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Tubular carcinoid tumor of the appendix – a clinical case

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Abstract. Objective: We present the clinical case of a young patient of 18 years old male, who was admitted in the surgical department of Cluj-Napoca County Hospital with symptoms of acute appendicitis. The appendectomy was performed, while during the surgery the macroscopic appearance of the appendix was of a slight catarrhal appendicitis, with no sign of a tumor, but the appendix was not sectioned longitudinally. The histopathological examination revealed a tubular carcinoid tumor on the tip of the appendix. We discuss the indication of a more extended surgery for such a tumor. Results: The patient is 18 months after surgery with no signs of tumor extension. Conclusions: The appendectomy is enough for carcinoid tumors of the tip of the appendix, of small sizes, without vascular or perineural invasion.
Key Words: young patient, acute appendicitis, carcinoid appendiceal tumor.

Rezumat. Obiectiv: Prezentăm cazul clinic al unui tânăr de 18 ani internat în serviciul de chirurgie al Spitalului Clinic Municipal Cluj-Napoca cu simptomatologia unei apendicite acute. S-a practicat apendicectomia de urgenţă, intraoperator aspectul macroscopic fiind al unei apendicite catarale, fără semne de tumoră, însă menţionând faptul că apendicele nu a fost secţionat longitudinal. Examenul histopatologic a evidenţiat un carcinoid tubular al vârfului apendicular. Luăm în discuţie indicaţia unei chirurgii extinse pentru acest tip de tumoră. Rezultate: Pacientul se află la 18 luni după intervenţia chirurgicală, fără semne de extensie tumorală. Concluzii: apendicectomia este suficientă pentru tumorile carcinoide apendiculare de mici dimensiuni, localizate la vârful apendicelui, fără invazie vasculară sau perineurală.
Cuvinte cheie: pacient tânăr, apendicită acută, carcinoid apendicular.

Introduction. We analyzed the case notes of an 18 years old boy, M. M., admitted in the surgical department of Cluj-Napoca County Hospital in July 2009 because of moderate pain in the right iliac fossa, discrete nausea, and slight alteration of the general status from the previous day before admission. The laboratory data showed a slight leucocitosis. The patient underwent direct appendectomy in rahidian anesthesia. The vermiform appendix had a discrete wall edema and a congestion of the submucosal vessels. The postoperative evolution was very good and the patient regained transit in the first postoperative day and was discharged in the second day. The pathological examination revealed a tubular carcinoid tumor of the tip of the appendix, a tumor of 0.5 cm in diameter, not beyond the submucosal layer, made of little tubular cells with pale eosinophilic cytoplasm some of them containing mucine, round and ellipsoidal nuclei with small nucleoli. The tumor cells showed focal positivity for chromogranine. It was not found either angiolymphatic invasion signs or perineural tumor infiltration. The mesoappendix and the margins of the appendix were tumor free. We proposed to the patient and his family to perform a right hemicolectomy but they refused. There was no other adjuvant therapy. The patient underwent a CT scan after surgery which revealed no tumor spread. Eighteen months have passed since the initial surgery and the patient is symptom-free. A new CT scan was performed and there were no signs of tumoral extension.

Discussion. Carcinoid tumors are a slow-growing cancer that can arise in many places throughout the human body. Gastrointestinal carcinoid accounts for more than 95% of all carcinoids and for 1.5% of all gastrointestinal tumors. They usually appear in the gastrointestinal tract (appendix, stomach, small intestine, colon and rectum) and in the lungs. Carcinoid tumors develop in neuroendocrine cells, from enterochromaffin cells of Kulchitsky, which are considered neural crest cells situated at the base of the crypts of Lieberkühn, performing some nerve cell functions and some hormone-producing endocrine cell functions (adrenaline, serotonin histamine, bradykinin and kallikrein). After reviewing the data about the carcinoid syndrome, Santacroce remarked that the first description of a carcinoid tumor was in 1888 by Lubarsch, even if only in 1907 Oberndorfer called this group of small, benign-appearing tumors karzinoide tumoren (carcinoid) (Santacroce 2010). Also in 1980, the World Health Organization (WHO) applied the term carcinoid to all tumors of the diffuse endocrine system (synonymous with amine precursor uptake and decarboxylation [APUD] and neuroendocrine cell system).

