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Russell Body Gastritis Concurrent with Eosinophilia: a case report

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ABSTRACT

A 64-year-old male patient with a histological diagnosis of Russell body gastritis and with eosinophilic infiltrate in biopsy specimens is reported. The patient continued hemodialysis and pseudomembranous enteritis was contracted. Upper gastrointestinal endoscopy was performed due to poor appetite and blood eosinophilia. During endoscopy, a flare, swollen mucous membrane, and multiple verrucous erosions were noted in the gastric antrum. Biopsy and histopathological examination of gastric mucosa showed infiltration of plasma cells containing Russell bodies and eosinophils. Plasma cells containing Russell bodies were positive for CD138, immunoglobulin A (IgA) and kappa-light chain. Giemsa stained biopsy specimen revealed that the patient was negative for *Helicobacter pylori*. The patient was diagnosed with Russell body gastritis with eosinophilia. This is the first report of Russell body gastritis concurrent with eosinophilia. We discussed the possible correlation between the presence of plasma cells containing Russell bodies and gastric eosinophilia.

Key words: *Russell body gastritis, Russell body, Plasma cell, Eosinophilia*

Russell bodies are eosinophilic globules and structures including spherical immunoglobulin derived from plasma cells. Russell bodies represent a general cell response to accumulation of abundant, non-degradable immunoglobulin[13)]. Therefore, Russell bodies can appear in various organs and different diseases, either benign or malignant[13)]. If present in the gastrointestinal tract, they manifest as chronic inflammation of the esophagus, stomach, and duodenum which is known as Russell body gastroenteritis[2)]. Plasma cells are important components of the gastric lamina propria in chronic gastritis. Russell body gastritis is considered to be a subtype of chronic gastritis. The main constituent of inflammation is the infiltrate of plasma cells containing Russell bodies in the gastric mucosa.

Eosinophils have an important role in diseases of Th2 type immune hyperfunction such as parasitic infection defense or allergic disease. Gastrointestinal eosinophilia, a broad term for an abnormal eosinophil accumulation in the gastrointestinal tract, involves many different disease identities[19)]. Small numbers of eosinophils are commonly found in inflammatory stomach diseases[12)]. When large numbers of eosinophils are present, eosinophilic gastritis is diagnosed[12)]. Another main constituent of inflammation is the infiltrate of eosinophils in the gastric mucosa.

Here, we describe a case of Russell body gastritis, which includes not only plasma cells containing Russell bodies but also large numbers of eosinophils in the gastric mucosa. Previously there have been some reports of Russell body gastritis alone but not concurrent with eosinophilia. We discussed the possible correlation between the presence of plasma cells containing Russell bodies and gastric eosinophilia.

CASE REPORT

A 64-year-old man with an allergy to iodine and some kind of hemodialyzer membrane was on hemodialysis for chronic renal failure. During hos-

Abbreviations
H. Pylori: Helicobacter pylori, HPF: High power field, MGUS: monoclonal gammopathy of undetermined signficance

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pitalization for pseudomembranous enterocolitis, upper gastrointestinal endoscopy was performed because of poor appetite and eosinophilia of the peripheral blood (3690/μl). A flare and swollen mucous membrane and multiple verrucous erosions were noted in the gastric antrum during an endoscopic examination (Fig. 1a). The biopsy of this area was performed, and histopathological examination revealed many plasma cells containing Russell bodies in the gastric mucosa. In addition, eosinophils were also present around plasma cells (Fig. 1b-d). Russell bodies stained positive for Periodic acid-Schiff (PAS) (Fig. 2a). The eosinophil count was >30/HPF (Fig. 2b). Main constituents of infiltrative cells were plasma cells and eosinophils without atypia. No malignant findings such as lymphoepithelial lesion were present. Immunohistochemically, plasma cells with Russell bodies stained positive for CD138, IgA and kappa-light chain, but were negative for AE1/AE3, IgG, IgM and lamda-light chain (Fig. 2c-f). The Ki-67 labeling index was lower than 1%. Hematoxylin-eosin staining (H & E) and Giemsa staining were negative for *Helicobacter pylori (H. pylori)*. The patient did not show clinical or laboratory signs of monoclonal gammopathy of undetermined significance (MGUS). He was diagnosed with Russell body gastritis concurrent with eosinophilia.

