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Case Report

Signet-Ring Cell Cholangiocarcinoma: A Case Report

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Abstract

Signet-ring cell carcinomas are malignant tumors that may affect the stomach and the colon, but extrahepatic bile duct localization is rare. Here we present a case (a 56-year-old Moroccan woman), without either pancreato-biliary mal-junction or liver disease. The patient had obstructive jaundice. Morphological studies by MRI and ERCP revealed a bile duct tumor obstructing the common bile duct and invading gallbladder and hepatic hilum. Pathological examination revealed a carcinoma containing signet-ring cells. The evolution was characterized by rapid disease progression; the patient died in about five months. The case of our patient is among the rare cases described in the mainly Asian literature, and the first case reported in North Africa.

Keywords: Obstructive jaundice, cholangiocarcinoma, signet-ring cell, case report.

INTRODUCTION

Signet-ring cell carcinoma is an undifferentiated malignant tumor occurring usually in the stomach and colon, but rarely in other digestive organs. Autonomous cell cholangiocarcinoma has been rarely reported in the literature.

Here, we report a rare case of infiltrative signet-ring biliary carcinoma by discussing the radiological and histological features, the diagnostic strategy and a review of the literature.

CASE PRESENTATION

A 56-year-old woman from North Africa, with no remarkable medical history, was admitted to hospital in February 2020 to explore a cholestatic jaundice evolving for 15 days preceding her admission, along with biliary-type abdominal pain. She also mentioned a recent weight loss of 8%.

The clinical examination revealed a good overall state, WHO: 1, a mucocutaneous jaundice, scratchy skin lesions, and a tenderness in the right hypochondrium.

The standard serum blood test was normal, particularly the blood count, and the standard metabolic work-up. The liver work-up showed: a Cholestasis (GGT: 10xN, Total Bilirubin: 40mg/l, Direct Bilirubin: 38mg/l) and a moderate Cytolysis (ASAT: 2xn, ALAT: 3xN). The Ca19-9 tumor marker was high up to 321 u/ml.

Cholangio-MRI showed a stenosis of the superior biliary junction extending to the left hepatic duct, and a thin bile duct on the cholangiography sequence, however, a thickening of the vesicular wall and an enlarged aspect of the head of the pancreas were noticed with no dilation of the Wirsung duct. No evidence of cystic biliary affection, biliary lithiasis or hepatopathy was detected (Figure 1).

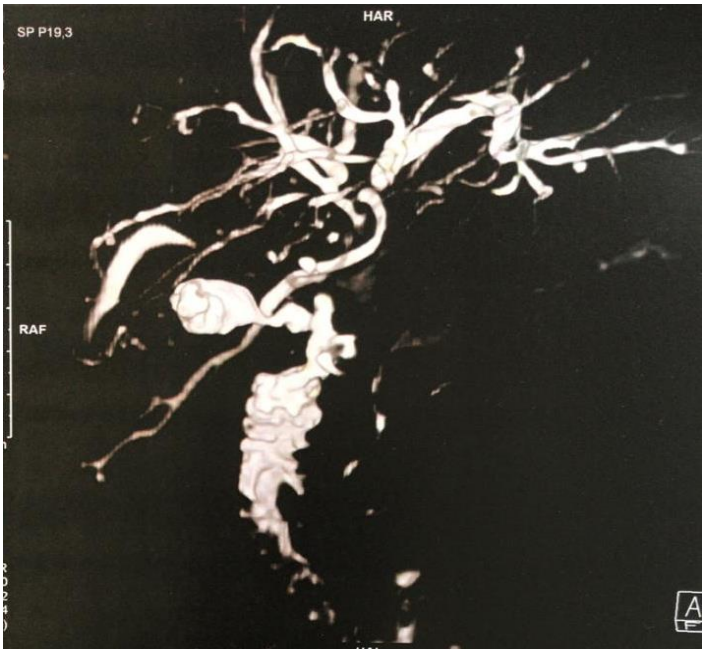

Figure 1: Cholangio-MRI shows a stenosis of upper biliary confluent with a virtual CBD.

Considering the multifocal radiological aspects of these findings, the morphological study was complemented by a bilio-pancreatic echo-endoscopy showing a thickened bile duct measuring 5 mm, making its lumen very thin. The gallbladder was thick-walled and measured 11 mm, along with subcentimetric lymph nodes found at the level of the hepatic hilum and 3 coelio-mesenteric adenopathies, of which the largest measured 10 mm (Figure 2).

