86607_Auto_Edited-check.docx

WORD COUNT	1723	TIME SUBMITTED	23-AUG-2023 05:03PM
		PAPER ID	102191275

Name of Journal: *World Journal of Gastrointestinal Surgery*

Manuscript NO: 86607

Manuscript Type: CASE REPORT

Epstein-Barr virus-positive mucocutaneous ulcer misdiagnosed as a small bowel adenocarcinoma: A case report

Song JH *et al*. EBV-MCU misdiagnosed as a small bowel adenocarcinoma

Abstract

BACKGROUND

Epstein-Barr virus-positive mucocutaneous ulcers (EBV-MCUs) represent an uncommon disorder characterized by ulcerative skin, oral, or gastrointestinal lesions in patients with iatrogenic or aging-induced immunosuppression. The non-specific 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 an 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 a 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 a comprehensive evaluation and accurate histopathological analyses.

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

Song JH, Choi JE, Kim JS. Epstein-Barr virus-positive mucocutaneous ulcer misdiagnosed as a small bowel adenocarcinoma: A case report. *World J Gastrointest Surg* 2023; In press

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 further emphasizes the importance of performing a comprehensive evaluation and an accurate histopathological analysis to guide appropriate management. Awareness of this rare entity is crucial for its timely diagnosis and prevention of unnecessary invasive procedures.

INTRODUCTION

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

However, EBV-MCU diagnosis is challenging due to the non-specific nature of the ulcerative lesions, which makes it difficult to distinguish them from other tumorous conditions (such as small bowel adenocarcinomas). Small bowel adenocarcinoma is a rare GI cancer, accounting for approximately 3% of all GI cancers[3]. The rarity of cases and the presence of non-specific symptoms often poses a challenge to achieving an 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 an EBV-MCU occurs in the GI tract, thereby mimicking a small bowel adenocarcinoma. Potential misdiagnosis may subject patients to unnecessary invasive procedures or inappropriate treatments. Thus, both conditions must be differentiated to ensure appropriate management. In this case report, we present a rare case of a surgically diagnosed and treated EBV-MCU that was initially misdiagnosed as a small bowel adenocarcinoma. By highlighting this case, we aim to raise awareness of the importance of accurately distinguishing between these two conditions to both ensure effective management and prevent potential harm to the patients.

CASE PRESENTATION

Chief complaints

A 69-year-old woman presented with hematuria during a 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). Furthermore, 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 ℃.

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 (being 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 cells 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

small number of large atypical lymphoid cells (Figures 2B and C). Immunohistochemical analyses revealed that these lymphoid cells were B cells with CD20 and CD30 positivity (Figures 2D and E). 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 an EBV-MCU was established.

TREATMENT

An exploratory laparotomy was performed for definitive diagnosis and treatment. During surgery, a mass of approximately 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 a 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

An 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 of EBV-MCUs 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 an EBV-MCU due to age-related immunosenescence.

A review by Sinit *et al*[2] discussed the first 100 reported cases of EBV-MCUs; it revealed that the most commonly affected site was the oropharyngeal mucosa, followed by the GI tract and skin. The treatments administered included immunosuppressive drugs reduction, systemic therapy, radiotherapy, and surgical resection in 50, 22, 10, and 6 cases, respectively. Notably, only one out of the six surgically treated cases involved the GI tract[7]. Furthermore, 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 a small bowel adenocarcinoma but subsequently confirmed to be an EBV-MCU through histopathological analyses.

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 aforementioned 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 an EBV-MCU, the pivotal aspect of clinical practice lies in its accurate differentiation from other related conditions, such as small bowel adenocarcinomas or intestinal tuberculosis. This differentiation hinges upon a 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 immunosuppressive therapy or undergoing age-related immunosenescence[8]. Notably, reduction in immunosuppressant dosage often leads to an improvement in the lesions; this offers a diagnostic clue for EBV-MCUs. EBV-MCUs often presents as ulcerative lesions with infiltrative margins in mucosal areas on imaging studies.

For small bowel adenocarcinomas, clinical manifestations may include non-specific 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].

Notably, while these clinical manifestations and imaging features could help differentiate an EBV-MCU from a small bowel adenocarcinoma or intestinal tuberculosis, there may be cases with overlapping characteristics. Thus, diagnosis of GI tract-associated EBV-MCUs remains challenging without surgery; accurate diagnosis requires a combination of clinical assessment, imaging studies, and histopathological analyses[7,8,11].

CONCLUSION

Although EBV-MCUs rarely affects 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 adenocarcinomas may lead to a misdiagnosis; this emphasizes the need for a comprehensive evaluation and accurate histopathological analyses. Increased awareness of this rare entity is crucial for timely diagnosis, optimal patient care, and prevention of unnecessary invasive procedures.

86607_Auto_Edited-check.docx

ORIGINALITY REPORT

4%
SIMILARITY INDEX

PRIMARY SOURCES

1	journals.lww.com Internet	21 words — 1%
2	f6publishing.blob.core.windows.net Internet	16 words — 1%
3	www.wjgnet.com Internet	16 words — 1%
4	academic.oup.com Internet	15 words — 1%

EXCLUDE QUOTES	ON	EXCLUDE SOURCES	< 15 WORDS
EXCLUDE BIBLIOGRAPHY	ON	EXCLUDE MATCHES	< 15 WORDS