DISCUSSION

Russell bodies are eosinophilic globules and structures including spherical immunoglobulin derived from plasma cells. In 1890, these were first described by Russell[14]. Russell bodies represent a general cell response to accumulation of abundant, non-degradable immunoglobulin[13]. Therefore, Russell bodies can appear in various organs and different diseases, either benign or malignant[13].

Russell body gastritis is considered to be a subtype of chronic gastritis. The main constituent of inflammation is the infiltrate of plasma cells containing Russell bodies in the gastric mucosa. In 1998, Tazawa et al reported a case of Russell body gastritis associated with *H. pylori* infection[16]. This case showed localized accumulation of plasma cells containing Russell bodies in multiple ulcer scars in the gastric antrum. Plasma cells are mature cells formed from lymphocytes that produce immunoglobulin. They have an important role as inflammatory cells along with polymorphs, lymphocytes, and macrophages. Regardless of anatomic location, it is likely that chronic inflammation causes aberrant chemokine expression, resulting in overstimulation of plasma cells, excessive immunoglobulin production, and subsequent Russell body formation[2]. It is important to exclude potential conditions such as signet cell cancer, mucosa-associated lymphoid tissue lymphoma (MALToma), malignant lymphoma, plasmacytoma, and MGUS[6]. In our case, immunohistochemical staining of plasma cells was positive for kappa-light chain and negative for lambda-light chain. This indicated Russell body gastritis showing IgA kappa-type monoclonality.

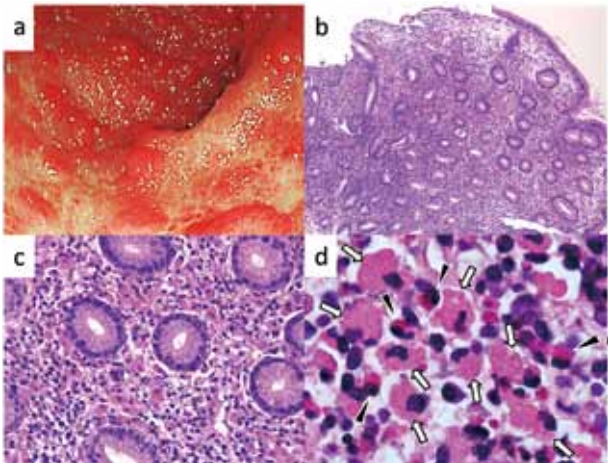

Fig. 1. Endoscopy and histopathological examination of biopsy specimens.
(a) Endoscopy of the gastric antrum. An inflamed and swollen mucous membrane and multiple verrucous erosions were noted.
(b)-(d) Biopsy and histopathological examination (hematoxylin and eosin staining).
Large numbers of plasma cells containing Russell bodies (arrows) and eosinophils (arrowheads) were present in the gastric mucosa.

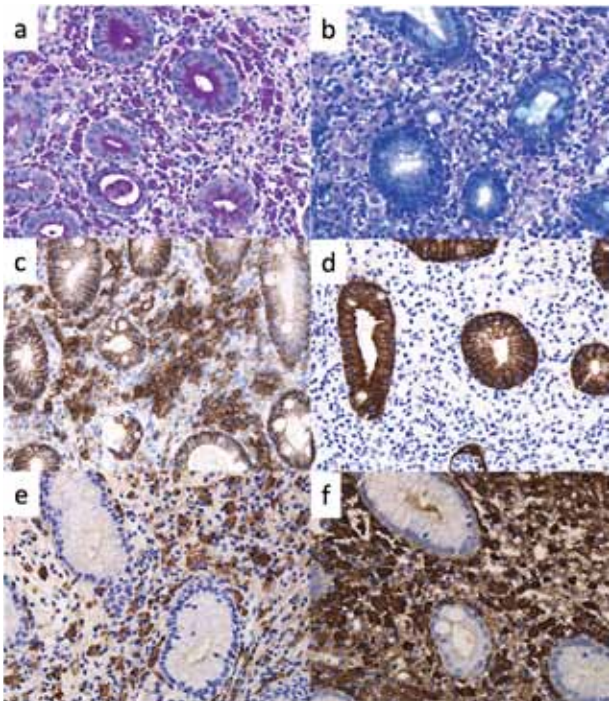

Fig. 2. Special staining and immunohistochemistry.
(a) The Russell bodies showed positive Periodic acid-Schiff staining.
(b) Large numbers of eosinophils were present in the mucosa (Giemsa staining).
(c)-(f) Plasma cells containing Russell bodies were positive for CD138 (c), negative for AE1/AE3 (d), and positive for IgA (e) and kappa-light chain (f).

