

Case Report

A Rare Form of Granulomatous Gastritis Presenting at an Unusual Age

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ABSTRACT

Isolated granulomatous gastritis is a rare disease of the middle-aged and it is a diagnosis of exclusion. It has not been reported earlier from Arab population. We are reporting a

case of isolated granulomatous gastritis in an adolescent Arab boy who was treated successfully with steroids and is doing well after one year of follow-up.

KEYWORDS: Arab, granulomatous gastritis, steroids

INTRODUCTION

Granulomatous gastritis is an uncommon diagnosis and it accounts for about 0.2-0.3% of all gastritis in various series^[1]. Isolated granulomatous gastritis refers to an idiopathic chronic granulomatous reaction limited to the stomach. This is a rare and poorly understood disorder. It was first established as a distinct clinicopathologic entity in 1963 by Fahimi *et al* who reported three cases^[2]. Fahimi *et al* suggested that isolated granulomatous gastritis could be considered a distinct clinicopathologic condition based on their own cases and the review of literature. The diagnosis is based on the exclusion of a number of conditions such as Crohn's disease, sarcoidosis, tuberculosis, neoplasm and foreign body^[1-7]. However the concept of isolated granulomatous gastritis is not universally accepted and it has been suggested that it only be used as an interim diagnosis, since an underlying cause for the granulomatous gastritis may eventually become evident on prolonged clinical follow-up. In this paper we report this rare clinical entity in a Kuwaiti teenager. This is an unusual age of presentation^[2,4,8]. In 1989 Barry *et al* reported the first case of isolated granulomatous gastritis in a 14-year old patient and no further cases in this age group have been reported since.

CASE REPORT

A 19-year-old Kuwaiti young man was admitted to the gastroenterology department of Mubarak Al-Kabeer hospital (Ministry of Health, Kuwait) on the 26th of September 2000 with a history of recurrent upper abdominal pain of 10 -14 days' duration that was related to meal and associated with nausea and

vomiting. There was weight loss of 6-7 kg over a period of two weeks associated with anorexia. Though he had no alteration of bowel habits, there was a history of vomiting of small amounts of altered blood twice, and melaena was noticed once. He gave no history of fever but had low grade fever while in the ward. There was no history of similar pain in the past.

Physical examination revealed a normal built, sick-looking and mildly dehydrated young man. The abdominal examination did not reveal any positive findings other than moderate tenderness in the epigastrium. All other systemic examinations including the respiratory, cardiovascular, neurological and musculoskeletal, were within normal limits.

Routine laboratory tests showed haemoglobin of 13.1 g/dL, white cell count of $13.5 \times 10^9/L$. Neutrophils 72%, lymphocytes 15%, monocytes 10%, eosinophils 3% and erythrocyte sedimentation rate of 75 mm/hour. The blood biochemistry profile was as follows: serum sodium 135 mmol/l, serum potassium 3.7 mmol/l, blood glucose 4.7 mmol/l, blood urea nitrogen 2.9 mmol/L, serum creatinine 73 micromol/L, serum calcium 2.21 mmol/L, total bilirubin 14 mol/L, serum alanine aminotransferase 33 IU/L, serum aspartate aminotransferase 26 IU/L, serum alkaline phosphatase 73 IU/L, total protein 55 g/L, serum albumin 28 g/L and serum amylase 28 IU/L. His chest X-ray and electrocardiogram were normal. Gastroscopy done on the 30th September showed acute gastric ulceration in the prepyloric area with severe erythematous and exudative gastritis and highly friable mucosa involving upper and lower stomach (Fig. 1). There was moderate diffuse erythematous erosive nodular bulbar and post bulbar duodenitis. Biopsies were taken from

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Fig. 1: Endoscopic picture showing the erythematous, ulcerated mucosa involving the antrum of the stomach diffusely



Fig. 3: Endoscopic picture of the antrum of stomach showing marked improvement after one year of treatment

pre-pyloric, lesser curve antrum and lesser curve mid-body and sent for histopathology, acid fast bacilli and fungal staining as well as mycobacterial culture.

Histopathology: Multiple fragments of gastric antral mucosa showed severe active chronic antral gastritis with extensive cryptitis. There was mild glandular atrophy with severe intestinal metaplasia but no dysplasia. There were multiple poorly formed and ill-defined epithelioid granulomata with Langhans type giant-cell reaction (Fig. 2). Special stains for acid bacilli, fungi and bacteria were negative. There was no *H. pylori* seen. Mycobacterial cultures were also negative.

