inactivating CaSR mutation who had episodes of psychosis and osteoporosis. After treatment with cinacalcet for 12 months, serum calcium levels gradually normalized. Festen-Spanjer et al. reported a 37-year-old female patient with FHH and a 10-year history of recurrent pancreatitis who was treated with cinacalcet 30 mg/day for four weeks. Alon and Van DeVoorde reported a 6-year-old boy with FHH in whom hypercalcemia appeared to interfere with tissue healing after a tympanoplasty. He was treated with cinacalcet for one year, and initially showed partial response to treatment with doses of 30 mg/day. When this dose was doubled, adequate healing and normalization of serum levels of Ca and PTH were achieved.

Cinacalcet is thought to interact with CaSR segments, enhancing transduction and activation signals from the receptor and inducing conformational changes in CaSR. However, the pharmacodynamic mechanisms by which cinacalcet increases sensitivity to Ca in the mutated CaSR are not known yet.

We report our positive clinical and analytical experience with cinacalcet in a 25-year-old patient with severe hypercalcemia due to FHH and an altered CaSR gene. Cinacalcet represents a new alternative for treating patients with hypercalcemia secondary to mutation in the calcium-sensing receptor.

References


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Well-differentiated gastric carcinoids treated with somatostatin analogues

Tratamiento de carcinoides gástricos bien diferenciados con análogos de somatostatina

Type 1 gastric carcinoids are tumors caused by the constant stimulation of hypergastrinemia on enterochromaffin-like cells occurring in chronic atrophic gastritis. They are the most common gastric carcinoids (70%) and have a good prognosis in most cases. Their indolent course is confirmed by the presence of a low number of mitoses, as measured by the Ki67 index, usually less than 30 per high magnification field, and by a 0–10% risk of angioinvasion or submucosal invasion. Metastases occur in 2–5% of cases, usually in regional lymph nodes or liver. Type 1 gastric carcinoids are located in the gastric body or fundus, are usually less than 2 cm in size, and are often multiple. Because of their association with chronic atrophic gastritis, the patients most commonly affected are women over 50 years of age, and tumors are incidentally found in gastroscopies performed for anemia or dyspepsia, which are among the symptoms of chronic atrophic gastritis.

Type 1 gastric carcinoids develop following a carcinogenesis model where hypergastrinemia initially causes hyperplasia of enterochromaffin-like cells, after which neoplasms are formed following a period of cell dysplasia. The presence of cell dysplasia involves a 26-fold greater risk for the subsequent formation of carcinoid tumors as compared to chronic atrophic gastritis without dysplasia. Molecular markers reported in the literature include elevation in most patients of V-MAT2, chromogranin A or synaptophysin, and occasionally histamine. Such elevations are quite non-specific as compared to other gastric neuroendocrine tumors.

Because of the indolent course of type 1 gastric carcinoids, the therapeutic approach is less aggressive than for other gastric exocrine tumors. In addition, optimal treatment and monitoring of patients are controversial because

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of the rarity of the disease, and no large, randomized clinical trials which could allow us to draw clear conclusions are available. Endoscopic resection is usually performed when lesion size and number allow. However, the recurrence rate is high. Antrectomy has been performed to eliminate the source of hypergastrinemia, which is essential in the pathophysiology of the disorder. More aggressive surgical procedures, including partial or total gastrectomy, have been performed on tumors of a bigger size or with submucosal invasion or angioinvasion. Somatostatin analogues may also be used as an effective treatment for gastric carcinoids because they control hypergastrinemia and subsequent hyperplasia of enterochromaffin-like cells. Some authors would advocate their use for "functioning" gastric carcinoids and in cases with more than six polypoid lesions less than one centimeter in diameter. Three cases of gastric carcinoids are reported below, including their medical treatment and subsequent course. None of the patients were being treated with proton pump inhibitors at diagnosis or during follow-up.

Case 1

The case of a 48-year-old female patient with a personal history of primary hypothyroidism of autoimmune origin since she was 30, alopecia universalis, vitiligo, and menopause at 35 years is reported. Routine laboratory tests incidentally found vitamin B12 levels of 24 pg/mL (No. > 200 pg/mL), with folic acid levels within the normal range. Gastrin levels were markedly elevated, 1023 pg/mL (No. < 108 pg/mL), and chromogranin A levels were 6 nmol/L (No. < 4 nmol/L). Autoimmune testing showed positive anti-parietal cell and anti-intrinsic factor antibodies. A gastroscopy was consistent with chronic atrophic gastritis. Two polyps one centimeter in diameter were also seen. An endoscopic ultrasound examination performed to better characterize the findings showed no submucosal invasion of the neoplasms. Endoscopic polypectomy was performed, during which multiple biopsy samples were taken along the gastric cavity. Findings were consistent with chronic atrophic gastritis. Helicobacter pylori was not found. Polyps were reported by the pathological laboratory to be consistent with well differentiated neuroendocrine tumors with no angioinvasion and a Ki 67 < 2%.