There are some case reports of Russell body gastritis showing monoclonal proliferation[1,3,18]. In one case, plasma cells containing Russell bodies were reported to be positive for *H. pylori* and concomitant MGUS[18]. In our case, the main constituents of infiltrative cells were plasma cells and eosinophils without atypia. In addition, there were no malignant findings such a lymphoepithelial lesion. The possibility of MGUS was also ruled out.

In 2014, Klair JS et al summarized findings of all Russell body gastritis cases reported[6]. However, all cases showed Russell body gastritis without eosinophilia. Our case had not only plasma cells containing Russell bodies but also infiltration of eosinophils in the gastric mucosa. Small number of eosinophils are normally present in the lamina propria in the gastrointestinal tract, except for the esophagus, and the highest concentrations are found in the cecum and appendix[5]. Matsushita T et al reported the number and distribution of eosinophils in the adult human gastrointestinal tract[9]. The number of eosinophils was: 0.07 ± 0.43 (mean ± SD/mm^2/HPF) for the esophagus, 12.18 ± 11.39 for the stomach, and 42.18 ± 35.28 for the terminal ileum[9]. In our case, the number of eosinophils was 30/HPF in the gastric mucosa.

We speculated that there is a possible correlation between the presence of plasma cells containing Russell bodies and gastric eosinophilia. First, eosinophils might promote or suppress a strong inflammation in Russell body gastritis. Eosinophils have an important role in diseases of Th2 type immune hyperfunction such as parasitic infection defense or allergic disease. Eosinophils have roles in both host defense and pathological processes[19]. For example, in the case of granuloma, which is a biological defense mechanism against the stimulant, inflammatory infiltrating cells are not only macrophages and lymphocytes but also eosinophils and plasma cells. Thus, it is thought that eosinophils and plasma cells appear together under a strong inflammatory reaction. On the other hand, eosinophils in the lung are mobilized by marrow through the bloodstream of the respiratory tract and can promote and control allergic inflammation[7]. It is said that eosinophils contribute to inflammatory convergence and homeostatic maintenance[7]. In addition, we understood that eosinophils contribute to various immunoreactions only as effector cells of the Th2 type inflammatory reactions[15,17]. We thought that eosinophils might have promotion and suppression functions under the inflammation in Russell body gastritis.

Second, Russell bodies might be induced by eosinophils. Eosinophilic gastrointestinal disorders (EGID) are defined by a large number of eosinophils infiltrating the gastrointestinal tract together with various digestive organ symptoms. In our case, the patient had a past history of iodine allergy. EGID are regarded as allergic reactions occurring in response to a food antigen in a gastrointestinal mucosa, but etiology and pathological conditions are unidentified. A disease with functional disorder and infiltration of eosinophils in stomach and small and large intestine is said to be eosinophilic gastroenteritis. Russell bodies appear as chronic inflammation of the esophagus, stomach, and duodenum[2]. Therefore, plasma cells containing Russell bodies might appear in chronic inflammation including eosinophilia.

Finally, blood eosinophilia might cause eosinophilia in organs throughout the body. There are some reports in which patients with Russell body gastritis had a chronic renal failure due to several different diseases[10,11]. However, those patients had Russell body gastritis without eosinophilia. There is a report of hemodialysis-associated eosinophilia and it is believed to be associated with allergic reactions to dialyzer materials[8]. In addition, there is also a report of clostridium difficile colitis associated with eosinophilia[4]. Our patient, with a past history of hemodialyzer membrane-induced allergy symptoms, was undergoing the treatment of pseudomembranous enteritis at the time of biopsy. Therefore, blood eosinophilia due to hemodialysis or pseudomembranous enteritis might cause eosinophilia in organs throughout the body including the gastric mucosa.