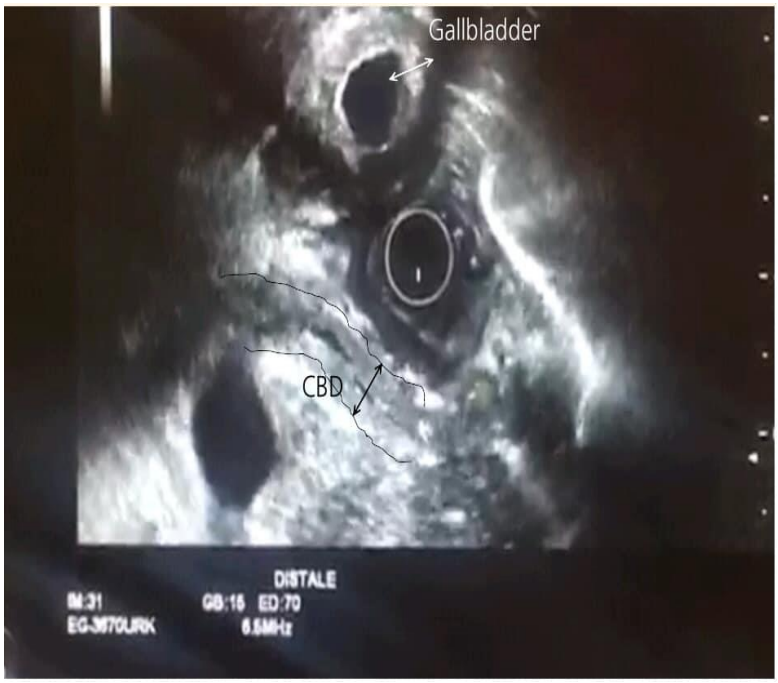

Figure 2: Biliary EUS shows a thin CBD.

A supplemental blood workup: IgG4 assay: 1.19g/l N, the test for NAA, AAMitochondria2, AA Gp200, AA Sp100, pANCA were negative.

ERCP was performed and showed an irregular narrowing of the entire bile duct with stenosis of the upper biliary convergence extending to the left and right segmental divisions. It was decided to perform a biliary drainage with a covered metal prosthesis and a double pigtail plastic prosthesis (Figure 3).

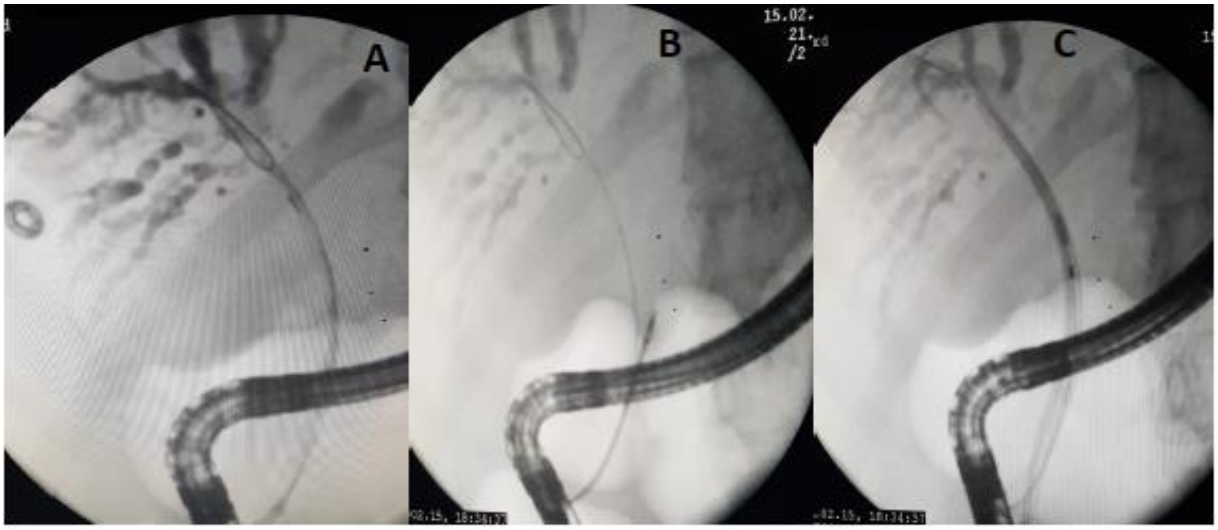

Figure 3: ERCP: A: cholangiography, B: biopsy of CBD with a pediatric forceps C: Biliary covary Stent placement and a plastic double pigtail stent.

The bile duct biopsies -performed using a pediatric biopsy forceps (0.5 mm diameter)- showed autonomous cells with eccentric nuclei and vacuolated cytoplasm evoking a carcinoma with non-cohesive Signet-ring cells. The immunohistochemical study demonstrated a positive marking for anti-CK20 and a negative marking for anti-CK7, while the hercept-test was negative (Figure 4).

