Carcinoid tumour of the gallbladder: laparoscopic resection and review of the literature

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Abstract

Carcinoid is a tumour with the ability to produce bioactive amines and polypeptides, most frequently serotonin. Typical symptoms include diarrhoea and facial flush. Carcinoid of the gallbladder is very uncommon, and only about 40 cases of that particular tumour location have been reported in the literature worldwide. Herein we describe a case of a 52-year-old patient who underwent cholecystectomy for chronic cholecystitis caused by gallstones. As the patient presented no symptoms of carcinoid, diagnosis was made on histopathological examination. The patient has been living for 10 years after cholecystectomy now, free from tumour recurrence, as confirmed by follow-up examination.

Key words: *carcinoid, gallbladder, laparoscopic cholecystectomy.*

Introduction

Carcinoid is a neoplasm originating from neuroendocrine Kulchitsky cells. They are capable of accumulation and excretion of bioactive amines and peptides. Most often these are serotonin, gastrin and vasoactive intestinal peptide [1, 2]. Carcinoid for the first time was described in 1929 [3]. Carcinoid is a rare neoplasm, and makes up less than 2% of all gastrointestinal tumours [4]. It is usually located in the appendix (35%), small intestine (25%), colon and rectum (19%), oesophagus and stomach (2%) or lungs and bronchi (14%) [5]. The gallbladder and extrahepatic bile ducts are extremely rare carcinoid locations. Tumours of this location account for 0.07-2% of all gastrointestinal tract carcinoids [4, 6, 7]. So far, there was case report on gallbladder carcinoid in the Polish literature.

Case report

The fifty-two-year old patient was qualified for laparoscopic cholecystectomy for symptomatic cholecystolithiasis. He had complained of biliary colic attacks for a few previous months, with occasional nausea and vomiting, mostly following dietary faults. For 5 years the patient had been treated for arterial hypertension (WHO stage II/III) and for ischaemic heart disease. No abnormalities were found on physical examination. Abdominal ultrasound revealed gallstones and liver steatosis, and ECG showed signs of cardiac ischaemia. Laparoscopic cholecystectomy was performed on 25 October 1999. Operative procedure and postoperative course were uneventful. The patient was discharged on the 2nd postoperative day. On histopathological examination of the removed gallbladder typical inflammatory changes were found in its thickened

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wall; however, a border of one slide contained neoplastic infiltration (Figures 1, 2). A striatal infiltrate consisted of uniform cells (Figure 3). Lack of mitotic figures and the substantial proportion of cells with fusiform nuclei drew the pathologist's attention. The whole picture was suggestive of carcinoid. Ten years following surgery, no signs of neoplasm recurrence were found.

Discussion

There are almost 80 cases of gallbladder carcinoid cases described in the literature. This cancer occurs more often in women than in men [1, 8, 9]. Mean age at diagnosis was 60 years [1, 8]. The majority of patients are operated on not for suspicion of cancer but for cholelithiasis, just as patients with carcinoid of the appendix undergo appendicectomy not for tumour, but for acute appendicitis [10]. Gallstones may accompany 89% of gallbladder carcinoids [1]. Similarly, in our patient chronic cholecystitis from biliary stones was an indication for surgery. Carcinoid diagnosis is usually made on routine histopathology examination of the gallbladder, following its removal for lithiasis [9, 11]. There is a small group of patients, 14-26% of all carcinoids, where suspicion of neoplasm was made on ultrasound prior to surgery [8, 9]. Preoperative diagnostics can be supplemented with computed tomography (CT), but both CT and ultrasound serve to establish the stage of disease and not to differentiate its character or to diagnose carcinoid [12, 13]. Nor is the intraoperative picture usually suggestive of carcinoid. There is a notion however, where in 22 cases of carcinoid, 17 tumours were diagnosed during surgery and 5 during autopsy, but this is rather unusual [8].

