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Original Research

Carcinoid tumors of the duodenum and the ampulla of Vater: Current diagnostic and therapeutic approach in a series of 8 patients. Case series

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ABSTRACT

Aim: To describe the specific characteristics of duodenal/perivaterian carcinoids and to analyze the diagnostic/therapeutic approach.
Material and methods: Eight patients were included in our study. Symptoms on admission included dyspepsia, upper gastrointestinal (GI) bleeding and anemia. All patients underwent upper GI endoscopy and gastrointestinal peptides (gastrin) and neuroendocrine markers (Chromogranin-A, CgA) measurement. Imaging studies were performed in all patients, including OCTREOSCAN, while in patients with ACs MRCP or ERCP was also performed, when necessary. Definite diagnosis was confirmed by histopathologic examination.
Results: Polypoid masses (carcinoids) were revealed at duodenal bulb and ampulla of Vater, in 5 and 3 patients, respectively. Serum gastrin was moderately increased in 4 patients, while in one patient it was more than 1000 pg/ml. Serum CgA was moderately increased in one patient, in whom OCTREOSCAN detected a solitary hepatic metastasis. Two patients with DC, of less than 1 cm of diameter, were treated by endoscopic polypectomy, while all the other patients underwent surgery. The patient with hepatic metastasis and positive OCTREOSCAN received also Octreotide LAR, resulting in stabilization of disease. No recurrence or metastases were observed during follow-up (range : 1.5–9.6 years).
Conclusions: In DC tumors <1 cm endoscopic excision with close follow-up is an adequate treatment, while in tumors >1 cm and in AC, surgical resection is the treatment of choice. In metastatic tumors, resection of the primary lesion with administration of somatostatin analogues may stabilize the disease and improve patient's quality of life.

1. Introduction

Carcinoids are rare, slow growing malignancies, predominantly arising from the Gastrointestinal (GI) tract. They are originated from a variety of different neuroendocrine cell types and are usually identified histologically by their affinity for silver salts and by positive reactions to neuroendocrine markers like neuron-specific enolase (NSE), synaptophysin and chromogranin. Appendix and the small bowel are the most frequent locations of carcinoid tumors within the GI tract, while carcinoids of the duodenum (DC) and especially of the ampulla of Vater (AC) are rare tumors, accounting for less than 2% and 0.3% of all gastrointestinal carcinoids, respectively.[1,2] According to the traditional classification, proposed by Williams et al.,[3] DC and AC belong to foregut cacinoids together with those of the respiratory tract, stomach and pancreas. However, a new classification, which takes into account not only their embryological origin, but also histologic variations of carcinoids, has recently been adopted by many authors.[4] According to this new classification system, neuroendocrine tumors of the duodenum and uppermost jejunum (including those of the ampullary region) are classified as well-differentiated endocrine tumors, well-differentiated endocrine carcinomas and poorly differentiated endocrine carcinomas.

In this paper, we present our experience with 8 patients with carcinoids located in the duodenum ($n = 5$) and the ampulla of Vater ($n = 3$). Clinical and pathologic features of these two rare entities are compared and our diagnostic and therapeutic approach is analyzed. The relevant literature is briefly reviewed.

Abbreviations: DC, Duodenal carcinoids; AC, Ampulla of vater carcinoids; US, Ultrasonography; CT, Computed tomography; EUS, Endoscopic ultrasonography.

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2. Material and methods

Among a total number of 114 patients with carcinoid tumors of all origins, including 103 patients with carcinoids of the GI tract/pancreas (Table 1), we present 8 cases in which carcinoids were located in the duodenum ($n = 5$) and the ampulla of Vater ($n = 3$). These patients had been treated in the Section of Neuroendocrinology, First Department of Propaedeutic Internal Medicine of Athens University Medical School, "Laiko" Hospital, Athens Greece, during the last 10 years. Five patients were females, aged from 36 to 67 years (median, 51 years) and three were males, aged from 62 to 77 years (median, 68.3 years). The diagnosis was based upon histopathological features and immunohistochemical markers, after biopsies taken during upper GI endoscopy or Endoscopic Retrograde Chollangio-Pancreatography (ERCP). The following immunohistochemical markers were used : NSE (Dako M0873, dilution 1:50), Chromogranin-A (Dako A 0430, dilution 1:100) and Synaptophysin (Dako M0776, dilution 1:10).

After confirmation of diagnosis and endoscopic or surgical treatment, all patients were evaluated several times per year with clinical, biochemical and radiographic assessments. The follow-up protocol included:

1) Measurement of 24 h secretion of urinary 5-hydroxy-indole-acetic acid (5-HIAA), and serum Chromogranin-A (CgA), every three months.
2) Measurement of serum neurohormonal peptides such as gastrin, somatostatin and pancreatic polypeptide (PP), when necessary.
3) Liver biochemistry tests every six months and in patients with hepatic metastases every four months.
4) Abdominal ultrasonography (US) every six months or every four months in patients with metastases and also endoscopic ultrasonography (EUS), when necessary.
5) Abdominal Computed Tomography (CT) scan once a year in all patients, and Magnetic Resonance Imaging (MRI) or Magnetic Resonance Chollangio-Pancreatography (MRCP), when necessary.
6) Somatostatin-Receptor-Scinitigraphy (OCTREOSCAN), once a year in all patients.
7) Upper GI endoscopy, once a year in all patients.

