CASE REPORT

Russell body gastritis associated with *Helicobacter pylori* infection: a case report

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An unusual and rare gastric mucosal lesion histologically consisting of a localised accumulation of Russell bodies and Russell body-containing plasma cells, the so-called Mott cells, has been recognised only recently and termed as ''Russell body gastritis''. This lesion, despite its densely monomorphous appearance is easily confirmed to be non-neoplastic by its polyclonal immunoreactive pattern to immunoglobulin light chains. However, the aetiology of Russell body gastritis is controversial and hence the optimal treatment for this disease has not been established. Two cases of Russell body gastritis associated with *Helicobacter pylori* infection are reported, and the possible role of *H pylori* infection in the pathogenesis is discussed.

Russell bodies are spherical immunoglobulin-containing structures derived from plasma cells. Mott cells are plasma cells whose rough endoplasmic reticulum is stuffed with Russell bodies. Although the presence of few Russell bodies in many types of chronic inflammation and in various B cell lymphocytic neoplasms is a well-recognised feature, an abundant homogeneous accumulation of Russell bodies and Mott cells simulating a neoplastic process is a rare event.

We report here two cases with unusual benign gastric mucosal lesions, histologically characterised by a dense monomorphous accumulation of Mott cells with numerous intracellular and extracellular Russell bodies. Despite the alarming monomorphous appearance simulating a neoplastic process, immunohistochemical analysis against immunoglobulin light chain showed a polyclonal pattern. Interestingly, both cases were intimately associated with *Helicobacter pylori* infection. These gastric lesions conform to a rare and peculiar gastric mucosal lesion, which was named only recently as Russell body gastritis by Tazawa and Tsutsumi.[1] To the best of our knowledge, this is the second documented report of Russell body gastritis associated with *H pylori* infection. This report highlights the clinicopathological characteristics of Russell body gastritis with emphasis on the possible role of *H pylori* infection in the pathogenesis.

CASE REPORTS

Case 1

A 47-year-old woman presented with mild epigastralgia. Physical examination and laboratory data did not show any abnormalities. The patient denied haematemesis, haematochezia, melaena, diarrhoea or weight loss. Upper gastroendoscopic examination showed focal erythematous swelling in the antrum. The gastric mucosal biopsy specimen under low power showed numerous spherical eosinophilic globules expanding the lamina propria, which at first glance looked like extravasated red blood cells (fig 1A). Under high power, these globules were shown to be Russell bodies, some of which were found in the cytoplasm of plasma cells—that is, Mott cells. Variable-sized extracellular Russell bodies, which coalesced to form larger masses were also present in the stroma (fig 1B). However, intranuclear inclusions—that is, Dutcher bodies, were absent. Thin wavy blue rods representing *H pylori* were readily identified in the mucus overlying or attached to the foveolar epithelium, on haematoxylin and eosin-stained slides. These organisms were confirmed to be *H pylori* antigen positive by immunohistochemical analysis using anti-*H pylori* antibody (Dako, Carpenteria, California, USA). Immunohistochemically, the Russell body-containing cells stained for CD79a and CD38 (Dako), but stained negative for CD20 (Dako), confirming them to be plasma cells. Small lymphoid follicles were found adjacent to but not within the collection of Mott cells (fig 1C). Initially, the possibility of a neoplastic process, such as mucosa-associated lymphoid tissue (MALT) lymphoma with extreme plasmacytic differentiation and plasmacytoma, was considered in the differential diagnoses due to the density and uniformity of the infiltrating Mott cells. However, on scrutiny, the absence of cytologic atypia, lymphoepithelial lesions and other cellular components such as centrocyte-like cells and monocytoid cells deemed MALT lymphoma to be an unlikely diagnosis. Furthermore, immunohistochemical staining against immunoglobulin κ and λ light chains (Dako) showed a polyclonal pattern confirming the plasma cells to be non-neoplastic.

Medication for the gastric lesion, including the eradication of *H pylori* with a 7-day course, was given. The patient soon became symptom free, and has been followed up in an outpatient clinic. Follow-up upper gastrointestinal endoscopy and biopsy will be planned.

