surgery protocol  
*Gu YX, Wang XY, Chen Y, Shao JX, Ni SX, Zhang XM, Shao SY, Zhang Y, Hu WJ, Ma YY, Liu MY, Yu H*
- 2201** Establishment and application of three predictive models of anastomotic leakage after rectal cancer sphincter-preserving surgery  
*Li HY, Zhou JT, Wang YN, Zhang N, Wu SF*
- 2211** Identification of multiple risk factors for colorectal cancer relapse after laparoscopic radical resection  
*Luo J, He MW, Luo T, Lv GQ*
- 2222** Examining the impact of early enteral nutritional support on postoperative recovery in patients undergoing surgical treatment for gastrointestinal neoplasms  
*Chen Z, Hong B, He JJ, Ye QQ, Hu QY*
- 2234** Predicting lymph node metastasis in colorectal cancer: An analysis of influencing factors to develop a risk model  
*Lei YP, Song QZ, Liu S, Xie JY, Lv GQ*
- 2247** Novel prognostic score based on the preoperative total bilirubin-albumin ratio and fibrinogen-albumin ratio in ampullary adenocarcinoma  
*Zhang XJ, Fei H, Sun CY, Li ZF, Li Z, Guo CG, Zhao DB*
- 2259** Analysis of textbook outcomes for ampullary carcinoma patients following pancreaticoduodenectomy  
*Zhang XJ, Fei H, Guo CG, Sun CY, Li ZF, Li Z, Chen YT, Che X, Zhao DB*
- 2272** Endoscopic retrograde cholangiopancreatography for diagnosing and treating pediatric biliary and pancreatic diseases  
*Qin XM, Yu FH, Lv CK, Liu ZM, Wu J*

**SYSTEMATIC REVIEWS**

- 2280** Systematic review of diagnostic tools for peritoneal metastasis in gastric cancer-staging laparoscopy and its alternatives  
*Ho SYA, Tay KV*
- 2294** Prediction of lymph node metastasis in early esophageal cancer  
*Li Y, Wang JX, Yibi RH*
- 2305** Hepatobiliary tuberculosis in the developing world  
*Esguerra-Paculan MJA, Soldera J*

**META-ANALYSIS**

- 2320** Timing of surgical operation for patients with intra-abdominal infection: A systematic review and meta-analysis  
*Song SR, Liu YY, Guan YT, Li RJ, Song L, Dong J, Wang PG*

- 2331** Bariatric surgery reduces colorectal cancer incidence in obese individuals: Systematic review and meta-analysis

*Liu YN, Gu JF, Zhang J, Xing DY, Wang GQ*

### CASE REPORT

- 2343** Postpolypectomy syndrome without abdominal pain led to sepsis/septic shock and gastrointestinal bleeding: A case report

*Chen FZ, Ouyang L, Zhong XL, Li JX, Zhou YY*

- 2351** Three-dimensional computed tomography reconstruction diagnosed digestive tract perforation and acute peritonitis caused by *Monopterus albus*: A case report

*Yang JH, Lan JY, Lin AY, Huang WB, Liao JY*

- 2357** Gastric adenosquamous carcinoma with an elevated serum level of alpha-fetoprotein: A case report

*Sun L, Wei JJ, An R, Cai HY, Lv Y, Li T, Shen XF, Du JF, Chen G*

- 2362** Mucocutaneous ulcer positive for Epstein-Barr virus, misdiagnosed as a small bowel adenocarcinoma: A case report

*Song JH, Choi JE, Kim JS*

- 2367** Hereditary hemorrhagic telangiectasia involving portal venous system: A case report and review of the literature

*Wu JL, Zhao ZZ, Chen J, Zhang HW, Luan Z, Li CY, Zhao YM, Jing YJ, Wang SF, Sun G*

- 2376** Giant dedifferentiated liposarcoma of the gastrocolic ligament: A case report

*Kassi ABF, Yenon KS, Kassi FMH, Adjeme AJ, Diarra KM, Bombet-Kouame C, Kouassi M*

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## Mucocutaneous ulcer positive for Epstein–Barr virus, misdiagnosed as a small bowel adenocarcinoma: A case report

