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Poorly Cohesive Cells Carcinoma of the Gallbladder

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Introduction

The majority of gallbladder tumours are adenocarcinomas with varying degrees of differentiation [1]. Poorly cohesive cells carcinoma is an extremely rare type of gallbladder carcinomas [2].

In the gastrointestinal system, carcinomas with infiltration by isolated cells or small cell clusters, that either contain Signet-ring cells or not, are now referred, according to the WHO 2010 classification as “poorly cohesive cells” type [3].

The infiltration of poorly cohesive cells should account for more than 50% of the tumour [4]. This tumour has as a characteristic the rapid dissemination in the abdomen, which may make it challenging to look for the primary site [5].

We report the case of a 60-year-old female patient presenting with a gallbladder poorly cohesive cells carcinoma, the patient deceased 15 days after a cephalic duodeno-pancreatectomy with a hepatic bisegmentectomy and a right colectomy. Death was secondary to due to septic choc.

Patient and observation

A 60-year-old female patient with a medical history of non-insulin-dependent diabetes mellitus under oral hypoglycemic agents and hypertension under Calcium channel blockers, hospitalized for transfixing epigastralgia with vomiting associated with moderate upper and lower digestive haemorrhage. Clinical examination revealed a blood pressure of 120 / 70 mmHg and a



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heart rate of 70 bpm. The abdomen was distended with epigastric sensitivity, without hepatosplenomegaly. Rectal examination revealed presence of blood, with no palpable mass.

The biological evaluation showed a lipaseemia at 437, K⁺ at 3.4meq / l, CRP at 1.26, hemoglobin at 13.4 mg / dl, White Blood Cells (WBC) at 8200, albuminemia at 47g / l, serum creatinine at 7mg / l, PR at 100%, with no associated cytolysis.

Oeso-gastroduodenal fibroscopy was performed showing stage B oesophagitis, congestive bulbitis, and post-bulbar stenosis. Biopsies were performed at the level of the stenosis; histopathological examination did not reveal tumoural proliferation.

A CT scan was performed showing a locally advanced bilio-digestive tract process at the gall bladder of approximately 7cm of diameter, extending to the duodenum, colon, pancreas and liver. (Figure 1).

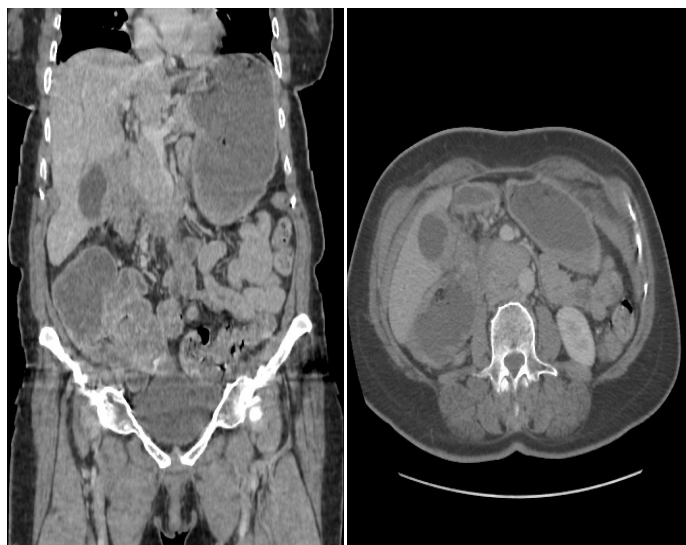


Figure 1: A CT scan showing a locally advanced bilio-digestive tract process at the gall bladder of approximately 7cm of diameter, extending to the duodenum, colon, pancreas and liver.

The patient subsequently benefited from cephalic duodeno-pancreatectomy with right hemicolectomy and hepatic bi-segmentectomy.

Macroscopic examination showed the presence of a whitish tumour with a hard consistency, measuring 7x5x7 cm, attached to a thin-walled gallbladder infiltrating its neck and engulfing the duodenum, the colon and invading the pancreas.

The histological study of the samples taken from the tumour has shown a proliferation of carcinomatous, poorly cohesive cells representing more than 50% of the tumor, with the presence of rare glandular lumens and nests. Neoplastic cells are round or oval, irregular in shape, with moderate cytonuclear atypia. The nuclei are vesicular, hyperchromatic and nucleolated. Several mitotic figures are observed. Presence of perineural invasion. This tumoural proliferation originates in the gallbladder (Figure 2a+b) and infiltrates the colon, duodenum (Figure 3a+b), pancreatic and hepatic parenchymas. Lymph node dissection showed 15N- / 15N. the tumour was classified pT4N-OMx.