These malignant tumors of the appendix still remain rare, but malignant carcinoid tumors are the most common, accounting for 85% of all appendiceal neoplasms, occurring in about one out of every 300 appendectomies. Appendiceal carcinoids are more common in women by a ratio of 2:1 or 3:1 and the average age is 4th or 5th decade of life.

Malignant carcinoid syndrome does not generally appear to be hereditary. Kulke et al (2008) studied the genetic alterations in small bowel carcinoid tumors and found a loss of all or most of chromosome 18. Heterozygosity was also lost on chromosome arms 9p and 16q.

Among the factors that are able to increase the risk of carcinoid tumors there are: age (older adults are more likely to be diagnosed with a carcinoid tumor than young people or children), female sex, family history (MEN multiple endocrine neoplasia type I in which there are tumors of the endocrine system), tobbacco, Zollinger-Ellison syndrome. Khan et al (2007) advocate even to perform appendectomy whenever it is operated a colo-rectal cancer, knowing that an individual with colorectal cancer has a 3 percent risk of synchronous colonic neoplasia and further 2 to 3 percent risk of metachronous cancer. They conducted a retrospective study on 169 patients who underwent colo-rectal resection and appendectomy, and they found 7 (4.1%) of 169 appendices with abnormalities: 3 mucinous cystadenomas, 2 cystadenocarcinomas, 1 carcinoid tumor, and 1 villous adenoma.

The complications of the disease consist of: gastric peptic ulcers, carcinoid syndrome (when the tumor cells secrete hormones), carcinoid heart disease (the hormones secreted by tumor cells can cause thickening of the lining of heart chambers, cardiac valves and heart failure) and Cushing's syndrome (a lung carcinoid tumor can produce in excess cortisol).

The diagnosis may be established using blood tests, urine tests, imaging tests (computerized tomography, magnetic resonance imaging, positron emission tomography, ultrasound, octreotide scan and X-ray, endoscopy (upper digestive endoscopy, bronchoscopy, colonoscopy or capsule endoscopy) and biopsies.

The treatment depends on the tumors location, presence of metastases, types of hormones secreted by tumor cells, patient overall health and patients' own preferences. Surgery is the treatment of choice when disease is early detected and the tumor may be completely removed. When the tumor is in an advanced stage, and cannot be completely removed, we may try to take out as much as possible to help control the symptoms and signs. For liver metastases it could be performed hepatic resection, hepatic artery embolization, radiofrequency ablation or cryoablation of the cancer cells.

According to current guidelines, an appendectomy may be performed for small carcinoid tumors less than 1 cm. It is stated that reasons for more extensive surgery than appendectomy are tumor size more than 2 cm, lymphatic invasion, lymph node involvement, spread to the mesoappendix, tumor-positive resection margins, and cellular pleomorphism with a high mitotic index (Fornaro et al 2007). The tumor size is still the main factor to produce an increased risk to develop metastasis for tumors greater than 2

cm, even if there is no evidence demonstrating a survival benefit for right hemicolectomy over simple appendectomy in patients with carcinoids greater than 2.0 cm in diameter. (Fornaro et al 2007).

O'Donnell et al reviewed 11 cases operated in a period of ten years, in which they have carcinoid appendiceal tumors and goblet-cell morphology, recommending the right hemicolectomy as the procedure of choice (O'Donnell et al 2007). However, appendectomy may be suitable for small appendiceal carcinoid tumors less than 2 cm in diameter at the tip of the appendix, with a low proliferative index, without angiolymphatic or mesoappendiceal extension. In this period of time they (O'Donnelll et al 2007) had also eight patients with adenocarcinomas and three patients with lymphomas of the appendix, the follow-up revealing that the patients with classical carcinoid tumours (CCT) had better outcomes[i] than patients with the goblet cell carcinoid, adenocarcinoma and lymphoma.