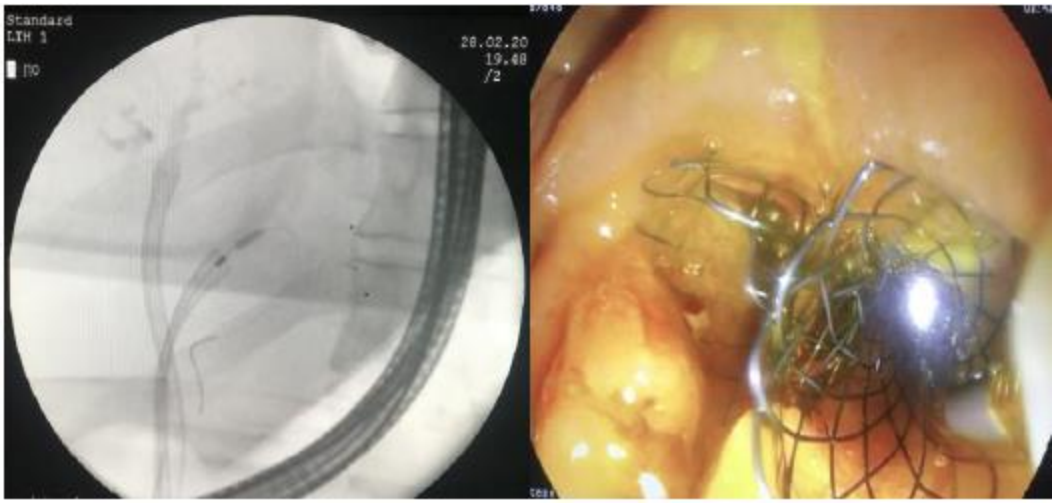

Figure 4: Stent change, placement of double metallic uncovered SEMS

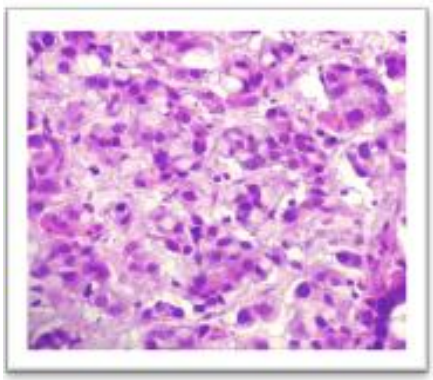

Figure 4.1 : biopsie shows a single ring cells Hemalun eosine G40x10

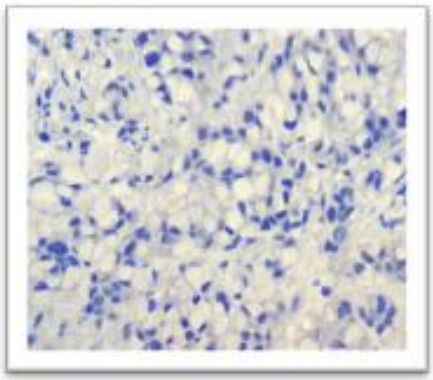

Figure 4.2: IHC; Anti body anti Ck7, Anti body anti Ck20 and Anti body anti Ck19: négative expression of tumoral cells G40x10

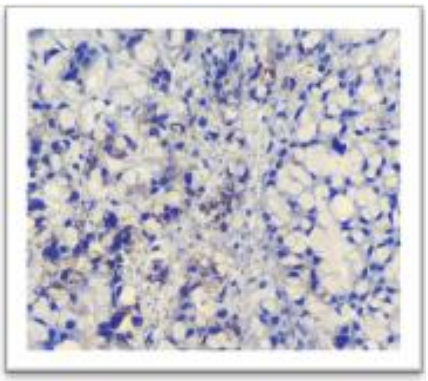

Figure 4.3: IHC; Anti body anti hepatocyte: heterogen expression cytoplasmic G40x10

The esophagogastroduodenoscopy was normal (no tumor lesions and good gastric distension on insufflation). Multiple antro-fundial biopsies x10 turned out to be normal.

Based on the histological, endoscopic and radiological analysis, the diagnosis of a primitive extrahepatic biliary carcinoma with Signet-ring cells was established.

The evolution was characterised by a fast deterioration of the jaundice and the onset of an angiocholitic syndrome. The post-drainage blood test on day 9 showed a significant cholestasis with: TB: 210mg/l, DB: 148mg/l, CRP: 92mg/l.

