

# Granulomatous gastritis: a diagnostic dilemma?

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## ABSTRACT

Granulomatous inflammation of the gastrointestinal tract is an uncommon entity; an aetiopathogenic diagnosis can be reached only by combining the morphological examination with clinical and laboratory investigations. We report two cases of granulomatous gastritis: a 27-year-old woman presenting with weight loss and a 55-year-old woman presenting with epigastric pain and vomiting. Upper oesophagoduodenoscopy in these cases showed antral hyperaemia and histopathology showed non-caseating gastric granulomatous inflammation. Both the cases were extensively worked-up for possible tuberculosis (TB) as the patients lived in an endemic area, before starting steroids for the possibility of Crohn's disease (CD). The first patient improved but the second patient had a flare of underlying undiagnosed TB. Granulomatous gastritis present a diagnostic challenge for treating physicians because of similar clinical, laboratory and endoscopic features between CD and intestinal TB.

**Keywords:** Crohn's disease, enteritis, gastritis, gastrointestinal tract inflammation, granulomatous gastritis, tuberculosis

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## INTRODUCTION

Granulomatous gastritis (GG) is a rare disease characterised by the presence of granulomas within the gastric mucosa or submucosa.<sup>(1)</sup> Common causes of GG are Crohn's disease (CD), disseminated sarcoidosis, infections (tuberculosis [TB], syphilis, fungal), foreign bodies, underlying malignancy or vasculitis.<sup>(2)</sup> Gastric TB should always be considered when dealing with granulomas in endemic areas. Moreover, gastric CD is rare in developing countries but can present as TB. The diagnosis of idiopathic GG is made only after the exclusion of other organic causes.<sup>(3,4)</sup>

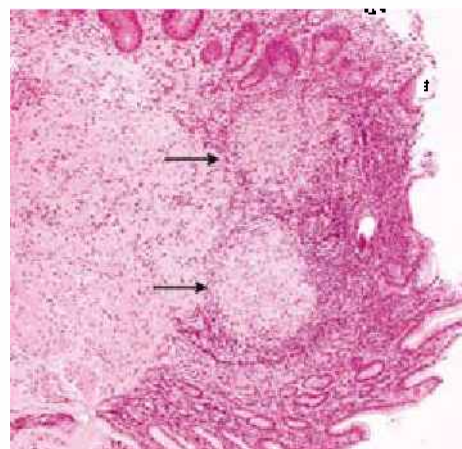
## CASE REPORTS

### Case 1

A 27-year-old woman presented to the gastroenterology clinic with a history of weight loss and diarrhoea of nine months' duration, without any history of fever, abdominal pain, rectal bleeding, rash, or joint pain.



**Fig. 1** Case 1. Endoscopic photograph shows nodular mucosa of the second part of the duodenum.



**Fig. 2** Case 1. Photomicrograph of gastric biopsy specimen shows non-caseating granulomas (arrows) (Haematoxylin & eosin, × 10).

There was no family history of TB and she did not travel outside the country in the past one year. Her past medical history was also insignificant. On examination, she was pale with a thin build. The rest of the general and physical examination was unremarkable. Laboratory investigation showed haemoglobin of 8.7 g/dL (hypochromic microcytic anaemia) with normal white blood cell (WBC) and platelet counts. Routine blood chemistry, including creatinine, electrolytes, calcium and liver function tests, were normal. She had a negative autoimmune, thyroid profile and purified protein derivative (PPD) test, with a normal chest radiograph and abdominal ultrasonography. Values of vitamin B12 193 (normal

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**Fig. 3** Case 2. Endoscopic photograph shows a hyperaemic antrum.

range 193–982) pg/ml, serum folic acid 2.8 (3.0–17) pg/ml, iron levels 19 (40–150) µg, ferritin 6.7 (15–150) ng/ml and albumin 1.7 (3.2–5.0) g/dL were low, suggesting malabsorption involving the proximal small intestine. Stool examination showed 4 WBC and cultures were negative, C-reactive protein (CRP) was 2.8, and erythrocyte sedimentation rate (ESR) was 60 mm at the first hour.

Oesophagoduodenoscopy (OGD) showed hyperaemia in the entire stomach with nodular appearance in the second part of the duodenum (Fig. 1). During OGD, biopsies were taken from the antrum and duodenum, which demonstrated multiple non-caseating granulomas (Fig. 2) on histopathology examination, using haematoxylin and eosin (H&E) staining. Furthermore, Ziehl-Neelsen stain and tissue culture for acid-fast bacillus (AFB) and fungus were non-yielding. Colonoscopy was also done to rule out similar lesions in the colon, which showed normal mucosa up to the terminal ileum. Subsequently, small bowel enema was done for evaluation of small intestine which was also normal. After ruling out the possibility of TB, the patient was started on prednisone 20 mg twice a day for the most likely possibility of CD. She underwent a close follow-up at the clinic. Subsequently, her symptoms improved and she started to gain weight with improved appetite. There was normalisation of CRP and ESR in next couple of weeks and a relook OGD showed resolution of hyperaemia and granulomas on repeat histopathology. Currently, the patient is on a tapering dose of steroids without any relapse.