Carcinoid may produce substances affecting the vascular system, the heart, lungs and digestive tract, which occurs infrequently [8]. Typical serotonin-dependent carcinoid symptoms are: diarrhoea, paroxysmal flushing of face and upper body, increase in arterial blood pressure, cardiological problems and abnormal respiration with wheezing [10]. Most often (60%) carcinoid syndrome is caused by a small bowel tumour [8]. Carcinoid syndrome is usually not seen in gallbladder carcinoid. All of the 17 cases were symptom-free [8], which was also the case in our patient. Another study shows that symptomatic disease does not occur more often than in 4% of all carcinoid cases [1]. Other authors

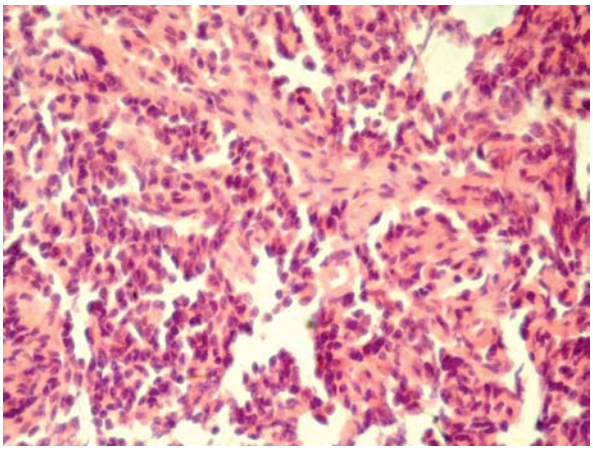

Figure 1. Carcinoid of the gallbladder, HE staining, magnification 400×

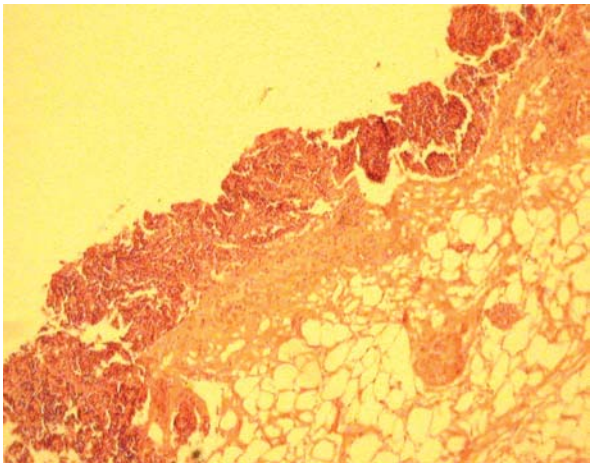

Figure 2. Carcinoid of the gallbladder, HE staining, magnification 50×

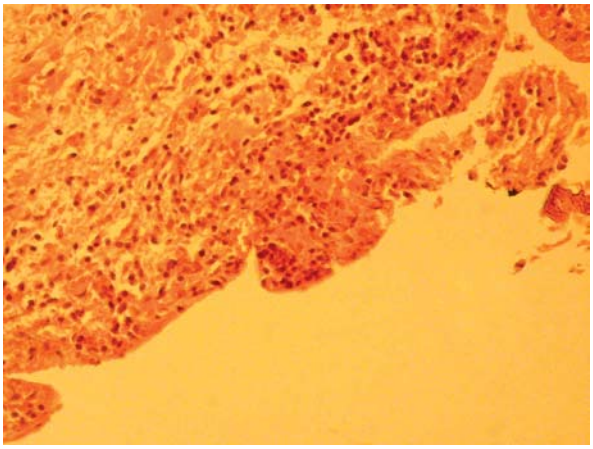

Figure 3. Carcinoid of the gallbladder, HE staining, magnification 200×

point out that carcinoid syndrome develops mainly in patients with metastases to the liver [8, 9].

Two histological classifications of carcinoid are used: Tahara's and WHO [14, 15]. Histopathological finding of carcinoid of the gallbladder in the majority of patients is accompanied by chronic or, less often, acute cholecystitis. Similarly, in our patient chronic inflammation of the gallbladder mucosa was found. It is believed that chronic cholangitis results in intestinal metaplasia of the mucous membrane, which in turn increases the number of Kulchitsky cells and promotes carcinoid development [16]. Within the gallbladder, carcinoid happens to coexist with intestinal-type adenocarcinoma [11, 17, 18]. Comorbidity with adenocarcinoma can be as common as 50% of these carcinoid cases [14]. Argyrophilia and neurosecretory granulations are often present in both cell types and confirm the close relation of both neoplasms [18, 19].

