ILEUS CAUSED BY CARCINOID TUMOR OF SMALL INTESTINE - A CASE REPORT

Saša Dragović, Nebojša Denić, Miloš Kostov and Marija Jelić

Carcinoids (argentoffinoma) are the tumors of enterochromatic cells which can appear anywhere in the gastrointestinal tract. They belong to the group of neuroendocrine tumors (NET). The term was introduced by Obendorfer in 1907. Case report. M.Z., 70-year-old patient had the first signs of the illness (diffuse abdominal pain accompanied by bloating and constipation) a month before he was hospitalized at the Surgical Ward of the Military Hospital in Niš. He was examined at the Gastrointestinal Ward of the Department of Internal Diseases and released to have home care because of the improved overall status. A month later he was hospitalized again at the same department because of strong subocclusive complaints, throwing up and lack of winds and defection. As ileus was diagnosed, the patient was moved to the Surgical Ward where he underwent laparatomy. The conglomerate of small intestine covered with small whitish tumorous changes was detected. The small intestine was resected and send to pathohistological verification which revealed a carcinoid tumor. Carcinoid is a rare type of tumour of the digestive tract and it usually is detected accidently during surgeries such as appendectomy, etc. Since health care centres in Serbia lack technical equipment, when detected, the disease has already advanced and survival period is short. Acta Medica Medianae 2012;51(3):47-51.

Key words: carcinoid, gastrointestinal tract, neuroendocrine tumours, serotonin, carcinoid syndrome

Introduction

Carcinoids (argentaffinoma) are the tumors that arise from the enterochromaffin cells and can occur anywhere in the gastrointestinal tract. This is a group of neuroendocrine tumors (NET) (1-4,11). The name „carcinoid“ was introduced by Obendorfer in 1907, with the aim to delimit a special group of small intestine neoplasms, which act less aggressive than most of intestinal adenocarcinoma (1). These are the most commonly well-differented endocrine neoplasms with morphological characteristics, containing most of the cells with cytoplasmic secretory granules which are indentified by histochemical, electron microscopy, and immunohistochemical and molecular biology techniques (1-3) They belong to the group of a very rare gastrointestinal tract cancers (1-10). In the last 25 years at the Military Hospital in Niš, Department of Surgery, there have not been the cases of gastrointestinal tract carcinoids in patients operated for any reason. Carcinoids are the tumors which are found in the gastrointestinal tract in 90% of cases, of which in 60% they affect the appendix, small intestine in 25%, and the the stomach and rectum in 2-5% cases. (3,4). This neoplasm is characterised by increased secretion of 5-HT serotonin (1-2,11). There is a different biological behavior of appendiceal carcinoid compared to small-bowel carcinoids (1,2,4,9). Small intestine carcinoid metastases most commonly occur in the regional lymph nodes and liver (1-3,7).

Small intestine carcinoid is clinically manifested in two ways:
1. Causing partial or complete intestinal obstruction (Ileus) or,
2. As the "carcinoid syndrome" described by Baeza in 1969, characterized by the following symptoms: "flash" - facial flushing, bronchospasm, hypotension, diarrhea, edema, and ascites.

All this occurs due to a sudden secretion of serotonin, bradykinin, and other vasoactive substances.

Histopathological features of the tumor: on the affected segments of the digestive tract the changes are macroscopically observed as small whitish-gray nodules measuring up to 4 centimetres in radius (1-3,9,11).

Frequently, a marked process of penetration deeply into the tissue can be noted, with the infiltration of mesenterium, as was the case
with our patient. Based on the histological structure of the modified Soga classification, these tumors can be divided into five groups (2):

- Type A – includes tumors with solid, nodular structure, the so-called "classic" or "insular" type (22.6%);
- Type B – characterized by trabecular or ribbon-like structures (21%),
- Type C - tubular, glandular or rosette-like structures (3.2%);
- Type D - poorly differentiated or atypical tumors (9.2%);
- Type E - mixed type tumors (43%);
- Type F – mucocellular type cells with abundant amphicrine cells ("adenocanceroids" or "goblet cell carcinoid" tumors).

Argentoffinoma metastasize to the lymph nodes, liver, lungs and bones.

They are usually of small dimensions and rarely manifest the clinical signs of ileus, however, in some cases their clinical manifestations can reach those of complete ileus, and they are most commonly found during surgery and subsequent histological verification.