**Fig. 4** Case 2. Chest radiographs show a cavitary lesion (arrow) in the right lung.

#### Case 2

A 55-year-old woman presented with epigastric pain, vomiting and weight loss for three months. There was no history of fever, diarrhoea or shortness of breath. She was known to have asthma which was well-controlled on salbutamol inhalers. General physical as well as systemic examination was unremarkable except for mild epigastric tenderness. Laboratory investigations including complete blood count, serum creatinine, electrolytes, calcium, liver function tests, stool examination, amylase, angiotensin converting enzyme levels, and PPD for tuberculosis were normal. Chest radiograph and abdominal ultrasonography were also unremarkable. Her serum albumin was 2.2 g/dL and CRP was 1.8. OGD showed antral hyperaemia with roughened prepyloric mucosa (Fig. 3) and biopsy showed non-caseating granulomas with active *Helicobacter pylori* (*H. pylori*) gastritis. The gastric tissue did not show AFB on staining, and cultures for mycobacteria and fungus were also negative. Colonoscopy and small bowel series were performed, both of which were normal. She was given a triple regimen treatment for eradication of *H. pylori*, which consisted of amoxicillin 1 g twice a day along with clarithromycin 500 mg twice a day for one week with capsule omeprazole for two weeks.

Her abdominal pain continued, and a repeat OGD with biopsy after three months again revealed non-caseating GG, but this time without *H. pylori* infection on Giemsa and H&E stains. As there was no evidence to suggest TB, she was also started on steroids 20 mg twice daily for the possible diagnosis of CD and advised

for regular follow-up. After three weeks, she presented with a dry cough and shortness of breath, and this time, her chest radiograph showed a cavitation in the mid-zone of her right lung (Fig. 4) suggestive of pulmonary TB. Her steroids were stopped immediately and she was put on a weight-based four-drug anti-TB regimen (isoniazid, rifampicin, ethambutol, pyrazinamide). She completed a six-month course of anti-TB medication, with marked improvement in abdominal pain, shortness of breath and chest radiograph findings.

## DISCUSSION

There are problems in distinguishing TB of the intestine from CD in Asians, and these have been described in the literature many years ago.<sup>(5)</sup> It is important to rule out TB as there is a close resemblance between the clinical features of CD and intestinal TB.<sup>(6)</sup> Both our patients were extensively investigated for TB, fungal infections, malignancy and sarcoidosis, before being considered for treatment of CD. In the first case, as the presenting complaints were diarrhoea and malabsorption with raised CRP and ESR and involvement of the small bowel on biopsy, a preliminary diagnosis of CD was made. Gastric TB was one of the differential diagnosis as the patient belonged to endemic area, but all supporting tests including negative PPD, normal chest radiograph, and absence of mycobacteria on culture of biopsy excluded this diagnosis. Symptomatic gastric sarcoidosis is rare and the diagnosis should be considered with evidence of systemic granulomatous disease.<sup>(7)</sup>

Symptomatic gastroduodenal involvement may occur in approximately 4% of patients in CD of the more distal small bowel and colon,<sup>(8,9)</sup> and endoscopic abnormalities are not always present. *H. pylori* has been associated with GG in some case reports<sup>(10,11)</sup> that resolves after treatment, but in the first case, there was no evidence of *H. pylori* on biopsy specimen. This patient improved with steroids and repeat biopsy showed resolution of granulomas. Gastroduodenal CD is rarely seen (0.5%–13%), and has distinct clinical, therapeutic and prognostic features.<sup>(12)</sup> Not much is known of the incidence and prevalence of this disease in Pakistan.<sup>(13)</sup> However, it has been observed that the incidence of CD is now increasing in geographical areas where the incidence was previously low.<sup>(14)</sup> Abbas et al described the clinical features of CD in the Pakistani population, and predominant features were abdominal pain and diarrhoea, whereas 10% had fistulising disease, 6% had isolated small bowel disease and extra-intestinal manifestations were less common, as compared to the West.<sup>(15)</sup>

In the second case, after treatment for *H. pylori* and without clear evidence of TB, the patient was also given steroids, but within three weeks, she presented with respiratory symptoms and chest radiograph showed cavitation. Gastric TB without evidence of TB

focus elsewhere is considered to be rare<sup>(15)</sup> and usually considered to be secondary to pulmonary TB,<sup>(16)</sup> as in our case. The endemicity of TB in Pakistan is high. Reported figures by the World Health Organisation showed an incidence of 181 cases/100,000 population/year and prevalence of 297 cases/100,000 population/year.<sup>(17)</sup>

GG is a very rare clinical entity, which is difficult to diagnose and it can be a serious challenge for the treating physician. It is one of the rare diseases which can have unusual presentations. Prognosis depends upon the causes which are myriad. The literature on this topic is limited, without long-term follow-up studies. Treatment should be carefully individualised with close follow-up. The possibility of gastric TB should always be kept in mind, especially when dealing with patients in endemic areas.

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