Case 2

A 53-year-old woman was referred from a private clinic with an abnormal gastric lesion found during an upper gastroendoscopic examination. She had epigastric bloating and hunger-pain lasting for several months. She had received *H pylor*i eradication treatment on the basis of a prior positive Campylobacter-like organism. Apart from that, her medical history and family history were unremarkable and she denied fever, chills or weight loss. A geographical yellowish raised lesion was noted on the anterior wall of the lower body on endoscopic examination (fig 2A). The surface was nodular without ulceration and the margin was smooth. Endoscopic ultrasonography disclosed a region of thickened gastric mucosal layer (longest diameter 2.5 cm), and there was no evidence of regional lymphadenopathy (fig 2B). A gastroendoscopic biopsy was carried out and the histological findings were similar to the first case except that *H pylori* could not be discerned by routine haematoxylin and eosin staining. The Russell body-containing plasma cells showed a

Abbreviations: Ig, immunoglobulin; MALT, mucosa-associated lymphoid tissue

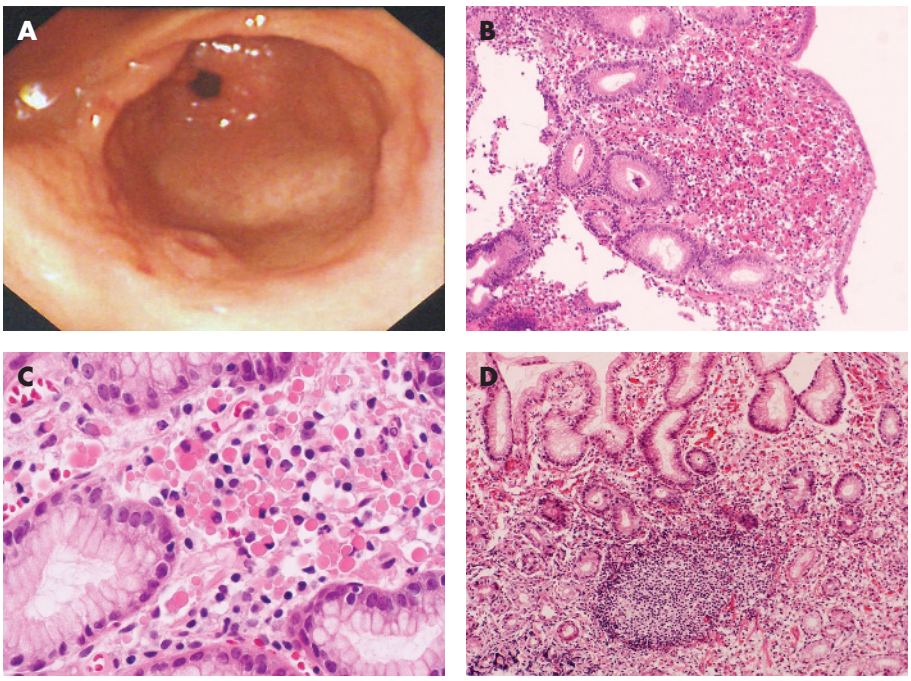

Figure 1 (A) Endoscopic view of patient 1. Focal mucosal swelling was noted in the antrum. (B) Gastric mucosa densely infiltrated by Mott cells—Russell body-containing plasma cells—in patient 1. Magnification ×100; haematoxylin and eosin (H&E). (C) High-power view of variable-sized intracellular and extracellular eosinophilic globules showing Russell bodies. Magnification ×400; H&E. (D) Note the presence of lymphoid follicle, an accompaniment of *Helicobacter pylori* infection, adjacent to the collection of Russell bodies. Magnification ×200; H&E.

polyclonal pattern on immunohistochemical examination against immunoglobulin light chains (upper gastrointestinal endoscopy was repeated 2 months later).

