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Case Report

Acute systemic infection-associated Russell body gastroesophagitis: A case report and literature review

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ABSTRACT

Russell body esophagitis/gastritis (RBG) is a rare gastrointestinal inflammatory condition characterized by accumulation of plasma cells containing dense eosinophilic cytoplasmic inclusions, i.e., Russell bodies. Herein, we report a case of RBG in a patient with a systemic inflammation background. A 61-year-old female presented with oral infection. Upper gastrointestinal endoscopy revealed patchy salmon-colored esophageal mucosa proximally to the gastroesophageal junction, suggestive of "Barrett's esophagus". Histologic examination of the biopsy tissue from the lower esophagus showed diffuse lymphoplasmacytic infiltration with abundant admixed enlarged plasma cells (Mott cells) containing bright eosinophilic, round, dense, homogenous inclusions (Russell bodies) in cytoplasm. Immunohistochemical study demonstrated membranous staining of CD138 in the Mott cells, while immunoglobulin light chain in situ hybridization revealed positivity of only kappa light chain, indicating kappa light chain restriction and clonality. A proton-pump inhibitor therapy was initiated, but the patient passed away due to generalized infection. Our case suggests that Russell body esophagitis/gastritis (RBG) can be a gastrointestinal presentation associated with acute systemic infection.

Introduction

Russell body was first described by William Russell as round eosinophilic cytoplasmic inclusions in plasma cells. Plasma cells containing numerous Russell bodies are referred as "Mott cells"; they can be seen in autoimmune diseases, chronic inflammatory conditions, and plasma cell dyscrasias [1].

Russell body gastritis (RBG) is a rare form of chronic gastritis with a localized accumulation of plasma cells containing Russell bodies [2]. It was first reported by Tazawa in a gastric biopsy in 1998 [3]. Since then, more than 40 cases of RBG have been appeared in scattered literature, in addition to 7 cases of Russell body esophagitis.

RBG can be associated with both neoplastic and non-neoplastic conditions. The former include gastric carcinomas, particularly gastric adenocarcinoma, signet ring cell carcinoma [4–6], gastric carcinoma associated with EBV [7], and malignant gastrointestinal tumor [8], while the latter are infections with H. pylori, HIV (human immunodeficiency virus) [9–10], HCV (hepatitis virus C) [11] and candida esophagitis [12] and chronic alcohol use [3,13]. Differential diagnosis of RBG includes signet ring carcinoma (SRC), especially eosinophilic variant [14], poorly differentiated carcinoma [6], hepatoid gastric carcinoma, epithelioid gastrointestinal stromal tumor, plasma cell dyscrasias, and lymphoproliferative diseases, including lymphomas with signet ring cell morphology (e.g., follicular lymphoma).

When entertaining a diagnosis of RBG entity, the clinical association and differential diagnosis are of particular importance, given the unique histomorphologic presentation and clinical significance of this condition. Here, we report a case of Russell body involving gastroesophageal junction, i.e., Russell body gastroesophagitis, in a patient with acute systemic inflammation.

Case presentation

A 61-year-old female presented with fever (104F), poor appetite, oral infection and worsening dysphagia. Her medical history was significant for cerebral palsy since birth.

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Physical exam revealed poor dentition, pus from Wharton's duct, and freely draining scalp abscess. Abdominal exam revealed no abnormalities. Imaging studies demonstrated right mandibular angle phlegmon/developing abscess. Abdominal CT scan revealed one 3.3 cm possible right adnexal mature dermoid, one benign appearing uterine polyp and cholelithiasis.

Upper endoscopy displayed patchy salmon-colored esophageal mucosa proximally to the gastroesophageal junction, suggestive of Barrett's esophagus (Fig. 1A). Gastric mucosa appeared unremarkable. There was localized erythema in the duodenal bulb, suggestive of duodenitis.

