

<i>Case report</i>
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## Evans' syndrome and enterochromaffin-like tumour (ECLoma)

G.E. Baltayiannis<sup>1</sup>, K.H. Katsanos<sup>1</sup>, A. Fotopoulos<sup>2</sup>, E.V. Tsianos<sup>1</sup>

### INTRODUCTION

Carcinoid tumours are extremely rare and are traditionally divided into endocrine growths of foregut, midgut and hindgut origin<sup>1</sup>. Foregut carcinoids, encompass human gastric and duodenal carcinoid tumors that have been identified as three main variants: types 1, 2 and 3. Types 1 (ECLoma) originate from the mucosal enterochromaffin-like (ECL) cells, which can synthesize and store histamine.

Evans' syndrome includes acquired autoimmune hemolytic anemia and thrombocytopenia and has been quite recently described (Dr Evans, 1912-). It is more frequent in adult women and has usually been reported during pregnancy.

Herein we present a female patient with ECLoma presenting with Evan's syndrome.

### CASE REPORT

A 75 year-old woman was admitted to our Department with a two-day history of abdominal pain and fever. The patient's medical history included diagnosis of autoimmune hemolytic anemia which had occasionally been treated with corticosteroids (methylprednisolone P.O. 0.5mg/kg/day) and blood transfusions over the last seven years. On admission the patient had a fever of 38 °C and pallor. Clinical examination showed tachycardia,

upper right quadrant abdominal tenderness, and hepatosplenomegaly. Abdominal and chest X-ray were within normal limits while abdominal ultrasound showed hepatosplenomegaly with diffuse liver steatosis and cholelithiasis. Laboratory tests showed a Coombs C<sub>3</sub>d strongly positive autoimmune hemolytic anemia (hemoglobin 7.5g/dl, reticulocytes 3.2%), lactate dehydrogenase (LDH) 1083 UI/L, indirect bilirubin 1.4 mg/dl, increased white cell blood count and thrombocytopenia (platelet count at 88X10<sup>9</sup>/L). No clinical or laboratory evidence was suggestive of diffuse intravascular coagulation (DIC).

The patient was started on triple therapy with ceftriaxone, metronidazole and amikacin with no clinical improvement during the following four days. Abdominal pain persisted in the upper right quadrant. In addition, the anemia and thrombocytopenia further deteriorated with platelet count at 58X10<sup>9</sup>/L and hemoglobin at 5.6g/L after 10 days of hospitalization. Bone marrow smear and biopsy showed a slight increase of all series. Chest and abdominal computed tomography were within normal limits.

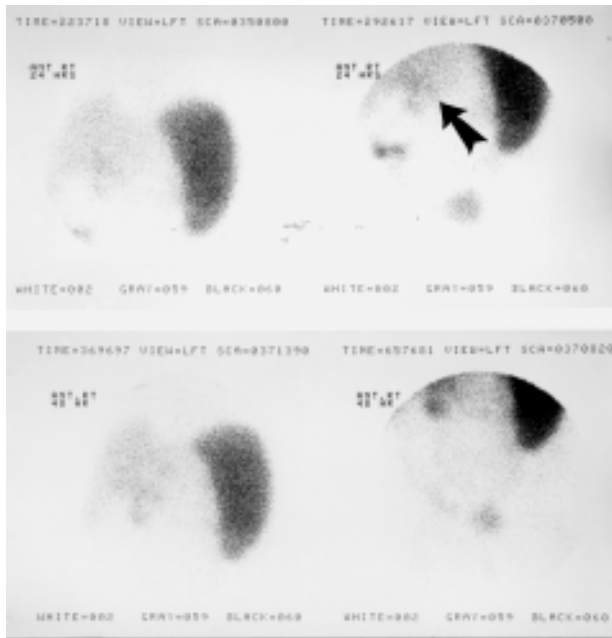
Because of the persisting symptoms of Evans' syndrome an upper gastrointestinal endoscopy was performed on day 12. An easily removable, non-bleeding duodenal polyp (0.5 cm in diameter) was the only pathologic finding. Histologic evaluation of the biopsy specimen showed neoplastic mucosal ECL cells suggestive of a polypoid duodenal carcinoid tumor (ECLoma). Random biopsies taken from gastric corpus, antrum and from other parts of the duodenum were normal.