The abdominal ultrasound was normal. The Computed tomogram of the abdomen and pelvis showed thickening of the wall of the stomach. There was no lymphadenopathy and the small bowel and mesentery appeared normal. The computed tomogram of the chest was also normal. Colonoscopy was normal up to the terminal ileum.

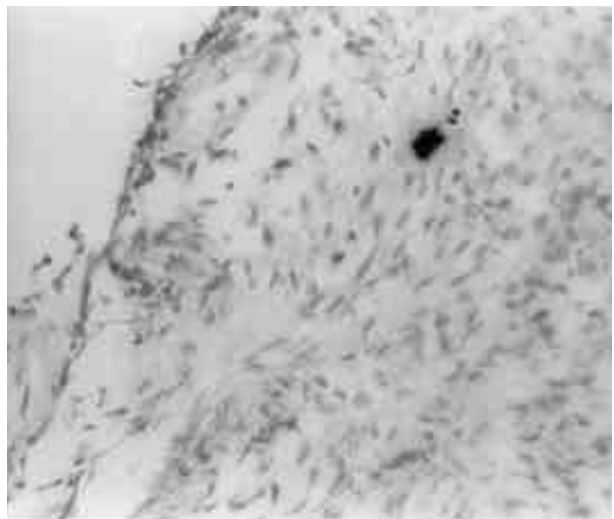


Fig. 2: An epithelioid granuloma; note the cigar shaped nuclei of the activated histiocytes with feathery appearance of the cytoplasm. (H&E, X 400)

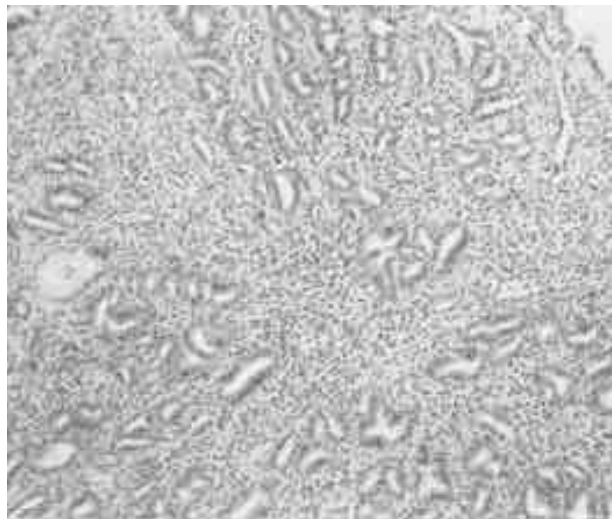


Fig. 4: Normal crypt architecture of gastric antral mucosa. There is mild chronic non-specific inflammation. (H&E, X10)

Multiple biopsies of the ileum and colon were normal. The barium meal study suggested Crohn's disease because of the cobble stone appearance of the gastric mucosa. The tuberculin test was non-reactive. The Venereal Disease Research Laboratory slide test was negative and angiotensin-converting enzyme level was normal.

With the clinical picture and endoscopic biopsy report of granulomatous gastritis, a presumptive diagnosis of gastric Crohn's disease was made and he was started on proton pump inhibitors. He continued to be symptomatic with persistent abdominal pain, vomiting and gastrointestinal bleeding in the form of haematemesis and melena resulting in a 4 gm drop in hemoglobin which required multiple transfusions. As he was not responding to the treatment of Crohn's gastritis and he had no positive tests that pointed to any other specific cause of granulomatous gastritis, he was started on prednisolone at a dose of 40 mg daily. This was slowly tapered over a period of two to three

months to a maintenance dose of 5 mg and he is still on this dose. He started improving within two to three weeks and he became asymptomatic after two months. One year later, the patient was asymptomatic and follow-up endoscopy showed marked improvement (Fig. 3) and biopsy showed disappearance of granuloma and significant reduction in the inflammation (Fig. 4).

