

## Gastric Ulcer: An Old Disease - A New Cause

Silke Urban<sup>1\*</sup>, Michael Manz<sup>1</sup>, Andreas Zettl<sup>2</sup>, Thomas Peters<sup>3</sup>, Katrin Baumann<sup>4</sup> and Markus von Flüe<sup>1</sup>

<sup>1</sup>Gastrointestinal Unit, St. Claraspital Basel, Switzerland

<sup>2</sup>Department of Pathology Viollier AG, Switzerland

<sup>3</sup>Department of Endocrinology St. Claraspital Basel, Switzerland

<sup>4</sup>GP surgery Dr. K. Baumann Muttenz, Switzerland

\*Corresponding author: Silke Urban, GI Unit, St. Claraspital Basel, Switzerland, Tel: 0041 61 685 8585; Fax: 0041 61 685 8182; E-mail: Silke.Urban@claraspital.ch

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### Abstract

A 73 year patient presented with melena to our endoscopy unit. He was hemodynamically stable and the haemoglobin was decreased with 113 g/l. The remaining blood tests were normal. Upper endoscopy showed a large bleeding ulcer along the lesser curvature, macroscopically suspicious for malignancy. To control the bleeding and to rule out gastric cancer, the patient was referred to surgery. Two thirds of the stomach, a segment of the transverse colon with mesocolon had to be resected en bloc. Final histology revealed a chronic ventricular ulcer with a distinct lymphofollicular, lymphoplasmacellular and eosinophilic inflammation. The number of IgG4 plasma cells was increased (60 IgG4 positive cells per microscopic visual field, 70-80% IgG4 out of all IgGs). Storiform fibrosis and obliterating phlebitis were found not only within the ulcer base but also extensively in the adjacent soft tissue. Summarizing, our patient suffered from a rare form of a chronic gastric ulceration as a manifestation of IgG4-related disease.

IgG4-related disease is an increasingly recognized condition presenting with specific pathological, serologic and clinical features. Its hallmark is the typical histopathological finding as in our case. Type 1 autoimmune pancreatitis and salivary gland disease are the two typical presentations, but IgG4-disease can affect each organ.

Because of no further organ involvement, consecutive immunosuppressant treatment was not required. Seven months later gastroscopy showed no signs of recurrence.

A gastric ulcer can be the first presentation of IgG4 related disease which needs to be considered as a differential diagnosis in refractory gastritis and cancer suspicious lesions.

**Keywords:** Gastric ulcer; Gastric cancer; IgG4 related Gastritis; IgG4 related disease

### Description

A 73-year-old man presented to our endoscopy unit with melena. He complained of upper abdominal pain, which had started two months earlier, permanent fatigue, low appetite and some weight loss. Beyond this, his general health condition was fine.

The GI bleeding was not life threatening, the haemoglobin was slightly decreased at 113 g/l. The remaining blood count, CRP, pancreatic enzymes, renal and liver function were normal. The upper panendoscopy revealed a huge bleeding ulcer along the lesser curvature (Figure 1). The biopsies showed pronounced chronic inflammation with plenty of eosinophils and scanty *Helicobacter pylori* without signs of malignancy.

CT scan showed the huge ulcer, enlarged perigastric lymphadenopathy and no distant metastases. To control chronic blood loss and to rule out definitely gastric cancer, we decided for surgical therapy.

Intraoperatively, a huge ulcer along the lesser curvature and dorsal gastric body infiltrating the transverse mesocolon was found. Perigastric lymph nodes were markedly enlarged. Two thirds of the stomach, a segment of the transverse colon including the mesocolon had to be resected en bloc.

Definite histology revealed a chronic gastric ulcer with a distinct lymphofollicular lymphoplasmacellular, eosinophilic infiltrate (Figure 2a), storiform fibrosis and obliterating phlebitis (Figure 2b/c) being indicative for IgG4 related disease. The latter could be confirmed by immunohistology with 60 IgG4 positive cells/ high power field (increased >30 cells/HPF) 3 and 70-80% IgG4/ IgG (increased >50%) (Figure 2c/d). In summary our patient suffered from a chronic gastric ulcer, a rare manifestation of IgG4-related disease.

