The General Practice Guide to Autoimmune Diseases

Edited by Y. Shoenfeld and P. L. Meroni

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Autoimmune gastritis

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1 Introduction

Pernicious anemia was first described by Thomas Addison in 1849 and was related to gastric disease by Austin Flint in 1860. Autoimmune gastritis, as a name, appeared later, when the identification of antibodies to anti-parietal cells and to intrinsic factor made the immunological pathogenesis clear.

Autoimmune gastritis which progresses with the loss of zymogenic and parietal cells of the gastric mucosa, mainly affects the gastric fundus and body, sparing the antrum. It is often manifested by the presence of pernicious anaemia, associated with cobalamin deficiency. While frequently remaining silent for 20 to 30 years, it can be detected early and before the development of anaemia, by the presence of anti-parietal cell and/or anti-intrinsic factor antibodies.

In spite of significant controversy several published studies favour a relationship with *Helicobacter pylori* infection, since antibiotic treatments induce an improvement in anaemia and cobalamin levels in nearly half the patients.

2 Clinical manifestations

Autoimmune gastritis can remain asymptomatic for many years or present solely by some sort of dyspeptic symptoms. The average age at diagnosis is 60 yo, and a higher prevalence in females is expected. Since pernicious anaemia is the main manifestation of this disease, signs and symptoms overlap significantly in both diseases (Table 1).

Neurological complications that also arise as a result of cobalamin deficiency are more common in advanced stages of the disease and range from peripheral neuropathy to spinal cord and cerebellum injuries, which progress to demyelination and axonal degeneration, and neuronal death.

Intestinal metaplasia in gastric mucosa is a risk factor for developing adenocarcinoma and in these patients it can reach an incidence of approximately 3 times that in the general population.

Table 1. Signs and symptoms of pernicious anemia at presentation (adapted from ref. 1).

Clinical haematologic manifestations
Anaemia with pallor and fatigue.
Constitutional symptoms
Loss of appetite Atrophic glossitis (sore, smooth, and red tongue)
Clinical gastrointestinal manifestations
Diarrhoea (cobalaminmalabsortion and intestinal changes)
Clinical neurologic manifestations
Peripheral numbness Muscle wasting Diminishing tendon reflexes Loss of perception to light touch and vibration Spastic ataxia

Haematologic manifestations: the inadequate production of intrinsic factor leads to malabsorption and hence to a cobalamin megaloblastic anaemia (Table 2).

Biochemical manifestations: typically gastric hypochlorhydria appears as a consequence of parietal cell loss and diminished concentration of pepsinogen. Hypergastrinaemia, due to over-stimulation of gastrin-producing cells because of the low amount of acid produced, is also frequently detected.

Gastric biopsy: histologically the gastric mucosa is characterized by a submucosal mononuclear cell infiltrate, together with parietal and zymogenic cell degeneration.

Table 2. Haematologic manifestations.

Megaloblastic anaemia
Macrocytosis
Neutrophil hypersegmentation
Leukopenia
Thrombocytopenia and púrpura
Megaloblastic bone marrow transformation

3 Diagnostic criteria

No definitive diagnostic criteria are internationally accepted for autoimmune gastritis. However, asymptomatic non-anaemic patients, parietal-cell and/or anti-intrinsic factor antibodies can be considered a sign of impending disease. In symptomatic patients the criteria of pernicious anaemia (macrocytic anaemia (MCV > 100 fL), cobalamin deficiency, confirmed cobalamin malabsorption with a positive Schilling test) should be complemented by the detection of anti-parietal cell or anti-intrinsic factor antibodies and the detection of hypergastrinaemia and/or low serum pepsinogen I.

Biopsies typically reveal a pattern of atrophic gastritis together with various stages of a lymphocytic-mononuclear infiltrate. However biopsies can be difficult to evaluate and are of limited use in the diagnosis of autoimmune component involvement.