At the endoscopic control performed one year later, six new gastric polyps were seen (Fig. 1). Three of them were resected, and were found to be consistent with well differentiated gastric carcinoid tumors.

At that time, treatment for the relapse of the disease was started with lanreotide at monthly doses of 90 mg for 12 months. Annual gastroscopies performed during the following three years showed an absence of tumors and disease remission (Fig. 2). One year after treatment, chromogranin A was within the normal range, 3 nmol/L, and gastrin levels were slightly elevated to 167 pg/mL.

Case 2

A 36-year-old female patient with a personal history of autoimmune polyglandular syndrome type II with Addison’s disease, primary hypothyroidism, and vitiligo. She was receiving hydrocortisone 20 mg/day, fludrocortisone 0.05 mg/day, and levothyroxine 100 mcg/day. In a routine visit, the patient reported non-specific asthenia, and laboratory test results revealed anemia with a hemoglobin value of 10.5 g/dL and an MCV of 99 fl. She also had a vitamin B12 level of 45 pg/mL (No. > 200 pg/mL) and a plasma gastrin level of 502 pg/mL (No. < 108 pg/mL). A gastroscopy showed three polyps each less than one centimeter in size.
The largest polyp (0.8 cm) was resected, and a pathological examination revealed a well differentiated neuroendocrine tumor with Ki 67 < 2%. Treatment was administered with octreotide LAR 20 mg monthly for 12 months, and in the next two annual endoscopic examinations the unresected polyps had disappeared, and no new neoplasms were found. Plasma gastrin level normalized after one year of treatment (101 pg/mL).

Case 3

A 28-year-old male with epigastric pain and intermittent nausea is reported. Laboratory tests found a plasma gastrin level of 1200 pg/mL (No. < 108 pg/mL) and a chromogranin A level of 6 nmol/L (No. < 4 nmol/L). Intragastric 24-h pH measurement showed a pH always higher than 4, and a gastroscopy revealed findings consistent with chronic atrophic gastritis and six polypoid lesions less than 0.8 cm in size, which were all resected. Pathological examination disclosed well differentiated carcinoid tumors with a Ki 67 < 2%. At six months, a repeat gastroscopy revealed four new lesions less than one centimeter in size, which were resected and again showed well differentiated carcinoid tumors. Treatment was started with octreotide LAR 20 mg/month by the IM route for six months. Gastroscopic monitoring at six and 12 months was normal, as well as plasma gastrin (103 pg/mL) and chromogranin A (3 nmol/L) levels.

Based on the courses of the three cases reported, treatment with somatostatin analogues appears to have an antiproliferative effect on well differentiated gastric carcinoids, and represents an alternative to other more invasive therapies. This is a well tolerated treatment with few side effects, but very expensive. Optimal treatment dosage and time, as well as its specific role in the guidelines for treatment of well differentiated gastric endocrine tumors, have not been elucidated yet. The reported cases show disease remission up to three years after treatment discontinuation.

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Pituitary apoplexy. A case report

Apoplejía pituitaria. A propósito de un caso

In 1898, Pearce Bailey reported the first case of pituitary apoplexy (PA); however, it was not until 1950 that Brougham et al. recognized this syndrome in five patients, reviewed the medical literature and coined the term PA.1

PA is a clinical syndrome characterized by headache, vomiting, visual defects, ophthalmoplegia, impaired consciousness and/or meningism due to infarction or bleeding from a pituitary adenoma.1,2 PA is an uncommon but potentially fatal endocrine emergency occurring in patients with pituitary adenomas, particularly non-secreting macroadenomas.3 In 80% of cases, PA is the first symptom of the pituitary adenoma.4,5

The incidence of PA in pituitary adenomas ranges from 2% to 7% in most series.5,6 However, the frequency of subclinical PA, i.e. incidentally detected pituitary hemorrhage and/or asymptomatic infarct, may be as high as 25%.2,5

Changes in visual acuity and field are due to the rapid growth of pituitary adenoma, which extends laterally into the cavernous sinus and compresses the third, fourth, and sixth cranial nerves; or upwards, compressing the optic chiasm.7,8

The case of a patient who attended the emergency room for headache, nausea, and diplopia is reported here. Magnetic resonance imaging (MRI) showed a pituitary macroadenoma with signs of hemorrhage. Transsphenoidal surgery resolved ocular changes.

A 71-year-old male patient with a history of dyslipidemia not treated with drugs attended the emergency room of our hospital complaining of headache, nausea, vomiting, diplopia, and impaired visual field for the previous two weeks. Three months before admission, the patient had experienced self-limited episodes of diplopia. One day

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