Another study performed by Groth et al, on 576 cases of appendiceal carcinoids, found that significant predictors of nodal involvement are: the tumor size of more than 2 cm and the histology (pure carcinoid tumors). It is helpful to identify which patients would benefit from a right hemicolectomy instead of an appendectomy alone. This study did not demonstrate a significant difference in adjusted survival rates between the two surgical procedures (Groth et al 2010) Usually, in children most appendiceal carcinoids present without lymph node metastasis, but there are cases with little tumor accompanied by lymph node metastasis (Cernaianu et al 2010).

Goblet cell carcinoids are uncommon tumours with histological features of both adenocarcinoma and carcinoid tumour. Maes et al reviewing the literature sustain that two-stage surgery for goblet cell carcinoid is advocated. But the debate still continues as to whether the goblet cell carcinoid should be treated by appendectomy alone, as for most carcinoids, or by right hemicolectomy, as for the appendiceal adenocarcinoma (Maes et al 2008).

In the case of carcinoid syndrome signs and symptoms depend on which chemicals the carcinoid tumor secretes into the bloodstream: skin flushing, facial skin lesions, diarrhea, difficult breathing and tachycardia. The carcinoid syndrome may produce complications such as carcinoid heart disease (a thickening of the heart valves), bowel obstructions and carcinoid crisis (flushing, low blood pressure, confusion and breathing difficulty).

Metastatic carcinoid tumors may be diagnosed by clinical findings and/or by elevated levels of 24-hour urinary 5-hydroxyindolacetic acid (5-HIAA). 5-HIAA is a metabolic product of the serotonin produced by the tumor. False positive 5-HIAA tests can be caused by foods such as bananas, avocados and pineapple, and by certain drugs.

Drugs that block the action of serotonin and/or histamine may be successful in relieving the symptoms. Octreotide (Sandostatin), which is a somatostatin agonist, may slow the rate of growth of carcinoid tumor and reduce signs and symptoms of carcinoid syndrome. Octreotide controls skin flushing and diarrhea in most people with carcinoid syndrome, but it has side effects, which include abdominal pain and bloating, diarrhea and nausea, though these effects may subside with time. Diarrhea and abdominal cramping may be treated with hydration and diphenoxylate with atropine.

Surgery is the treatment of choice whenever is possible to remove tumors or most of the tumors. Appendiceal, rectal, and small bowel carcinoids are treated surgically. Liver and lung carcinoids may also be treated surgically in some cases.

Medical therapy, using Interferon alfa, which stimulates the body's immune system to work better, is sometimes implemented in order to slow the growth of carcinoid tumors and to relieve symptoms. This drug may be prescribed alone or in combination with octreotide. Interferon also causes significant side effects, including fatigue, bone pain, headaches and vomiting.

Radiation and chemotherapy are not effective, but they may help relieve some of the more serious symptoms caused by carcinoid tumors. It has been reported a 30% limited response to chemotherapy. The metastatic tumors may be removed surgically. It has been reported 90% overall 5 year survival.

Conclusions. Carcinoid tumors appear more frequently in the appendix, and many times they are diagnosed after an appendectomy performed for acute appendicitis. For small tumors localized at the tip of the appendix, with no metastasis, a low proliferative index, no angiolymphatic and mesoappendiceal extension it is consider to be enough the appendectomy, rather than right hemicolectomy. For the clinical case we presented we consider that appendectomy was enough because it was a little tumor located at the tip of the appendix and it had no angiolymphatic or perineural invasion signs, no metastasis and also it was the patient's and his family preference.

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