Ji Hyeong Song, Ji Eun Choi, Jin Soo Kim

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### Abstract

#### BACKGROUND

Epstein–Barr virus (EBV)-positive mucocutaneous ulcers (MCUs) are an uncommon disorder characterized by ulcerative lesions in the skin, oral cavity or gastrointestinal tract in patients with iatrogenic or aging-induced immunosuppression. The nonspecific lesions are difficult to differentiate from small bowel adenocarcinomas. We present the case of a 69-year-old woman who was initially misdiagnosed with a small bowel adenocarcinoma but was later surgically diagnosed with and treated for EBV-MCU. Through this case, we aim to emphasize the importance of accurately distinguishing between the two conditions.

#### CASE SUMMARY

The patient presented with an incidental finding of a small bowel tumor during computed tomography (CT) examination performed for hematuria. The CT scan showed irregular thickening of the distal ileum, which was suggestive of a malignant small bowel tumor. An exploratory laparotomy revealed an 8-cm mass in the distal ileum; thus, a segment of the small intestine, including the mass, was resected. Histopathological analysis revealed an ulceroinfiltrative mass-like lesion with luminal narrowing, marked inflammatory cell infiltration, and large atypical lymphoid cells (positive for EBV-encoded small RNA). A final diagnosis of an EBV-MCU was established. The postoperative course was uneventful, and the patient was discharged on postoperative day 7. The patient remained recurrence-free until 12 mo after surgery.

#### CONCLUSION

This case highlights the diagnostic challenges for EBV-MCUs and emphasizes the importance of comprehensive evaluation and accurate histopathological analysis.



**Key Words:** Epstein–Barr virus; mucocutaneous ulcer; Misdiagnosis; Small bowel adenocarcinoma; Surgery; Case report

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**Core Tip:** We report a case that highlights the diagnostic challenges of distinguishing an Epstein–Barr virus-mucocutaneous ulcer from a small bowel adenocarcinoma in a 69-year-old woman. It emphasizes the importance of performing comprehensive evaluation and accurate histopathological analysis to guide appropriate management. Awareness of this rare entity is crucial for its timely diagnosis and prevention of unnecessary invasive procedures.

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## INTRODUCTION

Epstein–Barr virus (EBV)-positive mucocutaneous ulcer (MCU) is an uncommon disorder characterized by ulcerative lesions in the skin, oral cavity, or gastrointestinal (GI) tract. Previous reports have revealed that EBV-MCU is primarily associated with drug-induced immunosuppression or age-related immunosenescence[1]. Most cases of EBV-MCU respond well to conservative treatment, such as reduction of immunosuppressive drugs; surgical resection is required in only a minority of cases[2].

However, EBV-MCU diagnosis is challenging due to the nonspecific nature of the ulcerative lesions, which makes it difficult to distinguish from other tumorous conditions (such as small bowel adenocarcinoma). Small bowel adenocarcinoma is rare, accounting for ~3% of all GI cancers[3]. The rarity of cases and the presence of nonspecific symptoms often pose a challenge to achieving early and accurate diagnosis[4]. The complex etiology and histopathological heterogeneity of small bowel adenocarcinoma further contribute to the difficulty in establishing a definitive diagnosis[5].

A diagnostic challenge arises when EBV-MCU occurs in the GI tract, thereby mimicking small bowel adenocarcinoma. Potential misdiagnosis may subject patients to unnecessary invasive procedures or inappropriate treatment. Thus, both conditions must be differentiated to ensure appropriate management. In this case report, we present a rare case of surgically diagnosed and treated EBV-MCU that was initially misdiagnosed as small bowel adenocarcinoma. By highlighting this case, we aim to raise awareness of the importance of accurately distinguishing between these two conditions to ensure effective management and prevent potential harm to the patients.

## CASE PRESENTATION

### Chief complaints

A 69-year-old woman presented with hematuria during routine screening.

### History of present illness

Computed tomography (CT) urography was performed at the Department of Nephrology. Incidentally, a small bowel tumor was detected on the CT scan, prompting a referral to our department.

### History of past illness

The patient had no other underlying diseases, except for hypertension, and did not complain of GI symptoms (such as nausea, vomiting, or abdominal pain). There was no history of previous pulmonary tuberculosis.