After the interdisciplinary discussion, surgical management was not recommended considering the advanced state of the cancer. Instead, it was decided to replace the biliary prosthesis with a definitive double metal prosthesis (Figure 5), covered by antibiotics which were adjusted according to the bacteriological profile of the biliary sample.

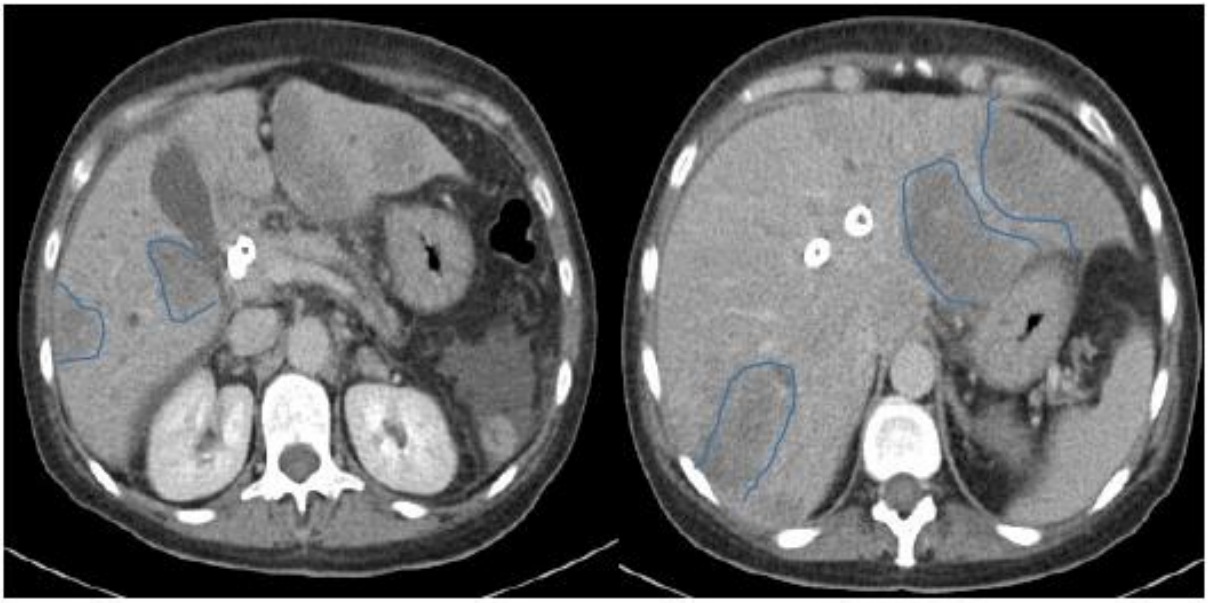

Figure 5: CT-scan shows hypodense lesions, Metastatic-like lesions.

At day 14, following the change of prosthesis and antibiotic therapy, we noticed a significant improvement in jaundice, infectious syndrome and pain. The check-up showed a total bilirubin of 37 mg/l and a CRP of 43 mg/l.

It was decided to provide a palliative support care based on analgesics by morphine titration and an oral corticosteroid therapy. A palliative chemotherapy was considered after an improvement of the hepatic function. However, because of the Covid 19 pandemic, the patient preferred home confinement which was approved by the oncology team, but with regular follow-up at a distance.

In May 2020, the patient was readmitted for significant impairment of her condition, WHO: 4, and an oedemato-ascitic syndrome: the blood work-up revealed an hepatocellular failure. The abdominal CT scan showed a disease progression through the detection of multiple secondary lesions of different sizes in the liver and a large peritoneal effusion (Figure 6).

A palliative support care was provided, including an evacuation of ascites, an albumin infusion, a nutritional support, an antibiotic therapy and an analgesic treatment. The state of health of the patient continued to deteriorate; she passed away in June 2020.

DISCUSSION

Cholangiocarcinoma is an unusual but an aggressive cancer, mostly well-differentiated mucin-producing adenocarcinoma, the other histological types include squamous cell adenocarcinoma, small cell carcinoma, and clear cell carcinoma.

Here we report on a rare case of Signet-ring cell carcinoma SRCC of the extrahepatic bile ducts. It is often found in the stomach but as far as we know, there are only rare cases of SRCC of the extrahepatic bile ducts described in the literature: 13 cases are reported in the (Table 1).

