Analysis of clinical and histopathological findings in Russell body gastritis and duodenitis

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ABSTRACT

Introduction: Russell body gastritis is considered as a rare, benign, incidental finding characterized by dense accumulation of plasma cells containing Russell bodies in the lamina propria. In this study, clinical and histopathological features of 12 cases of Russell body gastritis/duodenitis were presented.

Materials and methods: Clinical data, histopathological findings including Helicobacter pylori infection, Sydney system classification, Russell body density and immunohistochemical findings were evaluated in 11 gastric and 1 duodenal mucosal biopsy from 11 patients.

Results: Six cases were male, 5 were female and the mean age was 72 (44–87). The most common site was antrum (10/12), one case was located in cardia and one in heterotopic gastric mucosa of duodenal bulb. H. pylori was detected in half of the cases. One of the cases was accompanied by gastric tubular adenoma, one by gastric well-differentiated adenocarcinoma and one by plasma cell neoplasm. In all cases, globules were positive with PAS stain.

Conclusion: Russell body gastritis must be kept in mind while reporting endoscopic biopsies because this entity may be misdiagnosed as signet ring carcinoma and may be associated with neoplasms. Absence of nuclear atypia, mucin stains, cytokeratins, plasma cell and hematolymphoid antigen markers are useful in differential diagnosis. Associated H. pylori infection, as well as rarely carcinomas, adenomas and plasma cell neoplasms, may be observed.

1. Introduction

Russell bodies (RBs), dilated endoplasmic reticulum cisternae containing condensed immunoglobulins, are round eosinophilic cytoplasmic inclusions in mature plasma cells and represent a cellular response to excessive stimulation of plasma cells. Mott cells are plasma cells that have multiple globules of Russell bodies packed in their cytoplasm [1]. Russell body gastritis (RBG) was first described in 1998 by Tazawa as a rare, inflammatory process characterized by a dense accumulation of plasma cells containing RBs in the lamina propria, attended by chronic inflammation [2]. It is usually localized in gastric antrum but can be in the entire gastrointestinal tract [2-6]. Up to now there are only 40 cases of RBG [2-4,6-32], three cases of Russell body Barrett’s oesophagitis [5,40,41] and eight cases of Russell body duodenitis (RBD) [6,33-39] reported in the literature.

Although there are publications linking this entity with Helicobacter pylori (H. pylori), the aetiology has not been fully explained. There are cases of signet ring cell carcinoma and gastric adenocarcinoma accompanying the RBG [21,22]. Likewise, case reports about prominent Mott cell proliferation associated with Epstein-Barr virus-related gastric carcinoma and mucosa-associated lymphoid tissue lymphoma were reported [12,42,43]. While RBG is a benign process, it is important to recognize this entity because of the differential diagnosis and possible association with signet ring cell carcinoma, lymphomas and plasma cell neoplasms. Monoclonal plasma cell proliferation in RBG and RBD was reported earlier, and in these cases, differential diagnosis from MALT lymphoma with plasmacytic differentiation and plasmacytoma seems difficult due to the monoclonality of Mott cells [6,15,17,20,29]. In such cases, atypical morphology, nature of the background infiltrate and immunohistochemical stains provide important clues for the accurate diagnosis. In the present study, the clinical and histopathological findings of 12 cases with the diagnosis of Russell body gastritis/duodenitis were evaluated. This is the largest case series of Russell body gastritis reported in the English literature.

2. Materials and methods

A retrospective review was performed on database of our institution...
for the diagnosis of “Russell body gastritis”. There were 11 cases diagnosed as Russell body gastritis and 1 case as Russell body duodenitis between 2010 and 2018. Two gastric biopsy specimens of the same patient performed at different times were evaluated as different cases. Histopathologically all of the cases had at least localized dense accumulation of plasma cells containing RBs in the lamina propria, accompanied by chronic inflammation. All the slides were re-evaluated for pathological parameters including Sydney system classification (chronic inflammation, activation, glandular atrophy, intestinal metaplasia, \( H. pylori \)), extensiveness of RBs and dysplasia. The following data were recorded respectively; age, gender, localization, symptoms, accompanying lesions and neoplasms. RB density was scored as mild (focal) (1/3 of the lamina propria), moderate (2/3 of the lamina propria), severe (extensive) (3/3 of the lamina propria) according to the grade of involvement of the lamina propria by the lesion. Periodic acid Schiff-Alcian blue PH 2.5 (PAS-AB PH 2.5) and Warthin-Starry stainings were applied in all mucosal biopsies. CD38, CD138, pan-cytokeratin, Lambda and Kappa immunohistochemistry stainings were performed in 4 cases which had difficulties in differential diagnosis.