### Personal and family history

The patient had no relevant family history.

### Physical examination

A physical examination revealed normoactive bowel sounds, no abdominal distention, and no prominent tenderness. The vital signs were as follows: blood pressure, 141/86 mmHg; pulse rate, 70 beats/min; respiratory rate, 18 breaths/min; and body temperature, 36.2°C.

### Laboratory examinations

Laboratory tests indicated anemia, with the following findings: hemoglobin, 9.2 g/dL (reference: 12–16 g/dL); mean corpuscular volume, 87.8 fL (reference: 80–100 fL); mean corpuscular hemoglobin, 29.8 pg (reference: 26–38 pg); serum

iron, 82 µg/dL (reference: 29–164 µg/dL); ferritin, 116 ng/mL (reference: 13–150 ng/mL); and unsaturated iron binding capacity, 135 µg/dL (reference: 191–269 µg/dL). Tumor markers, namely carcinoembryonic antigen and carbohydrate antigen 19-9, were within their normal limits (0.697 ng/mL and 3.8 U/mL, respectively). No other abnormalities were noted.

### Imaging examinations

A CT scan revealed irregular thickening of the distal ileum, which caused proximal small bowel dilatation, and several enlarged lymph nodes in the mesentery and preaortic area (Figure 1). These findings suggested the presence of a malignant small bowel tumor with lymph node metastasis. No findings indicative of GI bleeding were observed during an endoscopic evaluation.

## FINAL DIAGNOSIS

The resected specimen was analyzed histopathologically. Grossly, the specimen showed a single ulcerative lesion with luminal obstruction, and the adjacent mucosa was edematous (Figure 2A). Microscopically, the mucosal surface showed ulceration with the formation of granulation tissue formation and marked inflammatory cell infiltration in all the layers of the colon wall; the inflammatory cells comprised a variable number of lymphocytes, plasma cells, eosinophils, and neutrophils, as well as a small number of large atypical lymphoid cells (Figure 2B and 2C). Immunohistochemical analyses revealed that these lymphoid cells were B cells with CD20 and CD30 positivity (Figure 2D and 2E). *In situ* hybridization further revealed that these cells were also positive for EBV-encoded small RNA (Figure 2F). No evidence of definite malignancy or tuberculosis was noted. Thus, a final diagnosis of EBV-MCU was established.

## TREATMENT

An exploratory laparotomy was performed for definitive diagnosis and treatment. During surgery, a mass of ~8 cm was identified at the distal ileum, 30 cm from the ileocecal valve. A 50-cm segment of the small intestine (including the mass) was resected, and D2 lymphadenectomy was performed. Anastomosis was performed using the hand-sewn method. The resected specimen showed a 7 cm × 4.5 cm ulceroinfiltrative mass-like lesion with luminal narrowing.

## OUTCOME AND FOLLOW-UP

The patient had an uneventful postoperative course, and was discharged on postoperative day 7. The patient remained recurrence-free until 12 mo after surgery.