**Case report**

Patient M. Z., 70 years old., had the first significant complaints a month before coming to our department. He felt a diffuse pain throughout the abdomen, accompanied by bloating and aggravated discharge of intestinal contents. He was examined at the Department of Gastroenterology in the Military Hospital in Niš. During examination, rectoscopy and irrigography were performed, however, without changes observed. The symptoms withdrew, and he was discharged to receive the home care. A month later, he was hospitalized at the Departement of Internal Diseases for marked subocclusive disorders, vomiting, lack of gases and defecation. Abdominal radiographs revealed the hydroaeric levels (Figure 4), which persisted, so that he was transferred for histopathological verification (Figure 2). Histological processing revealed the following: Macroscopic findings (resected small intestine): polyloid mucosal tumor change, measuring 25x20 mm, uneven granular white-yellow area, on the cross-section the material is of fibrous and homogeneouse structure, yellowish grey in color, of elastic and viscous consistency, with infiltration of the gut wall and mesentery (Figure 4). Tissue samples were histopathologically processed. For routine histological processing, the material was fixed in 10% buffered, neutral formalin, embedded in paraffin, cut with a microtome into slices 5 μm thick and treated with hematoxylin-eosin (H & E) method. For immunohistochemical verification of tumor neuroendocrine nature (hormonal markers), streptavidin-biotin-peroxidase technique was performed according to standard procedure (DAKO, LSAB Kit), using monoclonal antibodies to chromogranin A (Clone DAK-A3) (DAKO, Denmark). As a chromogenic substrate 3,3'-diaminobenzidine (DAB) was used and the sections contrasted with Mayer’s haematoxylin. Light microscopy showed that the tumor was composed of dense cells with solid growth, round regular nuclei and irregular cell boundaries (Figure 5). Immunohistochemically, an intensive enterochromophine reaction to chromogranin A was observed in the cytoplasm (Figure 6). The number of mitoses per 10 high-power fields (High-Power Filed HPF) per sample ranged from 2 to 5 mitotic figures/10 HPF, which corresponds to a moderately differentiated neuroendocrine carcinoma (G2). The definitive histopathological diagnosis was: carcinoma neuroendocrineum (malignant carcinoid tumor) multiplices / tres exulcerans infiltrativum intestine complexion et mesenterii, G2 (mitotic 2-20/10HPF) pT3c/ dN0MxV1L1 (TNM staging, Consensus Conference "ENets" 2006 Rome, Italy).

After one month, a reoperation for ileostomy closure was performed, supplemented by the right hemicolectomy and metastasectomy of the changes in the the second liver segment; digestive tract continuity established by latero-lateral ileo-transverse anastomosis. Definitive histopathological finding pointed to metastatic changes in the liver – carcinoma neuroendo-crinicum metastaticum in hepatie. The postoperative course was normal, established intestinal passage, feeding by mouth, wounds healed, stitches removed on the 14th postoperative day when he was discharged from hospital. Laboratory: except decrease in serum albumin to 21 and protein to 37.5, all other results were similar to the preoperative ones. Total length of hospital stay was 37 days.

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Figure 1. Hydroaeric level on abdomen nativ Ro.

Figure 2. Conglomeration of the small bowel loops caused by a carcinoid tumor.

Figure 3. Solitary metastasis in the left liver lobe.

Figure 4. The resected portion of the small intestine and mesentry associated with tumor.

Figure 5. Carcinoid (neuroendocrine) tumors, solid growth prospects (H&E, x200).

Figure 6. Positive cytoplasmic immunoreactivity for chromogranin A (L SAB, x200).
Discussion

Gastrointestinal tract carcinoid tumors can develop anywhere and are usually multicentric and divided on the basis of their origin into those that occur in the foregut, midgut and hindgut (1-11). 60-80% of them grow out of the midgut, mainly in the distal ileum and appendix, 25% in the rectum and partly in the colon, and the rest of them in other segments of the GIT (liver, bile ducts, pancreas) (1,2,7-8,10). Outside the GIT, the carcinoid tumors most usually affect the respiratory Airways and lungs (1,2,6) but can be found in the kidney, ovary, thymus and heart muscle (1,2,4,5). A considerable number of carcinoid tumors are found accidentally, i.e. the patients are asymptomatic. Symptoms usually cause intestinal obstruction, intestinal infarction or bleeding in the GIT (1-3,9). Local intramural invasion in these slow-growing tumors does not have the same significance as in adenocarcinoma, so that the differentiation among benign and malignant tumors is based on the presence or absence of metastases (1,2,9). More than two-thirds of these tumors that are larger than 2 cm have metastases at the time of detection (1,2) (Figure 5). 85% of all carcinoid tumors, which are characterized by deep local tissue penetration, metastasize in some stage of the disease with a fatal outcome in 65% of cases, whereas in tumors with superficial invasions that percentage is only 1% (1,2). When carcinoid syndrome occurs, survival period is less than one year (1,2). The aforesaid indicates that successful treatment of carcinoid tumor requires early detection. Diagnosis is based on anamnesis, clinical examination, biochemical analysis of serotonin in the blood and urine, diagnostic procedures such as endoscopy, barium gastroenteroscopy, radiography of the heart and lung (US, CT, MRI, angiography), endoscopic ultrasound, positron emission tomography (PET), scintigraphy (1-11). Given that in our country only a few tertiary health institutions are technically equipped for adequate diagnostics, timely diagnosis of carcinoid tumors is brought under question, and thus the success of treatment, because at the time of clinical manifestations, the disease has already advanced, with survival period up to one year.

Conclusion

Carcinoid (argentaffinoma) is an extremely rare malignant tumor of the digestive tract, belongs to the group of NET, most commonly affecting the appendix, then intestine, colon and rectum. It produces vasoactive substances, primarily 5-HT serotonin, bradykinin, etc. It often causes ileus and metastasizes into the regional lymph nodes, liver, lungs and bones. Carcinoid is usually detected accidentally, during surgery, e.g. appendectomy, etc. At the level of secondary health care, it is not possible to use diagnostic methods because of poor technical equipment (levels of serotonin, scintigraphy, PET scen etc..) and diagnosis is usually reached by laparotomy and histopathologic verification. The same was demonstrated in this case describing the distal ileum carcinoid, which caused ileus with the presence of metastases in the mesentery of the small intestine and the left lobe of the liver, which was discovered after an explorative laparotomy.

References

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Ključne reči: karcinoid, gastrointestinalni trakt, neuroendokrini tumori, serotonin, karcinoid sindrom