The patient was diagnosed with poorly cohesive cells carcinoma of the gallbladder and was classified: pT4N0Mx.

The patient died 15 days after surgery following septic shock.

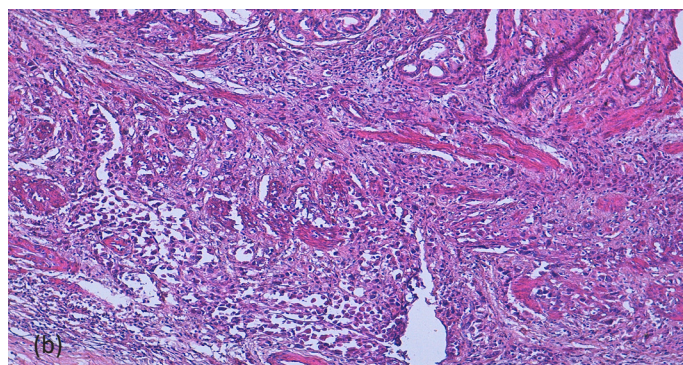
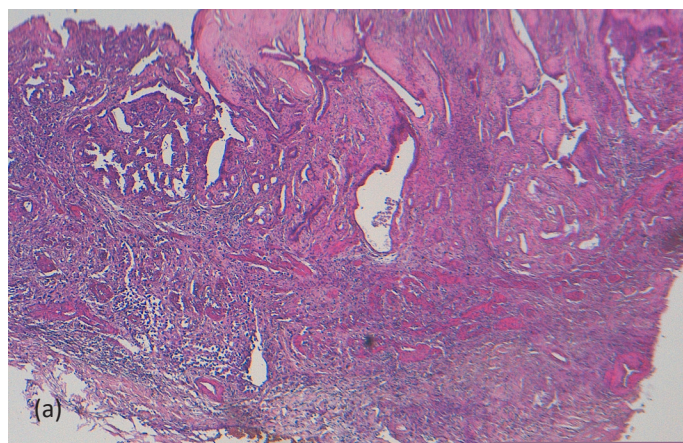


Figure 2a,b: Tumoural proliferation originates in the gallbladder made of poorly cohesive cells. Neoplastic cells are round or oval, irregular in shape, with moderate cytonuclear atypia. The nuclei are vesicular, hyperchromatic and nucleolated.

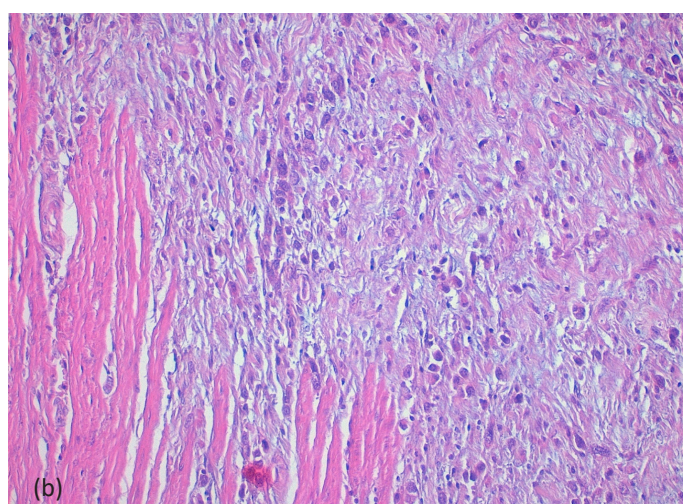
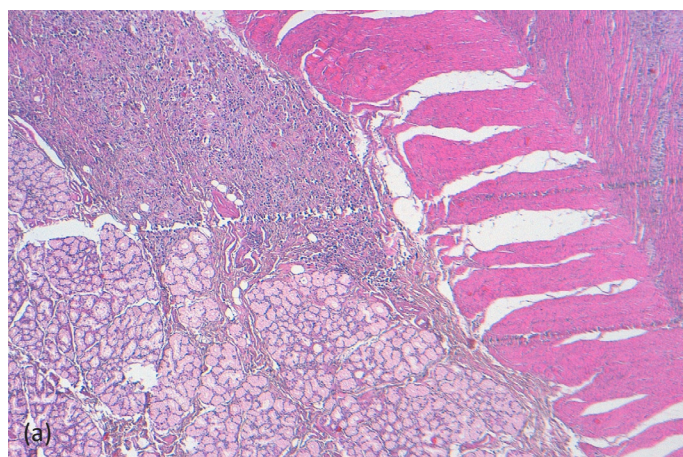


Figure 2a,b: Tumoural proliferation infiltrated the duodenum.

