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Gastroenterology I

Jaundice Revealing Multiple Primary Neoplasia and Krukenberg Tumour: A Case Report

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Abstract | **Case Report**

Krukenberg tumours are ovarian malignancies secondary to signet-ring cell adenocarcinomas. Gastric and colorectal cancers account for almost 90% of primary sites. Other less frequent primary sites are described in the literature. We report the case of a Krukenberg tumour discovered incidentally during the investigation of jaundice. This 55-year-old patient was referred to the emergency department for investigation of cutaneous jaundice associated with chronic epigastralgia resistant to symptomatic treatment. The initial radiological work-up showed dilatation of the bile ducts associated with the presence of 2 ovarian masses. Additional magnetic resonance cholangiography revealed a lesional process of the biliary bifurcation related to a cholangiocarcinoma, and the esophagogastroduodenoscopy performed as part of the exploration of chronic epigastralgia revealed a gastric tumour. The overall clinical picture suggested a multiple primary tumor syndrome with perihilar cholangiocarcinoma and gastric adenocarcinoma complicated by Krukenberg tumors. The patient underwent palliative biliary drainage with a transhepatic percutaneous prosthesis and died a few days later. Krukenberg's tumour is rare, and its prognosis is poor, especially when it occurs in the setting of multiple primary neoplasia. The aim of our work is to shed light on the rarity of this disease and its insidious evolution, responsible for erratic and delayed diagnosis.

Keywords: Case Report, Krukenberg, Multiple Primary Neoplasia.

INTRODUCTION

Krukenberg's tumour is an ovarian metastasis, often of digestive origin, notably gastric or colonic. Occurrence in the context of multiple primary neoplasia is exceptional.

We report the case of a Krukenberg tumour discovered incidentally during the investigation of jaundice and complicating a syndrome of multiple primary neoplasia. This case study highlights the rarity of this association and the importance of multidisciplinary management.

PATIENT AND OBSERVATION

Patient Information:

A 55-year-old woman, multiparous, with a history of type II diabetes on Liraglutide and Metformin since 2010, was admitted to the emergency department to investigate jaundice that had been evolving for 10 days. The patient's history revealed that she had been suffering from atypical epigastralgia for 05 months, which was resistant to symptomatic treatment.

Clinical Findings:

Clinical examination on admission revealed a patient in poor general condition, apyretic, icteric, with a sloping abdominal dullness with no hepatosplenomegaly or palpable mass.

Time Line:

Following the clinical examination, the patient underwent a biological workup, an abdominal ultrasonography, a CT scan, a magnetic resonance cholangiography, an esophagogastroduodenoscopy followed by a trans parietal biopsy.

Diagnostic Assessment:

The laboratory work-up showed a disturbed liver function, with ALAT at 256 UI/L, ASAT at 154 UI/L, an icteric cholestasis, with PAL at 531 UI/l , GGT at 724 UI/l and total bilirubin at 80 mg/L. Blood count showed anaemia at 10 g/dl, correct white blood cell count and a prothrombin level at 93%. CRP was elevated to 42.6 mg/l and tumour marker assays showed Ca19-9 at

4362 U/ml Reference range: <37 U/ml), and Ca 125 at 152.3U/ml (Reference range: <35 U/ml)

Abdominal and pelvic ultrasonography showed dilatation of the common bile duct (CBD) to 8 mm and dilatation of the proximal bile ducts without visible obstruction, with evidence of 2 latero-uterine masses, right and left, measuring 110 x90 mm and 70 x 60 mm respectively, and a moderately abundant pelvic effusion. An additional CT scan confirmed the ovarian origin of the 02 latero-uterine masses, with individualization of deep lymphadenopathies, peritoneal implants and peritoneal effusion associated with dilatation of the intrahepatic bile ducts and enhancement of the common bile duct after injection of iodine-based contrast material.

A magnetic resonance cholangiography was performed showing a poorly limited lesional process infiltrating the proximal portion of the biliary bifurcation consistent with a cholangiocarcinoma, responsible for dilatation of the intrahepatic bile ducts with a magma of mesenteric, intra- and retroperitoneal adenomegalies.