## DISCUSSION

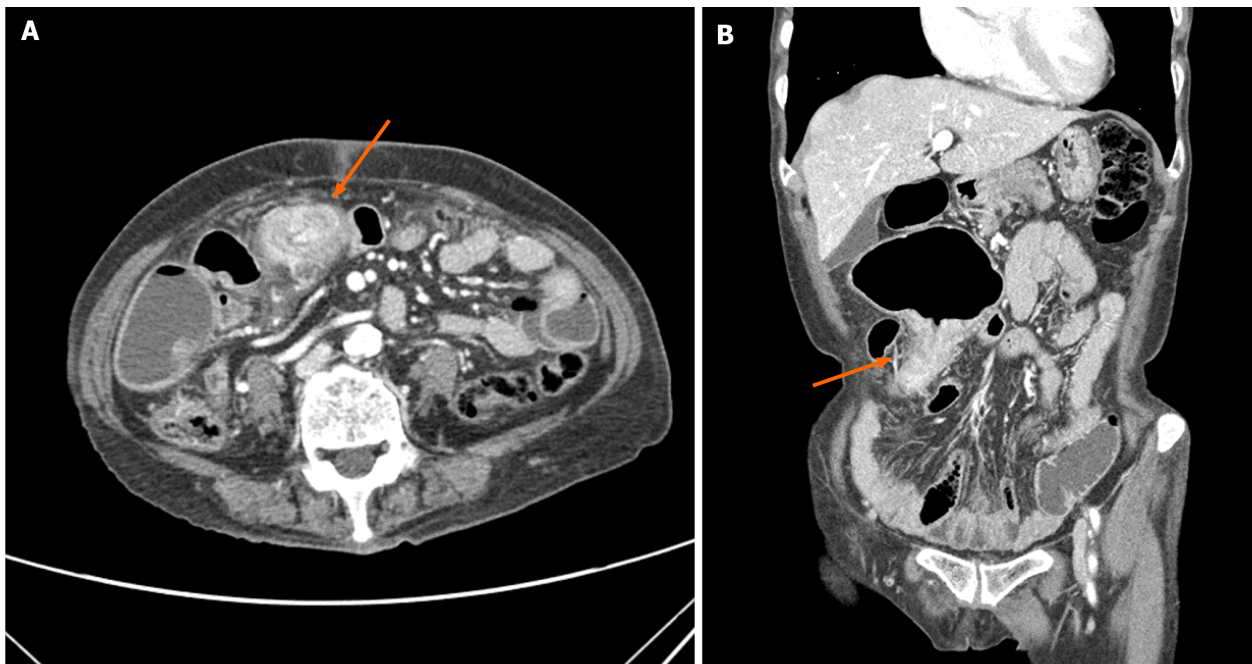
EBV-MCU was first identified as a B-cell lymphoproliferative disorder in 2010 by Dojcinov *et al*[1]. They reported a series of 26 EBV-MCU cases involving the oropharyngeal mucosa, skin, and GI tract; these were associated with drug-induced immunosuppression or age-related immunosenescence. Since then, several cases have been reported, and the 2016 World Health Organization classification recognized the condition as a newly identified entity[6]. Based on the absence of immunosuppression in the present case, the patient was considered to have developed EBV-MCU due to age-related immunosenescence.

A review by Sinit *et al*[2] discussed the first 100 reported cases of EBV-MCU, which revealed that the most commonly affected site was the oropharyngeal mucosa, followed by the GI tract and skin. The treatments administered included reduction of immunosuppressive drugs, systemic therapy, radiotherapy, and surgical resection in 50, 22, 10, and six cases, respectively. Only one of the six surgically treated cases involved the GI tract[7]. Only two out of the 100 small intestinal cases did not require surgical treatment. Conversely, the present case involved surgical resection of a tumorous lesion in the small intestine, which was initially misdiagnosed as small bowel adenocarcinoma but subsequently confirmed to be EBV-MCU through histopathological analysis.

Ishikawa *et al*[8] summarized 30 reported cases of EBV-MCUs involving the GI tract. The large intestine was the most commonly affected site, while the small intestine was only involved in three cases. Surgical treatment was undertaken in 10 of the 30 cases. Our case, however, presented with EBV-MCU-induced intestinal obstruction that required surgery; this is consistent with the findings reported by Morita *et al*[7]. Nonetheless, preoperative endoscopic access was challenging due to the location of the lesion in the small intestine. To the best of our knowledge, the present case is the first reported instance of an EBV-MCU causing small intestinal obstruction and necessitating surgical treatment.