Follow-up biopsy specimens disclosed persistence of Russell bodies and Mott cells with slightly decreased density as compared with the previous biopsy (fig 3A). Furthermore, numerous *H pylori* organisms, which were readily observed on haematoxylin and eosin staining as large colonies overlying the surface epithelium were present in the follow-up biopsy. These colonies were confirmed to be *H pylori* antigen positive on immunohistochemical examination (fig 3B). The foveolar epithelium in the vicinity of *H pylori* showed focal acute inflammatory-cell infiltration. The mucosa biopsied from the upper body disclosed, in addition, a prominent lymphoid follicle. Immunohistochemical staining of the initial biopsy specimen using *H pylori* antibody was carried out in retrograde showing focal apical staining of the cell membrane and staining in the gastric lumen above the epithelium corresponding to the presence of *H pylori* organisms that were not appreciable in the initial haematoxylin and eosin staining.

The patient received *H pylori* eradication treatment for 7 days, and has been followed up in an outpatient clinic. Follow-up biopsy will be planned.

DISCUSSION

Russell bodies occur as a result of a block in the normal pathways of immunoglobulin secretion in plasma cells. The sequestration of abnormal immunoglobulin within vesicles allows the cell to continue to function.[2] Mott cells are plasma cells whose rough endoplasmic reticulum is stuffed with Russell bodies; they occur in diseases, which are accompanied by plasmacytosis and in states of chronic hyperimmunisation, including lymphoid malignancies such as myeloma, B cell lymphomas as well as Hashimoto's thyroiditis, rheumatoid arthritis and ulcerative colitis.[3–5] Empirically, a small number of Russell bodies are occassionally identified in either chronic follicular gastritis or gastric MALT lymphoma. In these conditions, Mott cells and Russell bodies are usually found dispersed in small numbers among a larger component of polymorphous lymphocytic infiltrate.

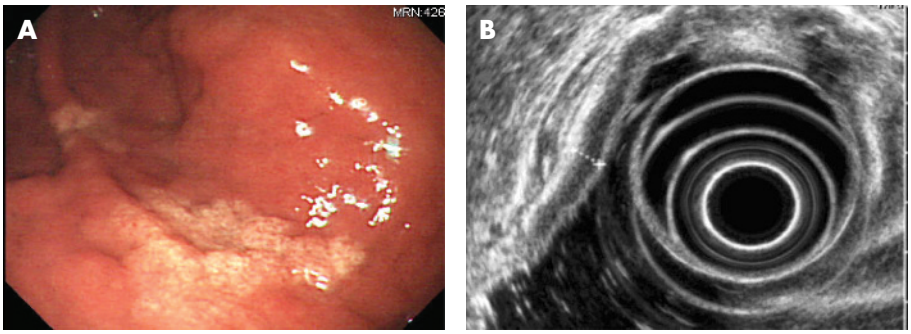

Figure 2 (A) Endoscopic view of patient 2. A yellowish nodular raised lesion was seen on the anterior wall of the lower body. (B) Endoscopic ultrasonographic finding of patient 2. Thickened mucosal layer without submucosal invasion was seen.

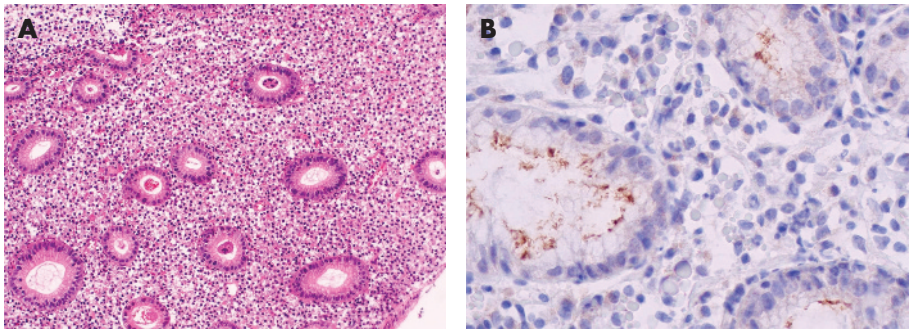

Figure 3 (A) Decreased intensity of Russell bodies and Mott cells in the follow-up biopsy of patient 2. Magnification ×100; haematoxylin and eosin. (B) Numerous readily visible *H pylori* stained by *H pylori* antigen. Magnification ×400; anti-*H pylori*.