Hematological studies found leukocytosis (WBC 11.7) with neutrophilia and left shift (87 % neutrophil: 11.48 absolute), mild anemia, and thrombocytosis (platelets 408). Additional laboratory findings included decreased total serum protein (5.1 g/dL), decreased serum albumin (2.4 g/dL), elevated AST and ALT (60 and 53 IU/L respectively), elevated D-Dimer and lactate levels (883 ng/mL and 5.3 mmol/L respectively), as well as elevated erythrocyte sedimentation rate (ESR, 69 mm/hour) and C-reactive protein (CRP, 2.3 mg/dL).

Hematoxylin and eosin sections of the lower esophageal biopsy specimen displayed expansion of lamina propria of metaplastic columnar mucosa of the esophagus by diffuse lymphoplasmacytic infiltration featuring dense accumulation of enlarged plasma cells, i.e., Mott cells (Fig. 1B, 1C). The Mott cells were filled up with bright eosinophilic, round, dense, homogenous inclusions (Russell bodies), which displaced nuclei to the periphery of the cell (Fig. 1D). The cell size, color and consistency of cytoplasm and eccentric nuclei of Mott cells imparted them a lantern appearance. No mitotic figures were noted in Mott cells. No intestinal metaplasia, dysplasia or lymphoepithelial lesions were identified in mucosal epithelium. Immunohistochemical (IHC) studies demonstrated positivity of CD138, a plasma cell marker, and negativity of CK AE1/3 in both plasma cells and Mott cells, confirming the origin of the latter (Fig. 2A, B). Kappa and lambda immunoglobulin light chain ISH (in situ hybridization) demonstrated polytypic light chain expression pattern with normal kappa/lambda ratio in normal plasma cells (Fig. 2C, D). In contrast, the Mott cells were positive only for kappa light chain, indicating kappa light chain restriction/clonality. Gastric antrum and body biopsies had no significant pathologic changes and were negative for H. pylori on immunohistochemical study.

A final diagnosis of Russell body gastroesophagitis was rendered on the basis of the overall histomorphologic features. The biopsy findings prompted additional work-up for possible underlying plasma cell dyscrasia. Serum protein electrophoresis was negative for monoclonal paraprotein. HIV and HCV screenings were negative.

A proton-pump inhibitor therapy was initiated through the PEG tube based on the GI biopsy result, but the patient passed away due to generalized infection at an outside hospital several weeks after the discharge from our institution. No medical documentation is available for further review.

Discussion

RBG is defined as localized accumulation of plasma cells with Russell bodies. Russell bodies represent accumulation of condensed non-degradable components of immunoglobulins in the dilated rough endoplasmic reticulum due to disturbance of immunoglobulin secretion secondary to chronic inflammatory cellular damage [15]. RBG was reported predominantly in males with a mean age of 60 years [16];