DISCUSSION

Isolated granulomatous gastritis is diagnosed by the presence of granulomatous inflammation limited to the stomach and by exclusion of a number of known causes as listed in table 1^[10]. To make a diagnosis, a detailed evaluation of the patient with endoscopy, imaging studies and various blood investigations along with a lengthy follow-up is necessary. In Fahimi *et al's* report, the most common symptoms were vomiting, upper abdominal pain and weight loss^[2]. In his series, 71% had symptoms for more than one year. The less common symptoms were anorexia, gastrointestinal bleed and diarrhea. The most common age of presentation was above 40 years in all series. Though there are no specific laboratory investigations to diagnose the disease, it is useful to rule out other causes of granulomatous gastritis. Gastroscopy with biopsy is the most important diagnostic tool. Gastroscopic examination shows focal gastritis usually involving the antrum with characteristic histological findings including diffuse non-caseating granulomas in the gastric mucosa and submucosa. The muscular and serosal layers in surgical specimens have been reported to have granulomas at times^[5].

The patient in this case report, had most of the features of isolated granulomatous gastritis described earlier. However he had certain atypical features. The endoscopy revealed diffuse gastritis involving the entire gastric mucosa unlike most of the reported cases. The age of presentation was an important rare feature as most of the cases reported are in the fourth and fifth decade. Only one case below 20 years of age has been reported so far in the literature^[8]. In our case there was diffuse gastric mucosal involvement with gastrointestinal bleed and the duration of symptoms were less than 2 weeks. This was unlike other cases reported where the duration of symptoms were usually more than one month and the gastric involvement was mostly confined to the antrum.

Before embarking on the diagnosis of idiopathic granulomatous gastritis we considered various other causes of granulomatous gastritis. Crohn's disease was the first differential diagnosis we considered because of the abdominal symptoms, age of presentation, raised erythrocyte sedi-

Table 1

Types of gastritis associated with granulomatous inflammation

Tuberculosis
Tertiary (gummatous) syphilis
<i>Helicobacter pylori</i>
Whipple's disease
Histoplasmosis
South American blastomycosis
Anisakiasis
Systemic disease- Associated (Non infectious)
Crohn's disease
Sarcoidosis
Wegner's granulomatosis
Other vasculitides
Confined to stomach (Non infectious)
Isolated granulomatous gastritis
Miscellaneous sporadic cases
Identifiable foreign substance (eg. barium, food, suture)
Tumor associated

mentation rate, and the presence of granulomas on biopsy. However endoscopic and histological abnormalities, which showed diffuse involvement of stomach, differed from the classical pathological findings of Crohn's disease where the lesions are focal or noncontinuous. Moreover gastric Crohn's is rare and to have isolated gastric Crohn's is still more rare^[10-12]. Symptomatic gastroduodenal Crohn's disease occur in 2-4% of patients with gastric involvement. All the investigations including colonoscopy, small intestinal biopsies and other imaging modalities failed to reveal any evidence of the disease outside the stomach. There were also no extra-intestinal manifestations to suggest Crohn's disease. Proton pump inhibitor therapy is reported to be an effective treatment in gastroduodenal Crohn's disease. Our patient did not respond to this therapy, clinically or endoscopically. With all the above points in mind, Crohn's disease was considered an unlikely diagnosis. The possibility of sarcoidosis, which is another important cause of granulomatous disease of the gut, was considered. Symptomatic gastric sarcoidosis is rare and the diagnosis can be made only when there is evidence of systemic granulomatous disease. It usually occurs in the setting of established sarcoidosis and possibly may present as a remnant of prior disseminated sarcoidosis. Here the possibility was ruled out by, a normal chest X-ray, a normal serum calcium and serum angiotensin-converting enzyme levels, an absence of systemic lymphadenopathy and an absence of evidence of organ involvement outside the gastrointestinal tract, or progression under observation^[13-16].

Tuberculosis does not spare any organ. So tuberculosis was also considered as a differential diagnosis though gastric tuberculosis is very rare. The normal chest X-ray, negative tuberculin test

and non-caseating granulomas on microscopy along with negative staining and culture for mycobacterial of the biopsy specimen helped to rule out the diagnosis^[5]. Moreover, the patient improved on corticosteroids. Other infective causes like syphilis were ruled out with negative Venereal Disease Research Laboratory slide test and other clinical features. The absence of identifiable organisms on histology and culture along with a negative serology for various fungi and viruses helped us to rule out other infective causes, which were still more unlikely especially with the remarkable improvement on steroid treatment. Though granulomas have been found in specimens of gastric carcinoma and lymphoma, no direct relation between granulomatous gastritis and cancer has been established. Tumours like carcinoma and lymphoma were a possibility endoscopically, but the young age with no evidence of malignancy on the repeated biopsies argued against this possibility, which was strengthened by the fact that the patient was doing well on steroid treatment one year later^[17].