The patient underwent an ultrasound-guided biopsy of the hepatic process. Pathological examination showed carcinomatous proliferation with positive staining for CK7 and CK19 and negative staining for CK20 and anti-hepatocyte antibody (Figure 1 and 2).

In view of the epigastralgia reported by the patient, an esophagogastroduodenoscopy was performed, showing a hemi-circumferential ulcerating process in the anterofundial region, taking the lesser curvature as far as the angulus, friable and bleeding easily on contact (Figure 3).

Pathological examination of the gastric biopsies showed a positive anti-CKAE1/AE3 antibody and a negative anti-CD20 and CD3 antibody staining in favour of a signet-ring cell adenocarcinoma (Figure 4 and 5).

The overall clinical, radiologic and pathologic picture was suggestive of a syndrome of multiple primary neoplasms consisting of a gastric adenocarcinoma with signet ring cells and a perihilar cholangiocarcinoma complicated by Krukenberg tumors with peritoneal carcinosis.

Therapeutic Intervention:

Her clinical presentation precluded palliative surgery. The patient underwent palliative biliary drainage with a transhepatic percutaneous prosthesis.

Follow-Up and Outcomes: the patient died few days after the biliary drainage.

Patient Perspective (After the Biliary Drainage):

"When I first came to the hospital, I was very worried, but thanks to the medical team who took the time to explain the diagnosis and support me, I felt reassured. Now that I have undergone the biliary drainage, I feel an improvement in the symptoms, and I hope that God will give me the strength to fight this cancer.**"**

Patient Consent: Informed consent has been obtained from the patient's for the publication of this case report.

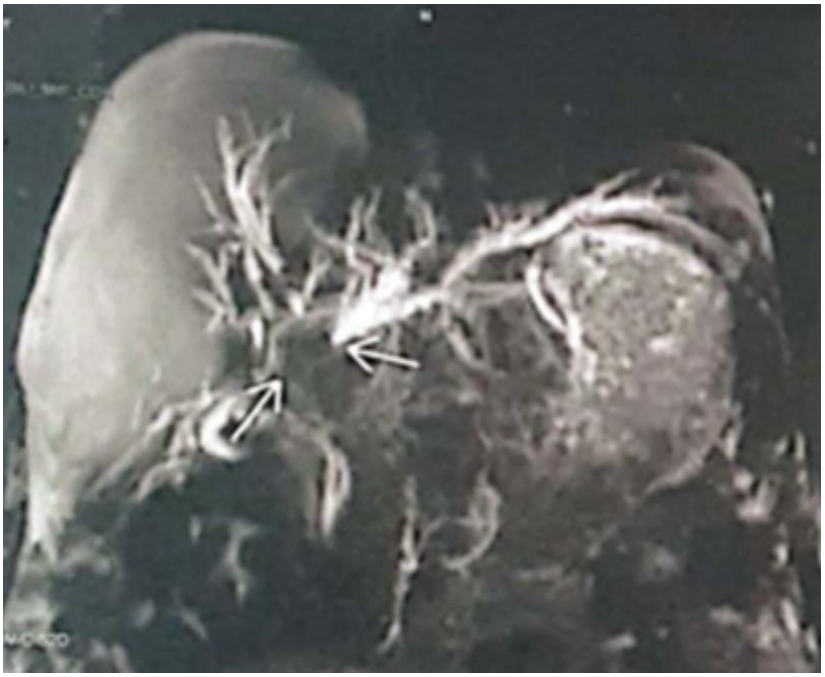


Figure 1: Coronal section of magnetic resonance cholangiography showing the peri hilar process