IgG4-related disease is an increasingly recognized condition presenting with specific pathological, serologic, and clinical features. Its hallmark is the histopathological finding of a lymphoplasmacytic tissue infiltrate with a predominance of IgG4-positive plasma cells accompanied by storiform fibrosis and obliterative phlebitis. Serum levels of IgG4 are often elevated. However, less than 40% of patients have normal serum IgG4 concentrations despite the presence of the classic histopathological changes in tissue [1]. Our case belonged to the latter minority with a normal IgG4-plasma level of 0.53 g/l (normal range 0.05–1.96 g/l).

IgG4-related disease affects mainly men (62 to 83%) aged over 50 and can involve multiple organs (in 60 to 90%) [2]. It usually presents subacutely or is found incidentally by radiology or histopathology. Most patients are not constitutionally ill; fever and raised CRP levels are uncommon. The disease was not recognized as a systemic condition until 2003, when extrapancreatic manifestations were identified in patients with autoimmune pancreatitis [3]. Even if type 1 autoimmune pancreatitis and salivary gland disease are the major

presentations of this condition, it can affect any organ. Lymphoplasmacytic gastritis associated with autoimmune pancreatitis and chronic gastric ulceration has been described so far only by a few case reports [4,5].

The term, IgG4-related disease, now includes a number of medical conditions, until 2003 not known to be interrelated (Table 1) [3]. Mikulicz's syndrome, Küttner's tumor and Riedel's thyroiditis may be reclassified in the future.

List of previously described conditions being reclassified as "IgG4 related disease" 3
Type 1 autoimmune pancreatitis
IgG4-related sclerosing cholangitis
Mikulicz's disease (sialadenitis)
Sclerosing sialadenitis (Suttner's tumor)
Inflammatory orbital pseudotumor
Chronic sclerosing dacryoadenitis (lacrimal glands)
"Idiopathic" retroperitoneal fibrosis (Ormond's disease)
Chronic sclerosing aortitis and periaortitis
Riedel's thyroiditis
IgG4-related interstitial pneumonitis and pulmonary inflammatory pseudotumors
IgG4-related kidney disease
IgG4-related hypophysitis
IgG4-related pachymeningitis

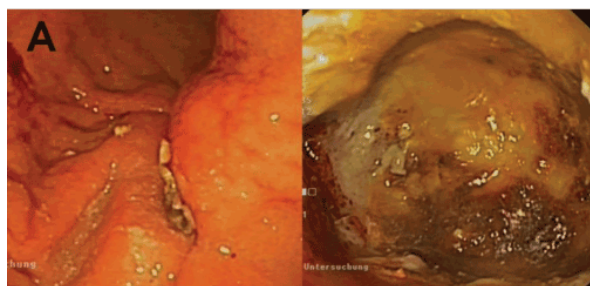
**Table 1:** List of IgG4 related disease.

Medical treatment includes glucocorticoids, azathioprine and mycophenolate [3].

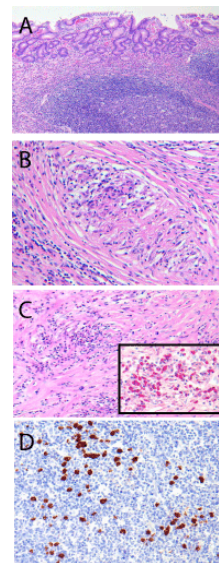
In our case diagnosis was made by histopathology - the hallmark of IgG4-related disease (Figure 2). Clinical examination, laboratory tests und CT scan did not reveal further organ involvement, making immunosuppressant treatment unnecessary.

Seven months later gastroscopy showed no signs of recurrence; blood tests were within normal range.

Concluding gastric ulcer can be the first presentation of IgG4-related disease, which has to be considered as a differential diagnosis in refractory gastritis and cancer-suspicious lesions.



**Figure 1:** extensive ulcer along the lesser curvature 5 cm in diameter und approximately 2 cm in depth



**Figure 2:** Histopathology: a) chronic ventricular ulcer with a distinct lymphofollicular partially lymphoplasmacellular infiltration (HE staining, 40x) b) storiform fibrosis and obliterating phlebitis (HE staining, 400x) c) eosinophilic inflammation, along with (HE staining and immunohistology, 40x/400x) d) an increased amount of IgG4 positive plasma cells (400x)

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