

## PANCREATIC NEUROENDOCRINE TUMOR PRESENTING WITH CARCINOID SYNDROME: CASE REPORT

Maja Berković<sup>1</sup>, Vanja Zjačić-Rotkvić<sup>1</sup>, Vesna Goldoni<sup>1</sup>, Davor Hrabar<sup>2</sup> and Nikola Karapandža<sup>3</sup>

<sup>1</sup>Department of Endocrinology, Diabetes and Metabolic Diseases, <sup>2</sup>Department of Gastroenterology, <sup>3</sup>University Department of Surgery, Sestre milosrdnice University Hospital, Zagreb, Croatia

**SUMMARY** – Carcinoid is the most common neuroendocrine tumor. It is primarily localized in the ileum and the appendix, whereas other localizations are rare. Only a small number of the carcinoids present with carcinoid syndrome (flushing, diarrhea), usually after tumor has already metastasized. A case of carcinoid tumor of uncommon localization is reported. A 54-year-old male patient presented for evaluation because of weight loss, flushing and diarrhea. Laboratory value of 5-HIAA was 775.5 mmol/l (normal values up to 72.8) and the pancreatic tumor marker CA 19-9 was increased. Ultrasonographic and magnetic resonance findings localized the tumor in the prepapillary pancreatic region and visualized the spread to the liver. The diagnosis was confirmed by pathohistologic evaluation of a liver biopsy specimen. The patient was treated with Sandostatin (octreotide analog), which led to significant relief of the symptoms, although control 5-HIAA values were not reduced.

**Key words:** *Neuroendocrine tumors, diagnosis; Pancreatic neoplasms, diagnosis; Pancreatic neoplasms, drug therapy; Carcinoid tumor, diagnosis; Carcinoid tumor, drug therapy; Case report*

### Introduction

Carcinoid is the most common neuroendocrine tumor<sup>1-5</sup>. It has traditionally been classified according to embryogenetic aspects into foregut, midgut and hindgut tumors, or to histologic characteristics as 'typical' or 'atypical' tumor. According to endocrinologic status, carcinoids are either functioning or nonfunctioning tumors<sup>6</sup>. Their metastatic potential correlates with the size and site of primary tumor, angioinvasiveness and number of mitoses<sup>7</sup>. If the tumor is greater than 2 cm in diameter, chances of spread are greater than 50%<sup>8</sup>. Approximately 20% (1/5) of the small intestine carcinoids will develop metastases and roughly 1/3 of those that have spread will develop symptoms of the carcinoid syndrome (hot red flushing of the face, diarrhea, and asthma-like wheezing attacks)<sup>9</sup>. The most common localization for carcinoids is the small intestine (39%),

followed by the appendix (26%), rectum (15%), lungs (10%), colon (5%-7%), stomach (2%-4%), pancreas (2%-3%) and liver (>1%), whereas other localizations such as gallbladder and bile ducts, ovaries, testicles, urinary bladder, prostate gland, breast, kidneys and the thymus gland are extremely rare. As much as 25% of all gastrointestinal tract carcinoids are associated with another tumor of non-carcinoid type (especially colon cancer, lung cancer, breast cancer and prostate cancer)<sup>4</sup>. If distant metastases are present when a carcinoid from any site of origin is found, the 5-year survival rate drops to 27% if not treated<sup>10</sup>. The potent chemicals and hormones produced by carcinoid tumors, through their effects on the cardiovascular, gastrointestinal, pulmonary and other body systems, cause the carcinoid syndrome, which is in many cases worse than the symptoms from the growth of the tumor itself<sup>11,12</sup>. Once considered, the diagnosis usually can be confirmed by performing a urine 5-HIAA test or by measuring chromogranin A (CgA) and serotonin in the blood<sup>13</sup>. A universally approved way of detecting carcinoid as well as other neuroendocrine tumors now is Sandostatin receptor scintigraphy (octreoscan). It is positive in up to 85% of carcino-

