

Letter to the Editor

**Achylia, Pernicious Anaemia, ECL Cells
and Gastric Carcinoids**

Sir,

Gastric endocrine tumours that are non-functioning or associated with the carcinoid syndrome are usually referred to as carcinoid tumours of the fore-gut type (Williams and Sandler 1963), while those giving rise to the Zollinger-Ellison syndrome are called gastrinomas (Creutzfeldt et al. 1975).

In a recent study on the clinical picture, morphology and immunocytochemistry of gastric carcinoids, concurrent pernicious anaemia (Wilander et al. 1979) was observed in 3 out of 9 cases examined. At least 8 additional cases of pernicious anaemia in association with gastric carcinoids are documented in the literature (Martin and Atkins 1952; Cattan et al. 1955; Pestana et al. 1963; Black and Haffner 1968; Sheahan et al. 1971; Gueller and Haddad 1975; Bader et al. 1977; Harris and Greenberg 1978) and Lattes and Grossi (1969) found that 3 out of 5 patients with gastric carcinoids had definite hyperchromic anaemia. Further, Fontolliet et al. (1976) reported one case of multiple gastric carcinoids with concomittant macrocytic anaemia. Some of the tumours referred to were examined with the silver nitrate stain of Sevier-Munger for the presence of argyrophilia and they were all argyrophil. This silver technique characteristically stains the enterochromaffin-like (ECL) cells of the gastric mucosa (Solcia et al. 1970).

In patients with pernicious anaemia, atrophic gastritis with a deficient production of "intrinsic factor" is a classical finding. In addition to achlorhydria, the majority of patients with atrophic gastritis have elevated serum gastrin levels (Stockbrügger et al. 1977). Several studies in man have revealed hyperplasia of ECL cells in association with increased gastrin levels (Solcia et al. 1970; Rubin 1973; Bordi et al. 1975).

In a recent report by Larsson et al. (1978) a patient with atrophic gastritis (without pernicious anaemia) with very high serum gastrin levels and multiple gastric endocrine tumours (carcinoids) was described. The majority of the tu-

Offprint requests to: Dr. Erik Wilander, University of Uppsala, Department of Pathology, P.O. Box 553, S-751 22 Uppsala, Sweden

Supported by grants from the Swedish Medical Research Council (Project No. 102)

mour cells were positively stained with the Sevier-Munger technique and like a previously described case (Hage and Hage 1976) they were of the ECL type ultrastructurally. It was concluded that "the raised serum gastrin levels, caused by decreased acid feed-back inhibition, may have been instrumental in bringing about hyperplasia and neoplasia of the ECL cells".

Apart from the report of Larsson et al. (1978) at least 6 other cases of gastric carcinoids without pernicious anaemia but with achylia are on record in the literature (Lützw-Holm 1952; Hines and Savage 1955; Eklöf 1967; Gueller and Haddad 1975; Bordi et al. 1976).

In conclusion it is indicated that achylia with or without pernicious anaemia is associated with gastric carcinoids at a higher frequency than has been suspected previously and that a relatively large number of these tumours may contain a majority of tumour cells of the ECL type.

The occurrence of the carcinoid syndrome in connection with gastric carcinoids is rare. Postlethwait (1966), was able to collect a total number of 8 cases in 1966, and at present achylia occasionally associated with pernicious anaemia seems to be the most distinct condition associated with these tumours.

References

- Bader LV, Lykke AWJ, Hinterberger H (1977) Multiple biogenic amine-secreting "carcinoid" tumour of the stomach: A case report. *Pathology* 9:353-358
- Black WC, Haffner HE (1968) Diffuse hyperplasia of gastric argyrophil cells and multiple carcinoid tumours. *Cancer* 21:1080-1099
- Bordi C, Costa A, Missale G (1975) ECL cell proliferation and gastrin levels. *Gastroenterology* 68:205-206
- Bordi C, Senatore S, Missale G (1976) Gastric carcinoid following gastro-jejunostomy. *Am J Dig Dis* 21:667-671
- Cattan R, Nallet J, Liebeskind M, Habib R, Pariente Pu (1955) Carcinoïde de l'estomac et anémie de Biermer. *Société Nationale Française de gastro-entérologie* juillet: 922-928
- Creutzfeldt W, Arnold R, Creutzfeldt C, Track NS (1975) Pathomorphologic, biochemical and diagnostic aspects of gastrinomas (Zollinger-Ellison syndrome). *Human Pathology* 6:47-76
- Eklöf O (1967) Carcinoid tumours of the stomach, 3 cases reported. *Acta Chir Scand* 121:118-126
- Fontollet Ch, Wertheim U, Arma S, Nosedà G, Theler A, Realini S (1976) Multiples Karzinoid des Magens. *Z Gastroenterol* 14:724
- Gueller R, Haddad JK (1975) Gastric carcinoids simulating benign polyps. Two cases diagnosed by endoscopic biopsy. *Gastrointest Endosc* 21:153-155
- Hage E, Hage J (1976) A gastric carcinoma identified as an ECL-oma associated with acanthosis nigricans. In: Fujita T (ed) *Endocrine gut and pancreas*, Amsterdam: Elsevier, pp 359-363
- Harris AI, Greenberg H (1978) Pernicious anaemia and the development of carcinoid tumours of the stomach. *JAMA* 239:1160-1161
- Hines CR, Savage JL (1955) Carcinoid tumours of the stomach. *Ann Intern Med* 43:859-867
- Larsson L-I, Rehfeld J, Stockbrügger R, Glohne G, Schöön IM, Lundqvist G, Kindblom L, Sæve-Söderberg J, Grimelius, L, Olbe L (1978) Mixed endocrine gastric tumours associated with hypergastrinemia of antral origin. *Am J Pathol* 93:53-68
- Lattes R, Grossi C (1956) Carcinoid tumours of the stomach. *Cancer* 9:698-711
- Lützw-Holm G (1952) Carcinoid tumours of the stomach. Two cases. *Acta Chir Scand* 104:193-200
- Martin JD, Atkins EL (1952) Carcinoid of the stomach. Review of reported cases. *Surgery* 31:698-704
- Pestana C, Beahrs OH, Woolner LB (1963) Multiple (seven) carcinoids of the stomach: Report of case. *Proc Mayo Clin* 38:453-456

- Postlethwait RW (1966) Gastrointestinal carcinoid tumours. A Review *Postgrad Med* 40:445–454
- Rubin W (1973) A fine structural characterization of the proliferated endocrine cells in atrophic gastric mucosa. *Am J Pathol* 70:109–118
- Sheahan DG, Horowitz SA, Zamcheck N (1971) Deletion of epithelial ABH isoantigens in primary gastric neoplasms and in metastatic cancer. *Am J Dig Dis* 16:961–969
- Solcia E, Capella C, Vassallo G (1970) Endocrine cells of the stomach and pancreas in states of gastric hypersecretion. *Rendic Gastroenterol* 2:147–158
- Stockbrügger R, Larsson L-I, Lundqvist G, Angervall L (1977) Antral gastrin cells and serum gastrin in achlorhydria. *Scand J Gastroenterol* 12:209–213
- Wilander E, Grimelius L, Lundqvist G, Skoog V (1979) Polypeptide hormones in argentaffin and argyrophil gastroduodenal endocrine tumours. *Am J Pathol* 96:519–526
- Williams ED, Sandler M (1963) The classification of carcinoid tumours. *Lancet* i:238–239

Accepted April 28, 1980

E. Wilander

Department of Pathology
University of Uppsala
Uppsala
Sweden