Since the disease was involving the stomach diffusely and there was no evidence of any foreign body on biopsy the diagnosis of foreign body granuloma was not entertained at any stage.

Recently *H. pylori* infection is also included in the differential diagnosis of granulomatous gastritis since rarely an inflammatory response to *H. pylori* infection can be granulomatous. The possible association of granulomatous gastritis with *H. pylori* has been examined by Dhillon and Sawyerr who reported cases of granulomatous gastritis associated with *campylobacter* like organisms and without other systemic granulomatous diseases^[18]. Joel *et al* found a statistically significant association of *H. pylori* infection with granulomatous gastritis without proven causes^[19]. However the association of *H. pylori* infection with granulomas of stomach has not been conclusively proved. In our patient since there was no evidence of *H. pylori* on multiple biopsies it was not considered a possibility.

Langerhan's histiocytosis is an illness in which multiple systems mainly lungs and bones are predominantly involved though gastric involvement has been reported rarely. Besides in Langerhan's histiocytosis the histopathology shows Langerhan's type cells without granuloma formation whereas definite granulomas are seen in isolated granulomatous gastritis. Langerhan's histiocytosis was very unlikely though it was considered in the differential diagnosis.

Menetrier's disease can clinically resemble isolated granulomatous gastritis. But it is a disease seen in the older age group and has markedly hypertrophied gastric folds with nodularity usually sparing the antrum. In Menetier's disease the main

abnormality on histopathologic examination is elongated and tortuous foveolae with cystic dilation. Unlike granulomatous gastritis, granulomas are not a feature of this condition.

There are no unique laboratory features to make a diagnosis of isolated granulomatous gastritis. The abnormalities observed in our patient were raised erythrocyte sedimentation rate and a low serum albumin. The raised erythrocyte sedimentation rate suggests a systemic inflammatory disease and it is normal in adolescent patients with peptic ulcer disease. However this is a non-specific finding indicating a significant inflammation. This may be useful in following up the patient since it returned to normal with treatment and it is a non-invasive measure of disease control. Probably as mentioned by Hirsch *et al*, a normal value in a patient with active gastritis may help to rule out granulomatous gastritis. The hypoproteinemia or hypoalbuminemia, which is another important finding in this case, may be a good indicator of the severity of the disease. This finding seems to be due to the loss of protein from the diffusely ulcerated gastric mucosa. This abnormality has not been observed in the series by Fahimi *et al* or in other case reports. There was significant hypoproteinemia at presentation in spite of a short symptomatic period of less than two weeks. This indicates a severe disease and also raises the possibility of isolated granulomatous gastritis having an asymptomatic period with gastric lesions.

Therapy of isolated granulomatous gastritis has been quite variable and no treatment has undergone a controlled trial. The natural history of the disease is unknown, so it is not clear whether any therapy is required at all for the milder forms of the disease. Various modalities of treatment like antacids and cimetidine have been tried with ambiguous results^[3,8]. There are also case reports of spontaneous resolution. Since our patient had no response to proton pump inhibitor therapy and a few case reports suggested success with steroids, we started him on steroids to which he responded^[20]. Previous reports of improvement with partial gastrectomy have been published, but we felt that in our patient surgery was not justifiable because of the young age, a good response to medical treatment and the extensive nature of the disease, which would have required a radical surgery like total gastrectomy. The medical treatment with steroids is based on the hypothesis that the disease is immune mediated though there was nothing positive on investigation to indicate this in our case. Almost one year after presentation, the patient was well while on steroids. There is no data on the optimal duration of treatment but recurrence upon discontinuation of treatment is well known^[15].

CONCLUSION

This 19-year old Arab male had an isolated granulomatous gastritis with certain unusual features. This is the second case reported in the literature at an age below 20 years and the first in an Arab. The acute presentation of symptoms and signs and involvement of the entire gastric mucosa with fierce looking endoscopic appearance were again features not reported in other cases. The significant hypoalbuminemia on presentation was not found in the previous reports. The patient's response to steroids, like in some previous cases reported, suggests that medical treatment with steroids should be tried in these patients before considering more aggressive treatment modalities like surgery.

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