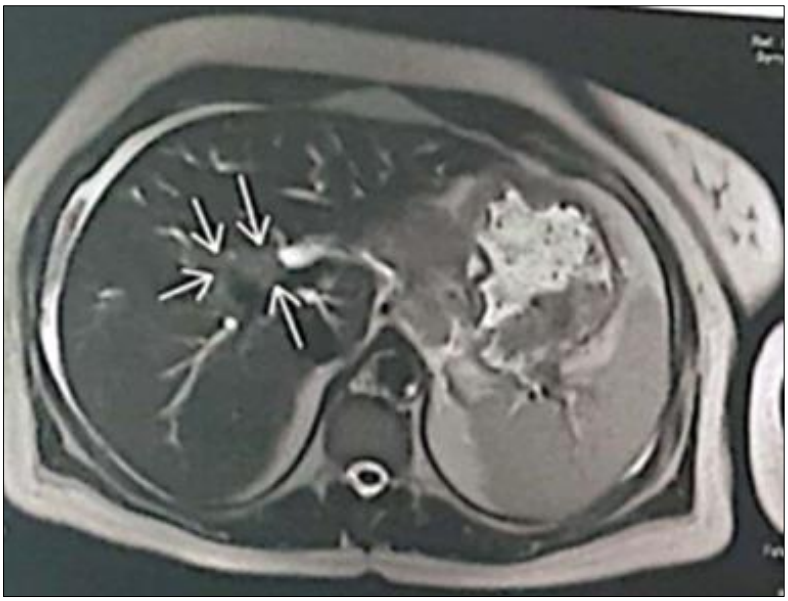


Figure 2: Axial section of magnetic resonance cholangiography showing the peri hilar process

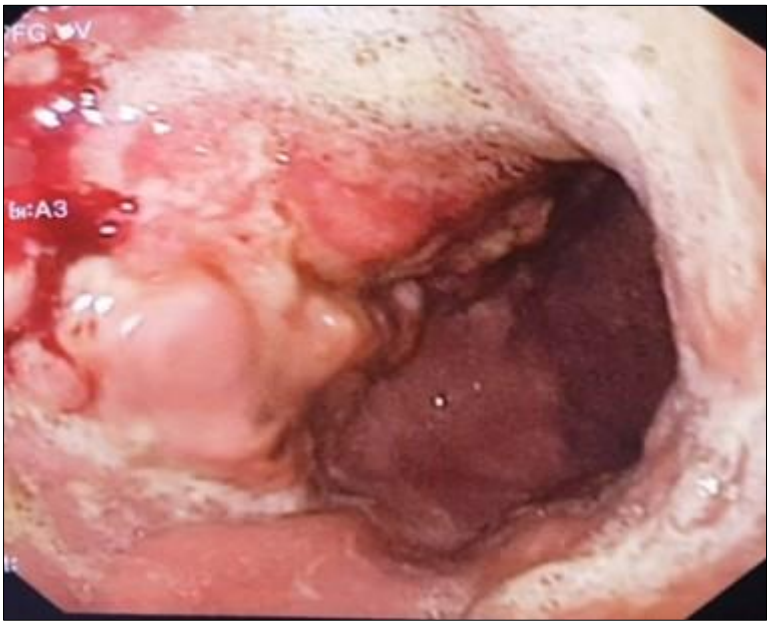
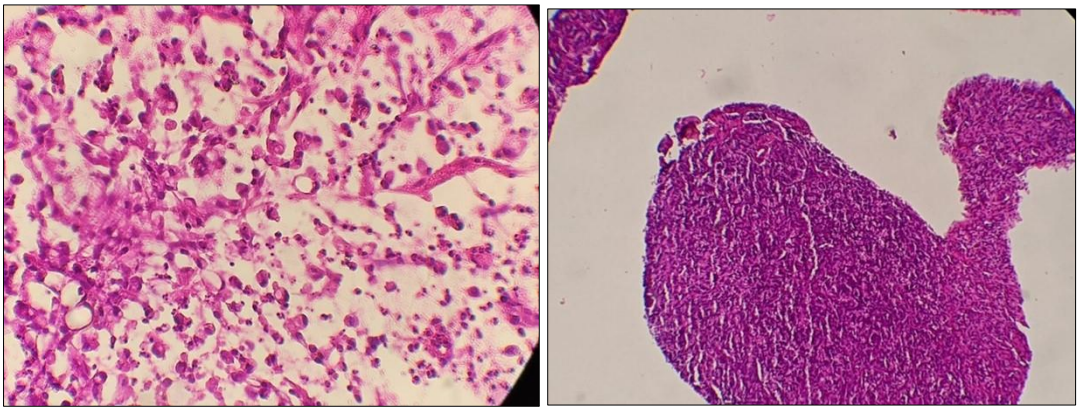