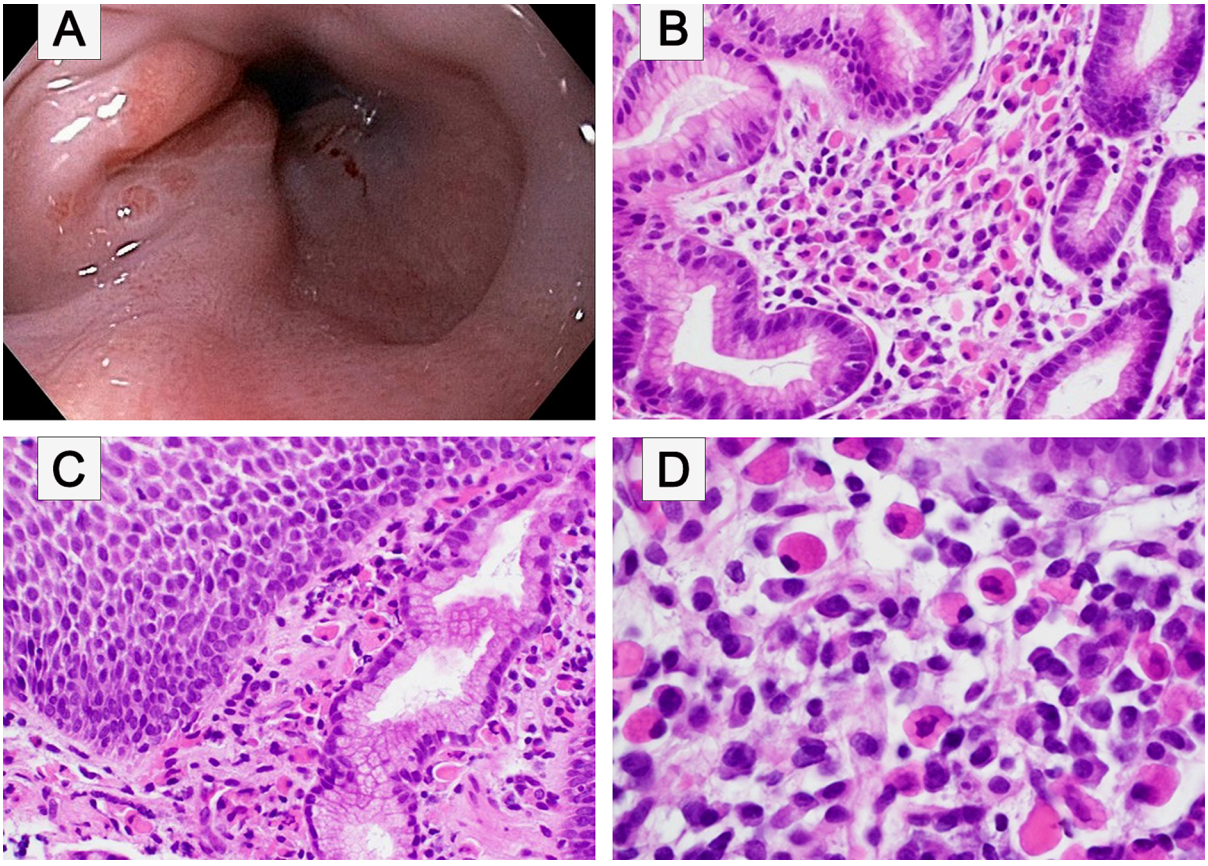

Fig. 1. EGD procedure displayed lower third of esophagus showing salmon-color mucosa (site of the biopsy) (A). H&E section of the lower esophageal biopsy. Heavy lymphoplasmacytic infiltrate and dense Mott cells in lamina propria of metaplastic columnar mucosa (B) (20× objective). Mott cells also infiltrated lamina propria of squamous mucosa (C) (20× objective). Lymphoplasmacytic infiltrate with Mott cells, i.e., enlarged plasma cells with abundant eosinophilic intracytoplasmic dense hyaline material (Russell bodies) (D) (40× objective).