3. Results

The mean age of the 12 cases was 72 (range between 44 and 87) and male to female ratio (M/F) was 6/5. Seven of the patients had dyspepsia, 2 had epigastric pain and 2 had gastrointestinal bleeding complaints. Two patients underwent endoscopy with suspicion of a gastric tumour. All of the 12 cases included in the study were endoscopic biopsy materials. Most of the cases were located in the antrum (10/12), 1 in cardia and 1 in duodenal bulb. Histopathological evaluation revealed infiltration of the lamina propria by variable number of plasma cells, at least localized but dense homogeneous round to oval shaped eosinophilic RBs and Mott cells. Lymphocytic infiltration was observed as well. Extensiveness of involvement of the lamina propria by RBs was mild (focal) in 3 cases, moderate in 6 cases and severe (extensive) in 3 cases (Fig. 1). In the case of RBD, Mott cells were present in the area of gastric heterotopia of the duodenal bulb (Fig. 2). Histochemically, RBs in all cases revealed intracytoplasmic PAS positivity with PAS-AB PH 2.5 staining (Fig. 3). Eight of the cases had polymorphonuclear leukocytes, four had intestinal metaplasia, six had glandular atrophy and half of the cases had \( H. pylori \) infection. In the case of RBD, no \( H. pylori \) was observed in gastric heterotopia area. Table 1 annotates the clinicopathologic findings of the specimens.

One of the cases was associated with gastric tubular adenoma, one with gastric well-differentiated adenocarcinoma and one with colonic tubular adenoma with high grade dysplasia. When the gastrectomy specimen was examined, Mott cell proliferation was seen intermingled to well-differentiated adenocarcinoma (Fig. 4). One patient diagnosed as RBD in two different gastric biopsies had a multiple myeloma diagnosis from bone marrow biopsy performed 3 years later. In this case, plasma cells showed polyclonal expression with Lambda and Kappa by immunohistochemistry.

In all cases which underwent immunohistochemical analysis, plasma cells showed positive staining with CD138 and CD38, negative with pan-cytokeratin and polyclonal expression with Lambda and Kappa.

4. Discussion

In the English literature, the publications about Mott cells and RBG are limited and the information about the aetiology is not clear. In relation to the mechanism of development, hypotheses have been proposed in the form of increased synthesis of immunoglobulin derivatives or increased immunoglobulins that cannot be sequenced due to altered secretion and genetic changes [28,38]. RBG is characterized by dense accumulation of plasma cells containing RBs in the lamina propria, attended by chronic inflammation. There is no information about the minimum number of RBs for the diagnosis of RBG in either text-books or the literature. Moreover, PAS staining used in cases suspected of RBG, facilitates the diagnosis because this stain clarifies RBs and Mott cells. RBG mostly appears in the antrum [40]. The presence of Mott cells in the upper and lower endoscopic biopsies was reported by Muthukumarana et al. [4] and they called this lesion as Russell body gastritis. In the literature, there are also cases of Russell body oesophagitis [5,40,41]. In the present study, ten of the cases were located in the antrum concordant with the literature findings. Muthukumarana et al. examined all cases in the literature and according to

![Fig. 1. Plasma cells containing Russell bodies (Mott cells) in lamina propria of gastric mucosa (HE × 200).](image-url)
their findings, the range of age was 24–88, the ratio of M/F was 1.6/1. In our study, the age range was 44–87, the ratio of M/F was 1.2/1 which was compatible with the literature in terms of male pre-
dominance.

Endoscopy was performed due to nonspecific gastrointestinal system complaints and Mott cells were identified incidentally in the reported cases [4,6]. Seven of our patients had a complaint of dyspepsia and 2 had epigastric pain. RBG is commonly associated with *H. pylori* infection in reported cases, and the relationship between these two entities is questioned to learn aetiology. In some cases, RBs disappeared on repeated biopsies after *H. pylori* eradication [2,6,7,10,17,19,25,26]; however, there are also *H. pylori* negative cases [4,6,11,14,20,24,30,32]. In our study, half of the cases had *H. pylori* infection. There are cases diagnosed as Russell body duodenitis in the literature, and in some of them Mott cells were observed in the area of gastric metaplasia [6,38], in addition, some of these cases are accom-
panied by *H. pylori* infection [6]. In the case of the only RBD in our study, Mott cells were observed in the area of gastric heterotopia and *H. pylori* was not accompanying it. In the present study, extensiveness of RB density was moderate in 5 and severe in 2 of *H. pylori* positive cases suggesting an association between density of RBs with presence of *H. pylori*.

