OUR EXPERIENCES IN THE TREATMENT OF CARCINOID NEOPLASMS OF THE GASTROINTESTINAL TRACT AT KARLOVAC GENERAL HOSPITAL – A RETROSPECTIVE STUDY

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Carcinoid is a slow-growing tumor of neuroendocrine origin from enterochromaffin APUD cells. About 2/3 of it arise in the digestive tract. Carcinoid tumors make up 1% of the cancers of the gastrointestinal tract and 50% of them are located in the area of the small intestine. They often are asymptomatic in the early stages of the disease, which makes them difficult to diagnose. It occurs most often in people at a mean age of 61.4 years. Epidemiological data show that the incidence is 2.47-4.48 *per* 100,000 and in the last 2-3 decades the incidence has been increasing. The cause of carcinoid tumors is unknown, but a genetic factor can play a role (it was observed in multiple endocrine neoplasia type 1, neurofibromatosis type 1, Von Hippel-Lindau disease) and inactivation of the tumor suppressor gene on the 11q chromosome. Carcinoids are hormonally active in about 10% of cases. A relative 5-year survival is 70%-90%. In our retrospective study conducted during the 2015-2019 period, we included 10 patients with carcinoid tumors of different locations who underwent surgical treatment with 5-year follow-up. The results of treatment were similar to those reported by other authors.

Key words: carcinoid, APUD cells, gastrointestinal tract

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INTRODUCTION

Carcinoid is a slow-growing tumor of neuroendocrine origin from enterochromaffin, amine precursor uptake and decarboxylation (APUD) cells. About 2/3 of carcinoid tumors arise in the digestive tract and make up 1% of the cancers of the gastrointestinal tract. The most common site is the area of the small intestine and appendix (more than 60%), then the rectum (15%), colon (5%-7%), stomach (2%-4%), liver (1%) and pancreas (2%-3%) (1-3). Carcinoid tumors are often asymptomatic until the late stage of the disease, and clinical presentation depends on the size, location, hormonal activity and presence of metastases. Obstruction occurs in about 1/3 of patients, followed by bleeding and appearance of carcinoid syndrome. The problems can last for years in the form of pain in the stomach and intermittent obstructions (4,5).

It most often occurs in people at a mean age of 61.4 years. Epidemiological data show that the incidence is 2.47-4.48 *per* 100,000 and in the last 2-3 decades the incidence has been increasing (1). The cause of carcinoid tumors is unknown, but a genetic factor can play a role (it was observed in multiple endocrine neoplasia (MEN) type 1, neurofibromatosis type 1, Von Hippel-Lindau disease) and inactivation of the tumor suppressor gene on the 11q chromosome (2).

About 10% of carcinoids are hormonally active and secrete excessive levels of hormones (the best known is serotonin 5-HT) (3).

Tumors smaller than 2 cm rarely metastasize (about 2%), unlike tumors larger than 2 cm (80%) (4,6). The metastatic disease that affects the liver can cause carcinoid syndrome, i.e., carcinoid crisis. The location of the tumor can be local, regional when the tumor has spread to the surrounding tissue or lymph nodes, metastatic when the tumor has spread to other parts of the body, and recurrent when the tumor has returned after treatment.

The diagnosis is based on clinical presentation, laboratory diagnostics (complete blood count, biochemical blood tests, 24-hour urine collection), gastrointestinal endoscopy, multi-slice computed tomography (MSCT), positron emission tomography, nuclear magnetic resonance, scintigraphy with somatostatin receptor, biopsy, angiogram (7).

Treatment and prognosis depend on the location of the tumor, size of the tumor, presence of metastases, and hormonal activity of the tumor (4). Treatment options for gastrointestinal carcinoids include surgery, radiation, chemotherapy, biological therapy, and hormone therapy. Relative 5-year survival is 70%-90% (1).

The prognosis of the disease is best in carcinoid of the appendix, and the prognosis of carcinoid of the small intestine is better than of carcinoid of the stomach and rectum (8).