Table 1

Author	Year	Patient age	sex	origin	localization	staging	Management	Evolution
Mizukami *et al.*, [1]	1999	74	M	Asian : Japan	Peri-Hilary	IVa	non	Died after 3weeks
Hiraki *et al.*, [2]	2007	78	F	Asian : Japan	distal	-	-	-
Lee *et al.*, [3]	2010	55	M	Asian : korea	distal	IIb	R1 resection + adjuvant radio-chemo (50.4Gy, gemcitabine/cisplatin)	Died after 24 months
Matsumoto *et al.*, [4]	2010	72	M	Asian : Japan	distal	IV	Gemcitabine	Died after 3 months
Ogata *et al.*, [5]	2010	42	F	Asian : Japan	distal	III	resection	Died after 6 months
Somer *et al.*, [6]	2012	66	F	Eastern Europe: Serbia	Peri-Hilary	II	resection	-
Kita *et al.*, [7]	2014	73	F	Asian : Japan	distal	III	R1 resection + adjuvant radio-chemo (50.4Gy, gemcitabine/cisplatin)	Died after 12 months
Kwon *et al.*, [8]	2014	63	M	Asian : Korea	distal	IIa	R0 Resection	Died after 15 months
Chedid *et al.*, [9]	2015	66	F	South American : Brasil	Peri-Hilary	IVa	R1 Resection	Died after 15 months
Hua *et al.*, [10]	2015	52	M	Asian : China	distal	III	Resection	Died after 6 months
Jessemae L. *et al.*, [11]	2016	55	F	American : USA	distal	IV	radio-chemo (50.4Gy, gemcitabine/cisplatin)	Died after 3 months
Millien VO *et al.*, [12]	2018	33	F	African : Niger	Peri-Hilary	Bismuth IIIa	Biliary drainage by prosthesis	
Conggui Zhang *et al.*, [13]	2018	32	F	Asian : Japan	Hepaticojejunal anastomosis		resection	Died after 5 months
Our case	2020	56	F	North Africa: Morocco	Peri-Hilary	Bismuth IV	Biliary drainage by prosthesis	Died after 4 months

Most of the reported cases 9/13 are from North-East Asia (Japan, Korea, China), only one case from Eastern Europe [6], and only one case of African origin as described in the publication of Millian Vo. [12] Our patient is the first North African case to be reported. The mean age of onset was 58 years, ranging from 32 to 78 years, this type of cholangiocarcinoma occurs at an earlier age than the usual form of cholangiocarcinoma and it is more common in women (9F/5H).

Signet-ring cell cholangiocarcinoma SRCCC was described as a cancer that exclusively affects northeast Asians, however, based on recent case reports including our own, it should no longer be considered as such.

Eight patients underwent a surgical resection, 2 of them received an adjuvant chemotherapy, 3 patients received a palliative chemotherapy and/or chemoradiotherapy. The overall survival was commonly very short between 3 weeks and 15 months. The longest survival was reported to be 2 years after surgical resection followed by adjuvant chemotherapy using Gemcitabine and Cisplatin [3].

Our case is the only one reported in North Africa, it is an unusual case of this type of cholangiocarcinoma to be diagnosed (in a woman in her fifteens). Like most described cases, our patient had no genetic, inflammatory or infectious risk factors.

She developed, as do most cases, a cholestatic jaundice, and the tumour was unresectable given the local extension and the celiac lymph node invasion [14].

The tumour was diffusely invasive and involved the entire height of the biliary duct with a possible involvement of the gallbladder.

It was diagnosed using intra-biliary biopsies under cholangiographic control, as the cholangioscope is not available in our country.

To date, there are several techniques for cytological or histological sampling of the bile duct, such as the aspiration of the bile fluid, the brushing of the bile duct, the biopsies by Trans papillary forceps and recently the Spyglass cholangioscope guided biopsies [15].

Although the optimal method remains debated, biliary fluid cytology is a simple technique but has poor sensitivity (6%-32%) [16], cytological brushing also remains with a low sensitivity (30-57%) [17]. In addition, the ERCP-guided trans-papillary biopsy has not been frequently used, considered technically difficult, yet its sensitivity is high and ranges from 43% to 81% [18]. Currently, Spyglass cholangioscopy guided biopsies have an equal sensitivity to the one described under ERCP but with a reduced risk of complications [15, 19]; trans-papillary biopsies are still the best technique to have a high quality histological sample, for which the results are also helpful in the therapeutic management (chemotherapy) according to the histological type of the cancer found.

For our patient, the disease progressed quickly due to the successive episodes of angiocholitis, making the use of any chemotherapeutic treatment restricted.

CONCLUSION

SRCCC of the extrahepatic bile ducts is a rarely described disease in the literature, but it is not reserved for the Asian population.

Given its aggressive nature and rapid advancement, histological evidence should be provided as soon as possible in order to guide further management.

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