The follow-up period ranged between 1.5 years and 9.6 years (mean, 4.2 years) and it is still in progress.

3. Results

3.1. Clinical features

Three out of five patients with DC were females and 2 were males, while 2 patients with AC were females and 1 was male. Four (4/5, 80%) of the patients with DC were referred to us, because of ulcer-like symptoms, while the other patient was admitted to our hospital for upper GI bleeding. On the contrary, one patient with AC presented with weakness and shortness of breath during the last 8 months due to a severe anemia (hematocrit, 18%), one patient referred to us because of painless jaundice of 4 weeks duration, while the other patient was admitted for malaena and painless jaundice of sudden onset. The latter patient had also a history of von Recklinghausen's disease. There were no clinical signs of "carcinoid syndrome" in any of the previous patients. The clinical features of all patients at the time of presentation, are summarized in Table 2.

3.2. Laboratory findings

On admission, one patient with DC and two patients with AC had anemia. Liver function tests were normal in all patients with DC, while in all patients with AC, γGT and alkaline phosphatase (ALP) were significantly elevated. Also, in the two patients with AC who presented with jaundice, a mild elevation of the amino-tranferases (AST, ALT) and increased serum bilirubin levels (up to 8.5 mg/dl) were found. Serum amylase and clotting parameters were normal in all patients.

Serum gastrin levels were significantly elevated in one patient (>1000 ng/L, normal values < 108 ng/L) and slightly increased in three patients (range, 158–395 ng/L, mean, 273 ng/L) with DC, while it was within normal limits in all patients with AC. Serum PP was moderately elevated (135 pmol/L, normal values : <100 pmol/L) in the patient with high values of serum gastrin, while it was normal in all the other patients. Serum somatostatin levels were normal in all patients. Serum and urine neuroendocrine markers were measured; serum CgA was found moderately increased in seven patients (mean, 266 ng/ml) and significantly elevated (>800 ng/ml) in one patient with DC. In this last patient, urinary 5-HIAA was found increased (19 mg%, normal values < 9 mg%) while the imaging studies revealed a solitary hepatic metastasis. Urinary 5-HIAA was normal in all the other patients (Table 3).

Table 1
Carcinoid tumors of the GI tract, treated in the section of neuroendocrinology, "Laikon" Hospital.

Tumor Location	No of Patients	%
Stomach	16	15.5
Duodenum and Ampulla of Vater	8	7.8
Pancreas	4	3.9
Small Intestine	31	30
Appendix	34	33
Colon and Rectum	10	9.8
Total	103	100

3.3. Endoscopic – imaging findings

On upper GI endoscopy, solitary polypoid lessions (up to 1 cm in 3 patients, 1.5 cm in one patient and more than 2 cm in one patient) were found in the bulb of the duodenum in patients with DC (Fig. 1). On the contrary, in one patient with AC an ulcerated, bleeding tumor with a diameter of 4 cm was revealed in the ampulla of Vater (Fig. 2), while in the remaining 2 patients with AC, the endoscopy raised the suspicion of a submosal tumor of the ampullary region. In these two patients, upper abdominal US demonstrated a dilatation of the extrahepatic and intrahepatic bile ducts, while in all the other patients US was without pathological findings. The biliary ductal dilatation in the previous two patients was confirmed by the abdominal CT scan or the MRCP (Fig. 3). These two patients underwent an ERCP, which revealed tumors of the ampulla of Vater (Fig. 4).

Based on the histological confirmation of the diagnosis, all the previous patients underwent a Somatostatin-Receptor-Scintigraphy, which showed no abnormalities in seven patients, while in the remaining patient with DC, a solitary hepatic metastasis was revealed (Fig. 5). Of note, in this patient, CT scan and US, performed at the same time, were without pathological findings.

3.4. Treatment

3.4.1. Endoscopic – surgical treatment

Endoscopic (snare) polypectomy was performed in 2 patients, who had polypoid lesions in the bulb < 1 cm. In these patients the infiltration of the regional lymph nodes was excluded by endoscopic ultrasonography (EUS), performed prior to polypectomy. In 2 patients with DC of diameter of 1.5 cm and 2.4 cm, respectively, as well as in the patient with a DC and diameter of the mass ~1 cm, who had already a hepatic metastasis, surgical local excision with regional lymph-node dissection was performed. Liver metastasectomy was not possible due to tumor location at the confluence of the hepatic veins/inferior vena cava.

On the contrary, in all three patients with AC a pancreatico-duodenectomy (Whipple procedure) with regional lymph-node resection was performed. During the operation, in the woman with AC and von Recklinghausen's disease, a second mass, of hard consistency, measuring 3.5 × 3.5 cm was found in the jejunum, approximately 15 cm distal to the ligament of Treitz, which was also resected. Postoperative course was uneventful in all patients, without any significant postoperative complication.