![Fig. 2. Mott cells in the area of the gastric heterotopia of duodenal bulb (HE ×100), inset: high power field of Mott cells (HE ×400).](image)

![Fig. 3. PAS positive Russell bodies in duodenal bulb (periodic acid-Schiff-Alcian blue stain (pH 2.5) ×100).](image)
In our study, we used immunohistochemistry in 4 cases which had differential diagnosis and in these cases, plasma cells were positive with CD138 and CD38, negative with pan-cytokeratin and positive with mucicarmine shows nuclear atypia and is positive for cytokeratin and mucicarmine whereas RBG lacks nuclear atypia and mitotic activity, negative for cytokeratins, and positive for plasma cell markers such as CD138 and CD38. PAS staining is very helpful for the recognition of Russell bodies, but it is not helpful to differentiate RBG from signet ring cell carcinoma because it also stains signet ring cells. Pathologists should not forget that signet ring cells and Mott cells can be found together in the same lesion, and, in particular, if clinical preliminary suspicion exists, detection of RBG should not be inhibitory in research for malignancy [4,22]. Shinozaki et al. presented 2 cases which showed the association of Mott cell proliferation and Epstein-Barr virus-associated gastric carcinoma [42]. They suggested that the expression of aberrant chemokine in these tumours led to plasma cell activation and Mott cell proliferation. In our study, associated gastric tubular adenoma in 1 patient, gastric well differentiated adenocarcinoma in 1 patient and colonic tubular adenoma with high grade dysplasia in 1 patient were observed.

It is important to be careful when examining biopsies containing RBs, not only due to the accompanying neoplasms but also due to the differential diagnosis with plasma cell neoplasms, MALT lymphoma and plasmablastic lymphoma. Histopathological findings favouring MALT lymphoma are the presence of atypical centrocyte-like cells and lymphoepithelial lesions. Ancillary tests such as serum protein electrophoresis, plasma cells and hematolymphoid antigen markers, in situ hybridization for EBV-encoded small RNA may be necessary. Clinical and radiological findings of the patient are also helpful in the differential diagnosis. In addition, Lambda and Kappa light chains can be used to show the polyclonal nature of plasma cell infiltrate. But there are also cases of RBG and RBD showing monoclonality in Mott cells [6,15,17,20,29]. Initially Zhang et al. reported the monoclonality of this entity on a large-scale basis, and they mentioned that the monoclonality of Mott cells can’t be used as an evidence of an existing neoplastic lesion and may represent a reactive process [6]. Additionally, monoclonal B cell proliferation has been reported in chronic inflammations such as Hashimoto thyroiditis, chronic hepatitis C, Sjögren’s syndrome and H. pylori associated chronic active gastritis. Monoclonal B cell proliferation in RBG is considered as a benign monoclonal condition associated with H. pylori gastritis. In our study, we used immunohistochemistry in 4 cases which had difficulty in differential diagnosis and in these cases, plasma cells were positive with CD138 and CD38, negative with pan-cytokeratin and positive with Lambda and Kappa. In the follow-up, one of our patients who was diagnosed as RBG by gastric tissue biopsies performed at two different times had a multiple myeloma diagnosis from bone marrow biopsy 3 years later. In this case, plasma cells were not diffusely infiltrating the mucosa and showed polyclonal expression with Lambda and Kappa. But extensiveness of RB density was severe (involving 3/3 of lamina propria) in this single case.

## 5. Conclusion

We presented the largest case series of Russell body gastritis reported in the English literature. According to our findings, Russell body gastritis is located mostly in the antrum and has a male predominance with an age range of 44–87. One of our cases was associated with

<table>
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<th>Case no.</th>
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<th>Activity</th>
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<th>Glandular atrophy</th>
<th>Histopathology</th>
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F: female, M: male, GI: gastrointestinal, LGD: low-grade dysplasia, HGD: high-grade dysplasia, 0: none, 1: mild, 2: moderate, 3: severe. *a Case no1 and no2: Two gastric biopsy specimens of the same patient performed at different times.*
gastric well-differentiated adenocarcinoma and one had multiple myeloma three years after RBG diagnosis. Our study has some limitations that need to be considered interpreting the findings. One of the limitations is the retrospective nature of the study and the other is the number of the patients. Although the number of the patients in the present study is small, there are only a few studies about RBG and its clinical significance in the literature. Albeit Russell body gastritis is a benign process, it is an entity that should be kept in mind especially in endoscopic biopsies, because of the presence of signet ring cell carcinomas, lymphomas and plasma cell neoplasms in the differential diagnosis and the possibility of accompanying neoplasms. In this respect, the absence of nuclear atypia, mucin stains, cytokeratins, hematolymphoid and plasma cell markers are useful. To better understand the relationship of these lesions with neoplasms and the underlying mechanisms, studies of larger series will be useful.

Declaration of interest

None.

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References