Discussion

Epidemiology

The prevalence of poorly cohesive cells carcinoma is variable from one population to another, for example, in the United States, the frequency is 1.43 / 100000, while in other countries such as Chile the frequency increases up to 17.8 / 100000 [1,6]. Prevalence also varies in different regions of the same country, which means that genetic and environmental alterations play an important role in developing the disease [7].

The poorly cohesive cells carcinoma of the gall bladder is most often found in subjects over the age of 60 [8], predominantly in women [9] (2 to 6 times more frequent than in men) with an incidence that tends to increase with age [10].

Positive diagnosis

This cancer poses a problem when it comes to early diagnosis because of the vague and non specific symptomatology represented mainly by biliary-type pain or epigastralgia, obstructive jaundice, digestive disorders made of nausea vomiting and gastrointestinal bleeding mainly melena (invasion of the duodenum) and alteration of the general state that is not significantly different from other gallbladder carcinomas [10,11]. As in our case, epigastralgia with vomiting associated with upper and lower gastrointestinal bleeding were the main symptoms.

The physical examination may show nonspecific signs attesting to the highly advanced stage of the illness such as a mass of the right hypochondrium, sensitivity to palpation of the right hypochondrium or epigastrium, hepatomegaly and ascites [12]. Our patient presented with atypical signs, that included abdominal distension and epigastric sensitivity.

Sometimes the symptomatology may cause confusion with certain benign biliary diseases, such as acute or chronic cholecystitis, for which an indication of cholecystectomy is indicated [10,12]. The diagnosis of gallbladder cancer is then made fortuitously after the pathological examination [11].

Despite improved imaging techniques, gallbladder carcinoma is diagnosed at an advanced stage. Radiological explorations contribute to the improvement of the preoperative diagnosis when they allow for the visualization of the tumour. They are mainly based on ultrasound and abdominal CT. These tests also make it possible to evaluate the locoregional extension [13]. As a matter of fact, in our case, the CT scan revealed a locally advanced process in the bilio-digestive junction.

Pathological examination remains the only test that confirms the diagnosis of biliary cancer [11]. In our observation, the histological examination enabled the diagnosis of poorly cohesive cell carcinoma of the gallbladder to be made.

Macroscopically, it can manifest as fibrosis and thickening of the vesicular wall, often associated with gallstones having a diameter >3cm [14].

Microscopically, the carcinoma with poorly cohesive cells is characterized by an infiltration of more than 50% of small cells, isolated or grouped in cord, nests or in sheets. Infiltration is very insidiously associated or not with signet-ring cells. The tumor cells are rounded or oval with hyperchromatic and nucleolated vesicular nuclei. They have an ability to dissect the stroma with an intense inflammatory response as a consequence. Lymphovascular invasion is less common than in other types of gallblad-

der carcinomas [5,15]. Indeed, in our patient the vascular embolisms were absent.

Immunohistochemically, the tumor cells have positive Mucin and CK labeling similar to the rest of the upper gastrointestinal tract but with more intense CDX2 labeling. E-cadherin is focally marked for carcinoma to those with poor cohesiveness [16].

Prognosis

Poorly cohesive cells carcinoma of the gallbladder is a very aggressive tumour. At the time of diagnosis, Most patients are classified as higher than T3 according to the TNM classification [4,17]. Our patient was classified T4.

The severity of this cancer is also explained by the rapidity of locoregional extension favoured by the histology of the vesicular wall (absence of muscularis mucosae, absence of the serosa facing the vesicular bed), extension by contiguity to the liver, to the duodenum. And to the right colic angle [18], venous extension to the portal venous system and upper hepatic veins, lymphatic and nervous extension to the hepatic pedicle, there are also possibilities of retro-pancreatic and celiac lymphatic dissemination [19]. In addition, the poorly cohesive cells carcinoma of the gallbladder has a tendency to metastasize at the level of the peritoneum, the ovaries and the lungs [20]. There are also extraordinary examples of the poorly cohesive cells carcinoma of the gallbladder metastasizing in the skin [21] and the breasts (invasive lobular carcinoma).

Most often, it is revealed at an advanced stage thus no longer permitting curative treatment. It has a very poor prognosis since the 5-year survival hardly exceeds 5% [22]. Our patient was deceased 15 days after surgery following septic shock.

Conclusion

The poorly cohesive cells carcinoma is rare, most often discovered fortuitously in women. it is defined by presence of poorly cohesive cells forming more than 50% of the tumour, classified most often higher than T3 at the time of diagnosis, with a very poor prognosis being the most aggressive gall bladder carcinoma. When a poorly cohesive cell carcinoma of the digestive tract with an indeterminate primary site is diagnosed, the gallbladder should be taken into consideration when searching for the primary site.

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