Correspondence to: *Maja Berković, M.D.*, Department of Endocrinology, Diabetes and Metabolism, Sestre milosrdnice University Hospital, Vinogradska c. 29, HR-10000 Zagreb, Croatia  
E-mail: [mberkovi@globalnet.hr](mailto:mberkovi@globalnet.hr)

Received June 5, 2003, accepted in revised form October 25, 2003



scribed, are infrequent and found incidentally or because of their local invasiveness when causing intestinal obstruction, changes in bowel habits or obscure bleeding. Only a small proportion of the pancreatic neuroendocrine tumors are responsible for symptoms of carcinoid syndrome<sup>11,12</sup>. The accompanying manifestations<sup>16</sup>, such as peptic ulcer, sometimes described with carcinoid tumors, especially those localized in the 'gastrinoma triangle', were also found in our patient, although gastrin values were within the normal range. Muscle wasting or Peyronie's disease<sup>17-19</sup> were not observed. Carcinoid heart disease, occurring in as much as 50% of patients with developed carcinoid syndrome, and being a major mortality and morbidity cause among those patients, was not present either<sup>20</sup>. The importance of carcinoid tumors is that they are slow growing and often curable. The progression of the illness in patients with carcinoid syndrome is usually more rapid than in those without the functioning tumor. However, this has been changed remarkably with the advent of Sandostatin (octreotide)<sup>21</sup>. In the last 10 years, since the introduction of effective combinations of treatment with Sandostatin, various types of surgery, chemotherapy, hepatic artery injections and biologic response mediators, the average survival time from the start of treatment has increased to more than 5 years. Sandostatin therapy not only relieves flushing and diarrhea in 75% to 80% of patients, but has also been shown to successfully reduce tumor growth<sup>22</sup>. This antiproliferative effect was not observed in our patient.

