**THE THYRO-GASTRIC SYNDROME:**

**FROM THYROID AUTOIMMUNITY TO NEUROENDOCRINE GASTRIC TUMORS.**

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In 1849, Prof Addison described a fatal case of anemia, or anemia perniciosa. Dr Biermer expanded this original description in 1872. Nowadays, this pathological condition associating a megaloglastic anemia associated with a metabolic polyneuropathy is recognized as Biermer disease. Biermer anemia or anemia perniciosa and its associated polyneuropathy are the consequence of vitamine B12 malabsorption, due to autoimmune gastritis. Autoimmune gastritis is caused by lymphocitc infiltration and the generation of parietal gastric antibodies and intrinsic factor antibodies. Parietal gastric antibodies are cytotoxic: they specifically recognize the gastric proton pump, causing mucosal gastric atrophia and acloridia. This pathological condition can later degenerate into gastrin enterochromaffin cell hyperplasia , progressing to gastrin neuroendocrine tumors in nearly 10% of cases.

In 1912 Dr Hakaru Hashimoto described the thyroid of four women affected by a struma lymphomatosa. This disease was later recognized as Hashimoto thyroiditis, being one of the most frequent causes of autoimmune hypothyroidism. Thyroid peroxodase (TPO) autoantibodies and lymphocytic infiltration are responsible for autoimmune thyroiditis and subsequent thyroid destruction.

The thyrogastric syndrome was described in the seventies, in patients which the serum crossreacted both with parietal gastric antigens and thyroid TPO antigens. Whereas autoimmune polyendocrinopathies type 1 and 2 are rare, the real prevalence of the thyrogastric autoimmune syndrome is unknown. We conducted a prospective study to determine the prevalence of vitamine B12 malabsorption and gastric autoimmunity in patients with Hashimoto Thyroiditis seen in our clinical practice. A second end point of the study was to analyse gastric histological characteristics in such patients.

A total of 240consecutive patients with Hashimoto Thyroiditis were studied in our clinic from 2008 to 2009. Patients underwent TSH, FT4, FT3, ATPO, ATG, parietal cell autoantibodies (PCA), intrinsic factor antibodies (IFA), gastrine, vitamin B12 determinations and thyroid ultrasound. Patients with PCA and/or IFA were invited to have a gastric endoscopy and biopsies for histology and immunohistochemical studies. Patients with Hashimoto thyroiditis and gastric autoimmunity had a mean age of 52±19 years (28F/4M) at inclusion. Mean TSH was21 ±28 µUI/ml (0.5-4) and 47% (15/32) of patients received levothyroxine treatment.Mean thyroid volume was 9.2±7 ml.  Parietal cell autoantibodies were present in 13% (32/240). Intrinsic factor autoantibodies were found in 37.5% (6/16).In 3/6 patients with intrinsic factor antibodies we did not found PCA. Hypergastrinemia (>120 pg/ml) was present in 37 % (12/32) of patients with a mean of 323±507pg/ml. No patient had megaloblastic anemia, whereas only two patients had  macrocytosis. Vitamine B12 was less  than 200 pg/ml in 18% (6/32) of patients. A total of 59% (19/32) with PCA underwent a gastroscopy, with mucosal abnormalities in 79% (15/19) gastroscopies. Gastric and duodenal biopsies shown in 68% (13/19) histological signs of lymphocitosis infiltration, 42% (8/19) had signs of metaplasia and ECC hyperplasia and 21% (4/19) had signs of mucosal atrophy. Interestingly, *H. pylori* infection was found in 16% (3/19) of patients. No gastric carcinoid was found in this prospective series.

In this oral presentation, we discuss the potential role of cross reacting epitopes between gastric proton pump ATP ase, thyroid autoantibodies and *H pylori* suggesting some physiopathological clues to explain this syndrome. Although the prevalence of the thyrogastric syndrome seems higher in our study, much of the previous studies were retrospective. Moreover, in these previous studies the physiopathological role of *H pylori* was not explored. Interestingly, in our experience, *H. pylori* can mimick gastric autoimmunity but this is reversible, after eradication. The high prevalence of autoimmune gastritis and vitamin B12 deficiency in this series provide a strong rationale for an early serologic screening and gastroscopic diagnosis in patients with Hashimoto's thyroiditis. The physiopathological model of the thyrogastric , or as already suggested gastro-thyroideal syndrome, shoud be revised in light of these new data.

**References**

**H Valdes-Socin, L Lutteri, A Latta, L Vroonen, D Betea, P Petrossians, V Geenen, A Beckers.** Prévalence de gastrite auto-immune et études histologiques dans une série prospective de 240 patients avec thyroïdite de Hashimoto**.** *Abstract book. ENEA (Liège) 2010.*

**H Valdes-Socin, L Lutteri, A Latta, L Vroonen, D Betea, P Petrossians, V Geenen, A Beckers.** Prévalence de gastrite auto-immune et études histologiques dans une série prospective de 240 patients avec thyroïdite de Hashimoto**.** In XXVII Congrès de la SFE *Abstract book. Annales d’Endocrinologie (Paris) 2010.*

**H Valdes-Socin, A Beckers.** Conférence pour médecins généralistes: «Le syndrome thyro-gastrique : de la carence en vitamine B12 aux tumeurs carcinoïdes de l’estomac». 18 mai 2011 à 20H00. Lieu : « Centre d’Endocrinologie d’Oupeye », Rue du Roi Albert, 261 – 4680 Oupeye.