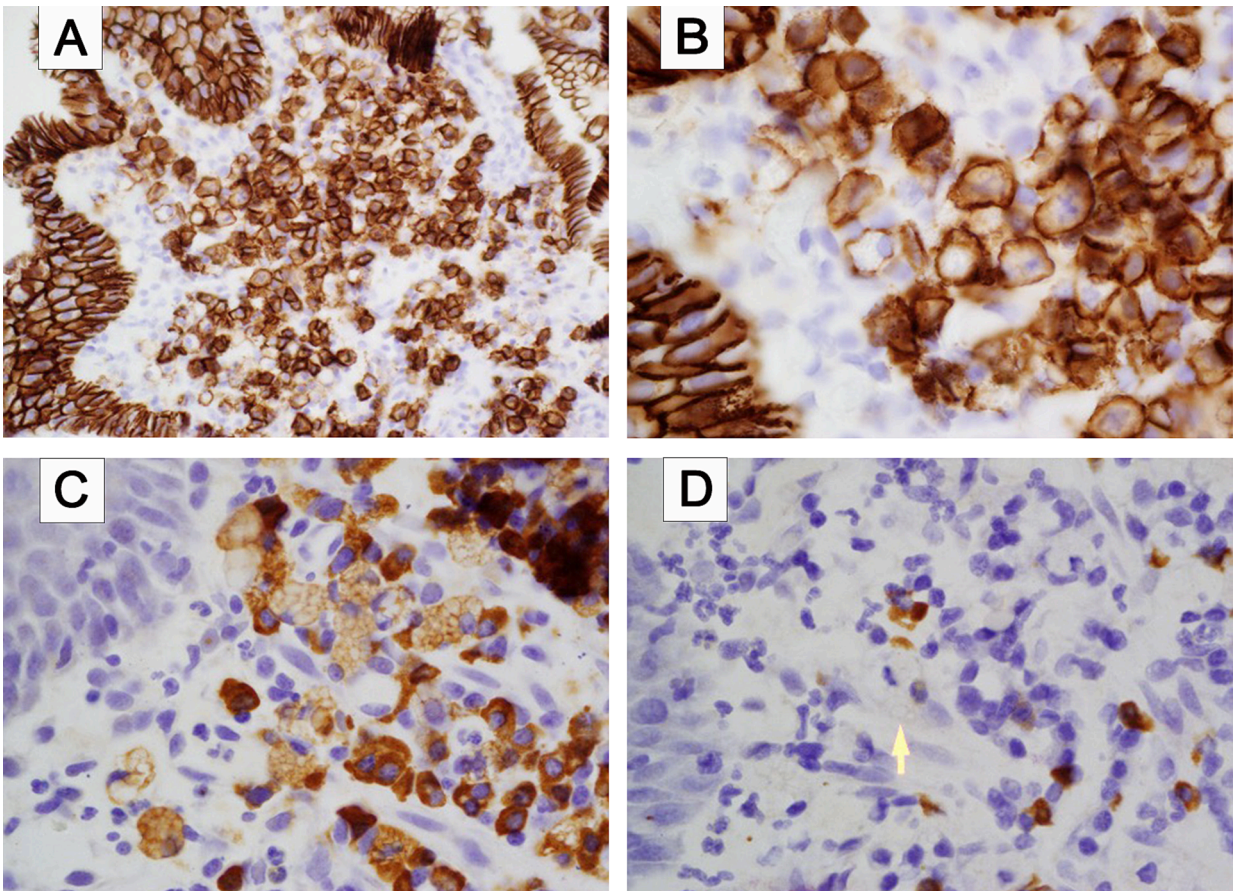

Fig. 2. CD138 immunostain highlighted both plasma cell and Mott cell component of the inflammatory infiltrates (A) in a membranous staining pattern (B). Epithelial cells served as a positive control (20× and 40× objective, respectively). Immunoglobulin light chain in situ hybridization showed expression of kappa light chain in both plasma cells and Mott cells (C). While lambda expression was present on infrequent, scattered plasma cells, it was lost on all Mott cells (D) (arrow) (40× objective).

however, pediatric cases were also reported [17]. Here we presented a case of a classic Russell body gastroesophagitis in the unusual location of gastroesophageal junction in a patient with acute systemic infection, as evidenced by her typical clinical presentation and alteration of serum markers indicating an acute inflammatory process.

The pathogenesis of RBG can be multifactorial. Some authors believe that localized Russell body-rich plasma cell infiltrate in the gastric mucosa represents a reactive response to H. pylori infection. In fact, 50–68 % of RBG cases are H. pylori positive [4,16]. H. pylori eradication usually results in clinical, endoscopic and microscopic improvement in these patients, further supporting the notion of H. pylori as a causative agent in RBG [16].

However, almost half of RBG cases are H. pylori negative. In addition, RBG occurrence does not correlate with the high prevalence of H. pylori infection in western countries [18]. Other causes, such as local degenerative or vascular-circulatory phenomena, are speculated to contribute to RBG [19]. Some investigators also hypothesize that immunoglobulin gene mutations may cause an excess of unsecreted immunoglobulin and subsequent RB formation in cases of RBG [20]. Therefore, the exact etiology of RBG still needs further investigation.