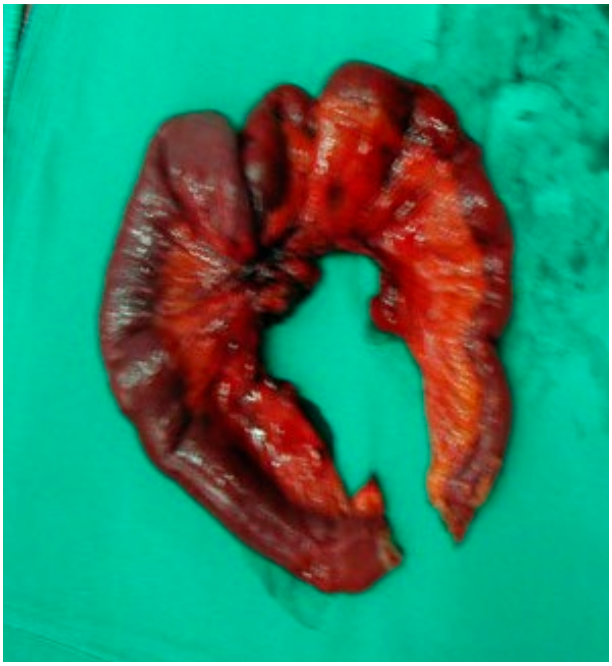

Figure 1. *Resected intestine with a tumor.*

MATERIALS AND METHODS

This retrospective study was conducted at Karlovac General Hospital, Department of Abdominal Surgery, during the 2015-2019 period. Data from medical records (history, letter of discharge) were evaluated. Data on 10 patients were included, 6 male patients in the age range of 55-69 years, and 4 female patients in the age range of 59-80 years. In 6 patients, carcinoid was diagnosed in the area of small intestine, in 3 patients in the area of stomach, and in 1 patient in the appendix. The disease was clinically manifested by bleeding from the digestive tract in 5 patients, obstruction of passage in 3 patients, subileus in 1 patient, and carcinoid syndrome in 1 patient.

The diagnostic methods we used were clinical presentation (gastrointestinal bleeding, passage obstruction, carcinoid syndrome), x-ray of the native abdomen (obstruction), gastrointestinal endoscopy, spiral MSCT, histopathologic diagnosis, immunohistochemical analysis (chromogranin, synaptophysin), and biochemical blood tests (serotonin, 5 HIAA in 24-hour urine).

Pathological macroscopic findings showed a 1.8-3 cm tumor growth, exophytic, partly ulcerated, mucosa with inflammatory changes of the epithelium, and preserved rough architecture (Figure 1). Histological findings showed solid clusters of trabecular and pseudo glandular formations, poorly differentiated uniform atypical epithelium with numerous mitoses, and hyperchromatic nuclei.

All patients underwent preoperative preparation, which included complete laboratory tests, x-ray of the heart and lungs, electrocardiogram, preoperative examination of the anesthesiologist (American Society of Anesthesiologists score) and were familiarized with treatment methods, possible complications, outcome and prognosis of the disease.

Operative procedures were performed by abdominal surgeons under general anesthesia, with early postoperative care in the intensive care unit and later on the abdominal surgery ward. Chemoprophylaxis was also carried out according to the scheme for abdominal surgery.

RESULTS

All 10 patients were operated on. In 6 patients, resection of the small intestine with a tumor, with formation of the side-to-side (LL) anastomosis was performed (Figures 2 and 3). In 3 patients, resection of the stomach with a tumor was performed according to the Billroth II method, and in one patient appendectomy was sufficient considering that the tumor size was less than 2 cm at the top of the apex of the appendix. In one patient, with the primary site in the stomach and metastatic liver disease, chemotherapy with Sandostatin was performed after gastric resection according to the Billroth II method.

All patients were monitored for 5 years. They had undergone MSCT of the abdomen and gastroscopy in pa-