Conflict of interest

The authors declare that they have no competing interests.

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REFERENCES

1. **Araki, D., Sudo, Y., Imamura, Y. and Tsutsumi, Y.** 2013. Russell body gastritis showing IgM kappa-type monoclonality. Pathol. Int. **63**: 565-567.
2. **Bhaijee, F., Brown, K.A., Long, B.W. and Brown, A.S.** 2013. Russell Body Gastroenteritis: An Aberrant Manifestation of Chronic Inflammation in Gastrointestinal Mucosa. Case Rep. Med. Article ID 797264, 5 pages
3. **Coyne, J.D. and Azadeh, B.** 2012. Russell body gastritis: A case report. Int. J. Surg. Pathol. **20**: 69-70.
4. **Holub, M., Arientová, S., Kořínková, M., Reisingerová, M. and Marešová, V**. 2013. Severe eosinophilia in a patient with clostridium colitis and gastric cancer. Klin. Mikrobiol. Infekc. Lek. **19**: 11-14.
5. **Khan, S.** 2005. Eosinophilic gastroenteritis. Best Pract. Res. Clin. Gastroenterol. **19**: 177-198.
6. **Klair, J.S., Girotra, M., Kaur, A. and Aduli, F.** 2014. Helicobacter pylori-negative Russell body gastritis: does the diagnosis call for screening for plasmacytic malignancies, especially multiple myeloma? BMJ Case Rep. doi:10.1136/bcr-2013-202672
7. **Kobayashi, Y. and Chihara, J.** 2012. Pathophysiology Focusing on Eosinophils. Jpn. J. Chest Dis. **71**: S47-50.

8. **Li, Z., Ma, L. and Zhao, S.** 2015. Effect of polyflux membranes on the improvement of hemodialysis-associated eosinophilia: a case series. Ren. Fail. **10**: 1-5.
9. **Matsushita, T., Riruke, M., Nahoko, I., Yuji, H., Asuka, A., Diane, C., et al.** 2015. The Number and Distribution of Eosinophils in the Adult Human Gastrointestinal Tract A Study and Comparison of Racial and Environmental Factors. Am. J. Surg. Pathol. **39**: 521-527.
10. **Munday, W.R., Kapur, L.H., Xu, M. and Zhang, X.** 2015. Russell body duodenitis with immunoglobulin kappa light chain restriction. World J. Gastrointest. Endosc. **7**: 73-76.
11. **Muthukumarana, V., Segura, S., O'Brien, M., Siddigui, R. and EI-Fanek, H.** 2015. Russell Body Gastroenterocolitis in a Posttransplant Patient: A Case Report and Review of Literature. Int. J. Surg. Pathol. **23**: 667-672.
12. **Owen, D.A.** 2003. Gastritis and Carditis. Mod. Pathol. **16**: 325-341.
13. **Paik, S., Kim, S-H., Kim, J-H., Yang, W.I. and Lee, Y.C.** 2006. Russell body gastritis associated with Helicobacter pylori infection: a case report. J. Clin. Pathol. **59**: 1316-1319.
14. **Russell, W.** 1890. An Address on a Characteristic Organism of Cancer. Br. Med. J. **1563**:1356-1360.
15. **Shamri, R., Xenakis, J.J. and Spencer, L.A.** 2011. Eosinophils in innate immunity: an evolving story. Cell Tissue Res. **343**: 57-83.
16. **Tazawa, K. and Tsutsumi, Y.** 1998. Localized accumulation of Russell body-containing plasma cells in gastric mucosa with Helicobacter pylori infection: 'Russell body gastritis'. Pathol. Int. **48**: 242-244.
17. **Weller, P.F.** 1991. The immunobiology of eosinophils. N. Engl. J. Med. **324**: 1110-1118.
18. **Wolkersdorfer, G.W., Haase, M., Morgner, A., Baretton, G. and Miehlke, S.** 2006. Monoclonal Gammopathy of Undetermined Significance and Russell Body Formation in Helicobacter pylori Gastritis. Helicobacter **11**: 506-510.
19. **Zuo, L. and Rothenberg, M.E.** 2007. Gastrointestinal eosinophilia. Immunol. Allergy Clin. North Am. **27**: 443-455.