H pylori is known to have a causative role in chronic gastritis, particularly in chronic follicular gastritis characterised by hyperplastic lymphoid follicles, and an aetiological role in MALT lymphoma.[6 7] This tiny spirally shaped bacterium could adhere to the surface of the gastric epithelium and generate considerable cellular and humoral responses through antigenic stimulation of mucosal monocytes and T cells. Consequently, T cell-driven activated B cells aggregate to form lymphoid follicles and may differentiate into immunoglobulin (Ig) M, IgA or IgG antibody-producing cells. Eradication of *H pylori* infection results not only in the decrease of these reactive lymphoid follicles and aggregates but also in the regression of early-stage MALT lymphoma.[7] This underscores the role of *H pylori* in the natural history of gastric MALT lymphoma, showing an example of antigen-mediated tissue stimulation and lymphoproliferation, with possible subsequent lymphomagenesis.

In 1997, Tazawa and Tsutsumi[1] reported a peculiar gastric mucosal lesion consisting of a localised accumulation of plasma cells filled with Russell bodies. They named this lesion Russell body gastritis and suggested that the associated *H pylori* infection may have provoked the accumulation of Russell bodies. Alternatively, Erbersdobler *et al*[8] proposed that the association with this infection could have been incidental, as their case failed to show *H pylori* infection even with immunohistochemical methods.

In both our patients, *H pylori* was readily identified at the surface epithelium overlying the Russell bodies. Furthermore, a variable amount of lymphoid follicles were found in the vicinity of the localised Mott cell collections. This implies that Russell body gastritis may have developed in the setting of chronic gastritis associated with *H pylori* infection. It is possible that the chronic infection with *H pylori* may have stimulated the plasma-cell hyperactivation and consequent hyperproduction of immunoglobulins with numerous Russell body formations. The disappearance of Russell bodies on the follow-up biopsy after the eradication of *H pylori* in the report by Tazawa and Tsutsumi lends further support to the causative role of *H pylori* in the development of Russell body gastritis. In our second patient, we had overlooked the possibility of residual *H pylori* infection in the initial examination due to the negative Campylobacter-like organism test and absence of obvious *H pylori* on haematoxylin and eosin staining. However, the emergence of conspicuously large colonies of *H pylori* in the follow-up biopsy and *H pylori* antigen positivity of the initial biopsy specimen discovered in retrograde does not indicate reinfection of *H pylori*, but rather a failure of *H pylori* eradication due to inadequate or inappropriate treatment.

Fujiyoshi *et al*[9] reported a primary gastric plasmacytoma with *H pylori* infection, distinguished by neoplastic plasma cells, most of which contained intracytoplasmic Russell bodies, the so-called Mott cell tumour. They also suggested that the associated *H pylori* may have influenced the immunological environment, which has resulted in the formation of Mott cells. In addition, noting the copresence of centrocyte-like cells and reactive lymphoid follicles, they also pointed out that the Mott cell tumour may actually represent a variant of MALT lymphoma associated with *H pylo*ri infection.

In summary, Russell bodies represent a general response of the cell to the accumulation of abundant, non-degradable immunoglubulin. Thus, Russell bodies can appear in various organs and different diseases, either benign or malignant, all in the context of imbalance of the local immunoglobulin system. Although bacterial infection may be the stimulus for the hyperactivation of plasma cells and the consequent hyperproduction of immunoglobulins in chronic dental pulp inflammation,[10] by analogy, chronic *H pylori* infection could be the antigenic stimulus for the formation and accumulation of Russell bodies in the gastric mucosa.

We have described two cases of Russell body gastritis associated with *H pylori* infection and discussed the pathogenic implications in this report. Although Russell body gastritis is by itself a benign condition, its long-term effect, such as its possible increased risk for the development of neoplasia, is unknown. Clinically, it may be worthwhile to implement *H pylori* eradication treatment in this peculiar disease entity. Histologically, awareness of this disease may prevent confusion with neoplasia. Also, immunohistochemical staining using anti-*H pylori* antibody may aid in the detection of residual microscopically inconspicuous *H pylori* during follow-up biopsy after eradication treatment.

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