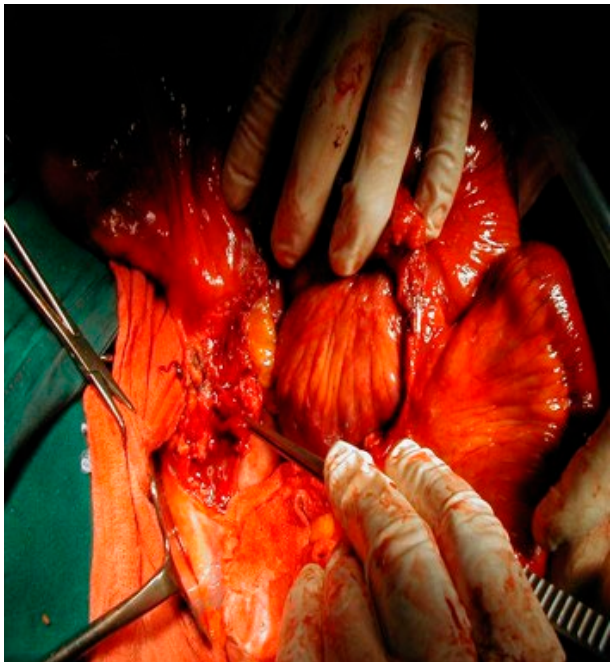

Figure 2. *Resection of the small intestine with a tumor.*

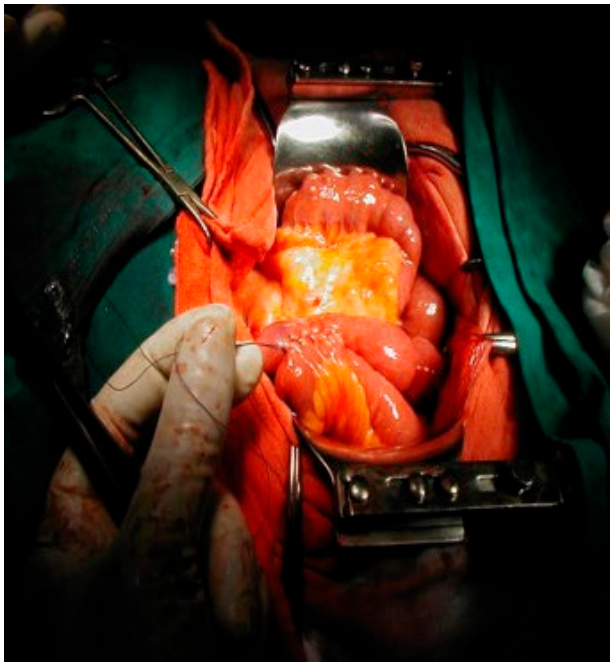

Figure 3. *Formation of the side-to-side (LL) anastomosis.*

tients with primary tumor sites in the stomach, with biochemical blood tests and determination of serotonin levels.

In 9 patients, there were no signs of the disease. In one of them, the disease relapsed in the stomach area with metastases in the liver two years after the operation; then, 6 cycles of chemotherapy with cisplatin and etoposide and Sandostatin were administered, after which the disease was under control. An 80-year-old female patient diagnosed with carcinoid of the stomach died within one year of gastric carcinoid diagnosis.

DISCUSSION

Carcinoid is a slow-growing tumor of neuroendocrine origin from enterochromaffin APUD cells. About 2/3 of carcinoid tumors arise in the digestive tract and make up 1% of the cancers of the gastrointestinal tract. The most common site is the area of small intestine and appendix (more than 60%), then the rectum (15%), colon (5%-7%), stomach (2%-4%), liver (1%) and pancreas (2%-3%) (1,3).

It most often occurs in people at a mean age of 61.4 years. Epidemiological data show that the incidence is 2.47-4.48 *per* 100,000 and in the last 2-3 decades the incidence has been increasing (1). The cause of carcinoid tumors is unknown, but a genetic factor can play a role (it was observed in MEN type 1, neurofibromatosis type 1, Von Hippel-Lindau disease) and inactivation of the tumor suppressor gene on the 11q chromosome (2). Carcinoids are hormonally active in about 10% of cases.

Gastrointestinal carcinoid tumors are clinically presented by obstruction, gastrointestinal bleeding, and secretion of excessive levels of hormones, the best known of which is serotonin 5-HT. Clinical presentation depends on the size, location, hormonal activity and presence of metastases (4,5). Tumors smaller than 2 cm rarely metastasize (2%), unlike tumors larger than 2 cm (80%) (4).

In our study, we showed that the mortality in non-metastatic disease was extremely low and that adjuvant chemotherapy in metastatic disease could have a significant effect on prolonging life.

CONCLUSION

Gastrointestinal carcinoid is a slow-growing tumor originating from neuroendocrine APUD cells and occurs most often in the small intestine and appendix, more than 60% of cases. Surgical treatment is the method of choice for non-metastatic disease, while lymphadenectomy and wide excision are unnecessary for localized disease. In the case of extended and metastatic disease, in addition to surgical treatment, adjuvant chemotherapy is also considered, which greatly prolongs median survival.

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SAŽETAK

NAŠA ISKUSTVA U LIJEČENJU KARCINOIDNIH NOVOTVORINA GASTROINTESTINALNOG TRAKTA, OPĆA BOLNICA KARLOVAC – RETROSPEKTIVNO ISTRAŽIVANJE

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Karcinoid je sporo-rastući tumor neuroendokrinog podrijetla iz enterokromafinih APUD stanica. Oko 2/3 karcinoida nastaje u probavnom traktu. Čine oko 1% raka u probavnom traktu, a primarno sijelo u 50 % karcinoida je u području tankog crijeva. U ranom stadiju bolesti bolesnici su često bez simptoma, što otežava postavljanje dijagnoze. Najčešće se javlja u osoba srednje dobi od 61,4 godine. Epidemiološki podatci pokazuju da je incidencija 2,47-4,48 na 100 000 stanovnika, a posljednjih 2-3 desetljeća incidencija je u porastu. Uzrok karcinoidnih tumora je nepoznat, ali ulogu može imati genetski čimbenik (uočeno je kod MEN tip 1, neurofibromatoze tip 1, Von Hippel-Lindau bolesti) te inaktivacija tumor supresorskog gena na kromosomu 11q. Karciniodi su u oko 10 % hormonski aktivni. Relativno petogodišnje preživljavanje je 70 %-90 %. U našoj retrospektivnoj studiji u razdoblju 2015.-2019. godine prikazujemo 10 bolesnika s karcinoidnim tumorom različitog sijela, koji su kirurški liječeni te praćeni tijekom 5 godina. Rezultati liječenja su slični podatcima koje iznose drugi autori.

Ključne riječi: karcinoid, stanice APUD, probavni trakt