On sigmoidoscopy and enteroclysis no abnormalities were seen. After an overnight fast, blood samples were drawn for analysis of plasma chromogranin A, gastrin, pancreatic polypeptide, calcitonin, parathormone, insulin and glucagons. Chromogranin A was 7.8.nmol/L (normal up to 4 nmol/L while all other hormones were within normal limits. Urinary 5-hydroxyindoloacetic acid

<sup>1</sup>Department of Internal Medicine (Section on Hepato-Gastroenterology), <sup>2</sup>Department of Nuclear Medicine, Medical School of Ioannina, Greece

#### Address for correspondence:

Epameinondas V. Tsianos, MD, Professor of Medicine-Gastroenterology, Department of Internal Medicine, Medical School of Ioannina, 45110 Ioannina Greece, Tel: + +30 26510- 99736, Fax: + +30 26510-97016, e-mail: etsianos@cc.uoi.gr



**Figure.** Anterior planar view of the abdomen 24h and 48h after injection of 120MBq/<sup>111</sup>In Pentetretotide (octreoscan) strongly suggestive of high amount of somatostatin receptors in the duodenum (arrow).

(5'HIAA) was twice assessed in two 24-hour urine collections and was within normal limits.

Anterior planar view of the abdomen 24h and 48h after injection of 120 MBq <sup>111</sup>I Pentetretotide (octreoscan) was strongly suggestive of high amount of somatostatin receptors in the duodenum (figure). It is remarkable that the patient never complained of a patchy, pruritic lobster-red flush on her face, neck and chest and upper extremities after meals or after emotional stress<sup>2,3</sup>. There was no history of diarrhea, cutaneous edema, lacrimation or bronchoconstriction as part of the secretion of histamine. On day 17 nephritic syndrome and sepsis overlapped with pernicious Evan's syndrome and the patient died five days later.

## DISCUSSION

Type 1 gastrointestinal carcinoid tumors are associated with type 1 chronic atrophic gastritis and achlorhydria<sup>4</sup>, although not evident in our case. Pernicious anemia (i.e. autoimmune hemolytic) may also coexist but Evan's syndrome is reported for the first time as presenting symptom according to the best of our knowledge.

Histologically, type1 carcinoid tumors stain positive with Grimelius' and Sevier-Munger's silver stains as well as for chromogranin A. The pathogenesis of these tumours is claimed to be the trophic effect of the hypergastrinaemia on the ECL cells in the fundus or corpus, but the chronic inflammation per se may also contribute to the hyperplasia of endocrine cells and the development of carcinoid tumors.

Although type 1 gastric carcinoids are considered to be the most benign of the three different types and have low malignant potential, metastases may, however, occur, most often to lymphnodes but also to the liver, although not evident in this fatal case. This case is not remarkable except for a non-metastatic carcinoid, as the overall frequency of metastases has been reported not to exceed one third of these cases<sup>1</sup>.

The most effective treatment of type 1 upper gastrointestinal tract carcinoids is under discussion. Treatment of type I carcinoids may include endoscopic polypectomy and limited surgery when feasible, although spontaneous resolution has been reported<sup>5</sup>. Treatment with interferon  $\alpha$  or octreotide or both is well documented for malignant midgut carcinoids and endocrine pancreatic tumours and can sometimes be of great help in decreasing the size of metastases. Octreotide has also been shown to decrease ECL cell content and plasma gastrin level in patients with forgut carcinoids. However, octreotide was not continued in this patient as a hypersensitivity reaction including symptomatic hypotension, occurred during initial drug administration.

We suggest that an insisting Evan's syndrome must always be suggestive of a carcinoid tumour (ECLoma) unless other diagnosis is proven.

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