Surgery is the treatment of choice for carcinoid of the gallbladder. Cholecystectomy is a sufficiently extensive procedure for the majority of affected patients. Most of the operations were done with classical open access [9, 13]. So far, only 2 cases treated with laparoscopy have been described [13]. The patient presented above is the third case treated with laparoscopy. During laparoscopic cholecystectomy, detailed assessment of the gallbladder, surface and hilum of the liver should always be performed. The wall of the gallbladder should not be damaged and neoplastic tissue should not be grabbed with forceps. When the gallbladder is divided from the liver, cancerous infiltration of the liver ought to be recognized. If the carcinoid affects the full thickness of the gallbladder wall or infiltrates liver parenchyma, some authors advise open cholecystectomy with hepatoduodenal ligament lymphadenectomy. Such procedures are completed with 2 cm adjacent liver margin resection or with right hepatectomy [13]. Such a situation, as statistics show, is unusual and may involve 13 to 22% of all patients operated on for carcinoid [8, 9]. Typically however, the correct diagnosis is made after the surgery on histological examination. This was also the case in 4 of 14 patients in whom the decision of re-laparotomy and hepatoduodenal ligament lymphadenectomy was made [9].

Other methods, i.e. radiotherapy and chemotherapy, have limited value [9]. In the literature an opinion that these tumours respond poorly to both chemo- and radiotherapy is common. There was a case of adjuvant chemotherapy following cholecystectomy with liver resection and radiotherapy for locally advanced carcinoid [20]. Cytosine arabinoside and 5-fluorouracil were administered, then chemotherapy with mitomycin C, doxorubicin and 5-fluorouracil was given for tumour progression. A short-term positive response was seen, followed by disease progression, and the patient passed away 21 months following surgery. Two other patients with locally advanced carcinoid and generalized disease were treated with chemotherapy [mechlorethamine, methysergide (Sansert)]. One patient received chemotherapy intravenously, the other into the hepatic artery [21, 22]. The first patient died after 6 months and the latter after 35 months. If the above-mentioned methods fail, the somatostatin analogue lanreotide can be given. The agent was given in 30 mg doses every 2 weeks for 6 months to carcinoid patients with 3 or more bowel motions a day and/or 1.5 or more episodes of upper body flushing [2]. Regression of symptoms, defined as a 50% decrease in symptom occurrence, was noted in 38% of patients. Although tumour size decreased only in 6% of patients, no tumour enlargement was seen in 81% of cases.

Results of treatment of carcinoid are not available in detail from the literature. In a meta-analysis of 22 patients with carcinoid, data concerning survival were published only for 13 of them [8]. Four patients died in the postoperative period (day 1, 3, 10 and 22), and four died from generalization of the disease (3, 3, 9 and 16 months following surgery). The rest of the patients were alive at data collection. Their survival time was 12 months – 7 years (2 patients had survived more than 5 years). Another publication on 18 patients operated on in various centres showed that their mean survival was 11 months [9]. Five-year survival can be as high as 30% [1]. Prognosis in carcinoid is dependent on tumour size and location. If the primary location is within the appendix, only 2% of patients develop metastases. Extra-appendicular site of carcinoid is believed to confirm its malignant character [8]. Metastases at diagnosis of carcinoid are found in 60% of patients with colonic and 30% with extrahepatic biliary duct location of the disease [8]. In carcinoid of the gallbladder, metastases or infiltration are seen in 43% of patients [1, 13]. Tumour size is another important factor [7]. Metastases of tumours smaller than 1 cm occur in 6-28% of patients and 40% of then die within 2 years [8, 13]. If carcinoid exceeds 2 cm, occurrence of metastases increases

to 70% [8]. If carcinoid diameter is 3 cm or more at diagnosis, metastases are present in every patient [13]. One meta-analysis showed that in each of 14 metastatic carcinoid cases tumour size was over 1 cm [14]. The prognosis in carcinoid depends on depth of gallbladder wall infiltration. The authors have noticed that if infiltrate reached the muscularis propria, 25% of patients died within 26 months. If the serosa was affected, 44% of patients passed away within a year [13].

Conclusions

1. Carcinoid of the gallbladder is a rare neoplasm of the gastrointestinal tract.
2. Tumour at this location usually does not cause symptomatic carcinoid syndrome.
3. Laparoscopic cholecystectomy is a sufficient method of treatment in early stages of carcinoid.

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