The clonality of the plasma cells in RBG is controversial. Although the Mott cells in most RB lesions in the GI tract are reported as polyclonal, a number of RBG cases do have light chain-restricted Mott cells [14,21] and are still considered as reactive proliferations. Zhang et al. suggested the term 'monoclonal RBG/RBD' for such cases [21]. Since serum light chain levels can be elevated in patients infected with H. pylori, it suggests that H. pylori disrupts immunoglobulin secretory system, which may explain reactive nature of light chain restriction in RBG cases [22]. Apparently, caution should be applied in the interpretation of the clonality in the setting of the reactive inflammatory conditions: a diagnosis of lymphoma cannot be based only on a light restriction of Mott cells [23]. On the other hand, light chain restriction in RBG may also raise concern for concomitant lymphoproliferative disorder. Factually, Joo reported a case of H. pylori-associated gastric MALT lymphoma with light-chain-restricted Mott cells [24], suggesting that these cells could be a part of neoplastic transformation. However, given a strong association of H. pylori infection with MALT [25] and gastric adenocarcinoma [26], RBG is potentially a concurrent event in patients with these conditions [14]. Moreover, RBG with polytypic Mott cells can be associated with multiple myeloma [4,27], implying independent proliferation of Mott cells from the neoplastic process. Interestingly, Mott cells of RBG in a patient with a monoclonal gammopathy of undetermined significance (MGUS) harbor both IgH and TCR-gamma rearrangement [20].

Stomach, especially antrum, is the most common site affected by Russell body accumulation in the GI tract [4,16]. However, these lesions can also be seen in duodenal heterotopic gastric mucosa, gastric cardia [4], and small and large intestine [13,28], including an unusual presentation of inflammatory polyp in the colon [29]. Considering wide anatomic distribution of Russell body inflammation, some authors suggest broader term, 'Russell body inflammation of the digestive tract' (RBIDT) [30]. In our case, although upper endoscopy revealed localized erythema in the duodenal bulb, no biopsy of this site was performed, precluding evaluation of the extent of Russell body-associated changes.

There are so far 7 cases of Russell body lesions reported in the esophagus or gastroesophageal junction [1,18,31–35], with 3 out of 7

cases negative for H. pylori (4 cases did not report H. pylori status). Interestingly, the majority of these cases (5/7) are associated with Barrett's esophagus. In our case, no histologic features of Barrett's esophagus were identified.

Patients with RBG usually have non-specific gastrointestinal symptoms, including reflux esophagitis, nausea, vomiting, abdominal discomfort, dyspepsia, diarrhea, or may be asymptomatic. Endoscopic images are varied with mucosal edema, hyperemia, ulceration, raised lesions and areas of mucosal granularity [21]. Due to the infrequency of RBG, the long-term prognosis and potential management approach still require further study. For H. pylori-associated RBG cases, antibiotic treatment results in clinical improvement and endoscopic and histological resolution [16]. As to H. pylori-negative cases, potentially associated conditions should be addressed for appropriate management.

In summary, we report a rare RBG case with typical morphology in an uncommon location in a background of systemic infection. Our case emphasizes the importance of recognizing the histomorphology of RBG and careful search of potential causes for differential diagnosis, including systemic infection, of this uncommon condition.

Author disclosure statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Ethics statement including patient consent statement

Informed telephone consent for the publication of this case report was obtained from the patient's legal next to kin, as the patient deceased. No personal details which may identify the patient are included in the submission. This study adhered to the guidelines set forth by the Office of Human Research Protection that is supported by U. S. Department of Health & Human Services.

Patient consent statement

All endoscopic and histologic imaging and text in this case report in entirely anonymized. Informed telephone consent for the publication of this case report was obtained from the patient's legal next to kin, as the patient deceased. No personal details which may identify the patient are included in the submission. This study adhered to the guidelines set forth by the Office of Human Research Protection that is supported by U. S. Department of Health & Human Services.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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