4 Diagnostic tests

Autoimmune gastritis is characterized by the presence of circulating autoantibodies against parietal cells and/or intrinsic factor. Anti-parietal cells are present in virtually 100 % of patients with autoimmune gastritis and anti-intrinsic factor in 60 to 70 % of those.

Cobalamin assays are widely available and at least one determination should be performed. The Schilling test (even if outdated) confirms cobalamin deficiency by intestinal malabsorption as caused by lack of intrinsic factor. There is also an increased cobalamin urinary fraction excretion, when the vitamin is orally administered with intrinsic factor.

Gastrin and pepsinogen determinations can be used to check for hypergastrinaemia and low serum pepsinogen I.

The clinical significance of all these results is uncertain in the absence of anaemia or macrocytosis. In those circumstances, a re-evaluation can be suggested, at 6 month to 1 year interval, with a full blood count, serum gastrin and serum cobalamin.

5 Diagnostic measurements for experts

Autoimmune gastritis can be found associated with other endocrine pathologies, such as type 1 diabetes and Hashimoto's disease. Seldom, Addison's disease, primary ovarian failure and hyperparathyroidism can also be found.

20–30 % of relatives can have detectable antibodies to parietal cells or intrinsic factor and a concordance has been found between monozygotic twins. Several HLA susceptibility markers have been suggested but no clinical usefulness has been established so far for those determinations.

6 Requirements for family practitioners

Autoimmune gastritis should be considered in older patients whenever macrocytosis is detected, with or without anaemia. Approximately 2 % of the population over 60 is considered to have undiagnosed pernicious anaemia.

Dyspeptic history should be carefully evaluated but can be expected to be either trivial or very variable and so should be considered of limited usefulness. The association with gastric cancer and concomitant autoimmune diseases should be remembered.

Autoimmune markers can easily be performed, but should only be of clinical implication in the presence of haematologic abnormalities.

7 Management/treatment

Steroids and other immunomodulatory drugs have been used with some success in decreasing parietal cell and intrinsic factor antibodies, thus increasing the available intrinsic factor and cobalamin absorption and reversing gastric mucosal atrophy with parietal and zymogenic cell regeneration. However, no clear protocols are established and the preferred treatment is cobalamin replacement. Monthly intramuscular 1000 μg of cobalamin is the standard maintenance treatment, whereas oral surcharge can also be considered but has a more unpredictable outcome. 1000 to 2000 μg daily dose can be considered in this situation (Table 3).

Table 3. Replacement therapy for pernicious anaemia.

Reposition of body stores
- 6 intramuscular 1000 μg injections of cobalamin at 3 to 7 days interval (or) - Daily oral doses (1000 to 2000 μg) cobalamin
Maintenance treatment
- 1000 μg intramuscular cobalamin every 3 months (or) - 1000 μg intramuscular cobalamin monthly (poorer retemption) (or) - 1000 to 2000 μg oral doses

8 Follow up

Anaemia correction and cobalamin serum levels normalization are the best evidence of treatment efficacy. In those cases where oral treatment has been chosen, a re-evaluation should be considered 1 to 2 months afterthe first approach, with a full blood count and fasting serum cobalamin testing. With parenteral treatment, laboratory testing should be considered after a 6 to 12 months interval.

No significant value has been established for the reappraisal of autoimmune markers in clinically diagnosed patients.

In those patients where autoimmune markers have been found in the absence of anaemia or macrocytosis, a re-evaluation should be suggested, at a 6–12 month interval, of a full blood count, serum gastrin and serum cobalamin levels.

Since autoimmune gastritis has been associated with an increased risk of gastric carcinoma and carcinoid tumour, a periodic endoscopic evaluation should be considered.

9 Prognosis

Prognosis has not been established for non-anaemic patients with autoimmune markers. In symptomatic patients, replacement therapy when started before the onset of neurologic complications carries a good prognosis, when patient compliance is achieved.

Gastric neoplastic complications should not be forgotten but are beyond the scope of this review.

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