## References

- MODLIN IM, TANG LH. Approach to the diagnosis of gut neuroendocrine tumors: the last word today. *Gastroenterology* 1997;112:583-90.
- OBERG K. Carcinoid tumors: molecular genetics, tumor biology and update of diagnosis and treatment. *Curr Opin Oncol* 2002;14:38-45.
- JENSEN RT. Carcinoid and pancreatic endocrine tumors: recent advances in molecular pathogenesis, localization, and treatment. *Curr Opin Oncol* 2000;12:368-77.
- KULKE MH, MAYER RJ. Carcinoid tumors. *N Engl J Med* 1999;340:858-68.
- MARTENSSON H, NOBIN A, SUNDLER F. Carcinoid tumors of the gastrointestinal tract: an analysis of 156 cases. *Acta Chir Scand* 1983;149:607-16.
- WILLIAMS ED, SANDLER M. The classification of carcinoid tumours. *Lancet* 1963;1:238-9.
- KLOPPEL G, PERREN A, HEITZ PU. From carcinoids to a biologically and prognostically relevant classification of the neuroendocrine tumors of the gastrointestinal tract and the pancreas. *Acta Clin Croat* 2002;41:285-94.
- LOFTUS JP, Van HEERDEN JA. Surgical management of gastrointestinal carcinoid tumors. *Adv Surg* 1995;28:317-36.
- BURKE AP, THOMAS RM, ELSAYED AM, SOBIN LH. Carcinoids of the jejunum and ileum: an immunohistochemical and clinicopathologic study of 167 cases. *Cancer* 1997;79:1086-93.
- MODLIN IM, SANDOR A. An analysis of 8305 cases of carcinoid tumors. *Cancer* 1997;79:813-29.
- FELDMAN JM. Carcinoid tumor and syndrome. *Semin Oncol* 1987;14:237-46.
- WAREING TH, SAWYERS JL. Carcinoids and the carcinoid syndrome. *Am J Surg* 1983;145:769-72.
- FELDMAN JM. Urinary serotonin in the diagnosis of carcinoid syndrome. *Clin Chem* 1986;32:840-4.
- KVOLS LK, BROWN ML, O'CONNOR MK, HUNG JC, HAY-OSTEK RJ, REUBI JC, LAMBERT SW. Evaluation of a radiolabeled somatostatin analog (I-123 octreotide) in the detection and localization of carcinoid and islet cell tumors. *Radiology* 1993;187:129-33.
- KLÖPPEL G, INTVELD PA, KOMMINOTH P, HEITZ PU. The endocrine pancreas. In: KOVACS K, ASA SL, eds. *Functional endocrine pathology*, 2<sup>nd</sup> ed. Boston: Blackwell; 1998:415-87.
- GOUGH DB, THOMPSON GB, CROTTY TB. The diverse clinical and pathological features of gastric carcinoid and the relevance of hypergastrinemia. *World J Surg* 1994;18:473-9.
- MORIN LJ, ZUERNER RT. Retroperitoneal fibrosis and carcinoid syndrome. *JAMA* 1971;216:1647.
- BIVENS CH, MARECEK RL, FELDMAN JM. Peyronie's disease: presenting complaint of carcinoid syndrome. *N Engl J Med* 1973;289:844.
- LAROSAS, SESSA F, CAPELLA C, RIVA C, LEONE BE, KLETSY C, RINDY G, SOLCIA E. Prognostic criteria in nonfunctioning pancreatic endocrine tumours. *Virchows Arch* 1996;429:323-33.
- WESTBERG G, WANGBERG B, AHLMAN H, BERGH CH, BECKMAN-SUURKULA M, CAIDAHL K. Prediction of prognosis by echocardiography in patients with midgut carcinoid syndrome. *Br J Surg* 2001;88:865-72.
- DE VRIES EG, KEMA IP, SLOOFF MJ, VERSCHUEREN RC, KLEIBEUKER JH, MULDER NH, SLEIJFER DT, WILLEMSE PH. Recent developments in diagnosis and treatment of metastatic carcinoid tumors. *Scand J Gastroenterol Suppl* 1993;200:87-93.
- O'TOOLE D, DUCREUX M, BOMMELAER G, WEMEAU JL, BOUCHE O, CATUS F, BLUMBERG J, RUSZNIEWSKI P. Treatment of carcinoid syndrome: a prospective crossover evaluation of lanreotide *versus* octreotide in terms of efficacy, patient acceptability, and tolerance. *Cancer* 2000;88:770-6.

## Sažetak

## NEUROENDOKRINI TUMOR GUŠTERAČE S IZRAŽENIM KARCINOIDNIM SINDROMOM: PRIKAZ SLUČAJA

*M. Berković, V. Zjačić-Rotkvić, V. Goldoni, D. Hrabar i N. Karapandža*

Iako su karcinoidi rijetki, predstavljaju najčešći tip neuroendokrinih tumora, primarno smještenih u tankom crijevu i apendiksu. Mali broj ovih tumora, nakon što metastazira u jetru, prezentira se simptomima karcinoidnog sindroma (rumenjača, proljevi). Prikazan je karcinoid gušterače, neuobičajene lokalizacije za ovu vrst tumora. Bolesnik u dobi od 54 godine upućen je u kliniku zbog gubitka na težini, rumenjače i proljeva. Vrijednosti 5-HIAA i CA 19-9 bile su izrazito povišene. Ultrazvučno i magnetskom rezonancom prikazan je tumor predpapilarnog područja te uvećana jetra prožeta višestrukim sekundarizmima, a patohistološki nalaz govorio je u prilog neuroendokrinih tumora tipa karcinoida. S obzirom na proširenost procesa odustalo se od kirurškog liječenja te je započeta terapija Sandostatinom uza značajno kliničko poboljšanje, no bez učinka na 5-HIAA.

*Ključne riječi: Neuroendokrini tumori, dijagnostika; Neoplazme gušterače, dijagnostika; Neoplazme gušterače, lijekovi; Karcinoidni tumor, dijagnostika; Karcinoidni tumor, lijekovi; Prikaz slučaja*