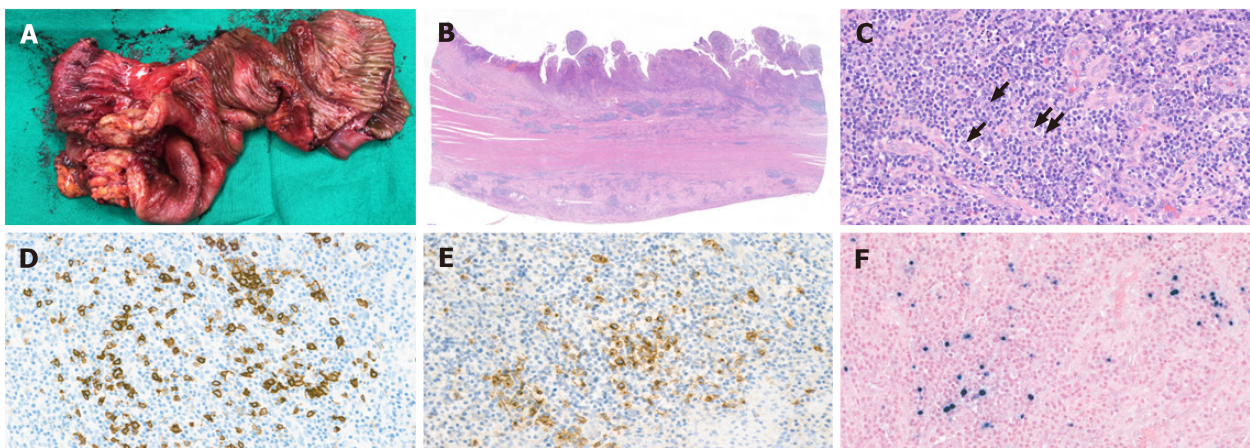
For EBV-MCU, the pivotal aspect in clinical practice is its accurate differentiation from other related conditions, such as small bowel adenocarcinoma or intestinal tuberculosis. This differentiation hinges upon comprehensive assessment of the clinical manifestations and imaging features, which enables precise diagnosis and development of tailored treatment strategies. EBV-MCUs frequently emerge in immunocompromised patients, especially those receiving immunosup-





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**Figure 1** Computed tomography scan demonstrating irregular thickening of the distal ileum, resulting in proximal small bowel dilatation (arrow). A: Axial view; B: Coronal view.



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**Figure 2** Histopathological analysis of the resected specimen. A: The resected specimen showed a single ulcerative lesion with luminal obstruction; B: Histopathologically, the mucosal surface was ulcerated with granulation tissue formation. Beneath the ulcer, the specimen revealed marked infiltration of various inflammatory cells as well as dense fibrosis in all layers of the colon wall (hematoxylin–eosin stain, scan view); C: The infiltrated inflammatory cells consisted of lymphocytes, plasma cells, eosinophils and neutrophils, as well as a few scattered large atypical lymphoid cells (arrow) (hematoxylin–eosin stain, original magnification, 400×); D–F: The large atypical lymphoid cells were CD20-positive, CD30-positive, and Epstein–Barr virus (EBV)-positive. CD20 (D), CD30 (E), and *in situ* hybridization for EBV-encoded RNA (F) (original magnification, 400×).

pressive therapy or undergoing age-related immunosenescence[8]. A reduction in immunosuppressant dose often leads to an improvement in the lesions, which offers a diagnostic clue for EBV-MCU. EBV-MCUs often present as ulcerative lesions with infiltrative margins in mucosal areas on imaging studies.

For small bowel adenocarcinoma, clinical manifestations may include nonspecific signs, such as weight loss, anemia, and abdominal discomfort[9]; conversely, common imaging findings include nodular or irregular thickening of the small bowel wall, which is often accompanied by luminal narrowing. In case of intestinal tuberculosis, patients may present with constitutional symptoms, such as fever, night sweats, and weight loss; imaging findings may include thickened intestinal walls or nodules, mostly in the ileocecal area[10].

While these clinical manifestations and imaging features could help differentiate EBV-MCU from small bowel adenocarcinoma or intestinal tuberculosis, there may be cases with overlapping characteristics. Thus, diagnosis of GI-tract-associated EBV-MCU remains challenging without surgery, and accurate diagnosis requires a combination of

clinical assessment, imaging studies, and histopathological analysis[7,8,11].

## CONCLUSION

Although EBV-MCUs rarely affect the GI tract, particularly the small intestine, they should be considered when chronic inflammation with ulceration is observed. The overlapping clinical features between EBV-MCUs and small bowel adenocarcinoma may lead to misdiagnosis, which emphasizes the need for comprehensive evaluation and accurate histopathological analysis. Increased awareness of this rare entity is crucial for timely diagnosis, optimal patient care, and prevention of unnecessary invasive procedures.

## FOOTNOTES

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