Figure 3: Endoscopic view of gastric tumour



Figures 4-5: Histological sections of gastric biopsy showing infiltration by multiple signet-ring cells

DISCUSSION

Krukenberg tumours are ovarian malignancies secondary to signet-ring cell adenocarcinomas [1]. They account for 1-2% of all ovarian tumours, and in over 80% of cases are bilateral due to their metastatic nature [2].

This tumour often affects multiparous women, during the period of genital activity [2]. The average age of diagnosis is between 35 and 45. However, the disease can be observed in all age groups [2]. Krukenberg's tumour is further defined as a synchronous metastasis, when it is discovered within three months of the diagnosis of the primary tumour, or as a metachronous metastasis, when it is discovered after three months, often after completion of the initial curative treatment [3].

From a pathophysiological standpoint, several hypotheses have been put forward concerning the mode of dissemination between a digestive neoplasia and an ovarian metastasis: the hematogenous route, the lymphatic route and the trans coelomic route. The average age of diagnosis is associated with increased vascularization of the ovaries, confirming the hypothesis of lymphatic and hematogenous dissemination.

Clinical presentation of Krukenberg tumours is highly variable. Symptoms can be nonspecific, or asymptomatic, which explains why they are often diagnosed late during extension workup for the primary cancer or following imaging for another pathology [2]. In our case, the discovery was fortuitous, following an abdominopelvic ultrasound performed as part of the investigation of cholestatic jaundice.

On imaging, ovarian metastases are often bilateral, less than 10 cm in size and appear as tissue masses with clear, regular contours [4]. Pathologically, Krukenberg's tumour is characterized by the presence of signet-ring cells, associated with a pseudo sarcomatous stroma [5]. Histological examination of ovarian biopsies is the only way to confirm the metastatic nature of ovarian tumours. Our patient did not benefit from histological examination because of peritoneal carcinosis, making surgery unnecessary [2].

In terms of etiology, gastric and colorectal cancers account for almost 90% of primary sites of Krukenberg tumours [2]. Other less frequent primary sites described in the literature include the appendix, small intestine, gallbladder and bile ducts, pancreas, ampulla of Vater, bladder, breast and cervix [2]. Occasionally, Krukenberg's tumour may precede or occur at a distance from the diagnosis of the primary tumour, posing a problem of differential diagnosis with a primary ovarian tumour. In both these cases, histological examination coupled with immunohistochemistry can help rectify the diagnosis [6].

In our observation, the patient presented 2 primary tumours: a gastric adenocarcinoma with signet-ring cells and a cholangiocarcinoma.

The syndrome of multiple primary malignant tumours, also known as multiple primary cancers, corresponds to the existence of more than one primary cancer in different organs, or the presence of more than one cancer, within the same organ, developed from different cell types. This is a fairly rare phenomenon, the incidence of which is gradually increasing as a result of improvements in complementary investigations. Many cases of multiple primary cancers of the gastrointestinal tract have been reported. According to an Italian study, synchronous double cancers account for 6% of all primary multiple gastrointestinal cancers [7].

A Japanese study of 3,291 patients showed that 3.4% (111 patients) of all gastric cancer patients had synchronous cancer [8]. To confirm the syndrome of multiple synchronous primary malignancies, it is essential to ensure that the second lesion is not a metastasis or local extension [9]. In our case, it was a combination of peri hilar cholangiocarcinoma and gastric adenocarcinoma. For peri hilar cholangiocarcinoma, histological confirmation is often difficult to obtain; the diagnosis may be established on an evocative image with a Ca 19-9 level > 100ng/ml [10].

The stomach is also an unusual site for metastasis. The most common primary tumours for gastric metastases are breast cancer, lung cancer and melanoma [9]. Histological confirmation is obtained after anatomopathological study of the gastric biopsy taken during upper digestive endoscopy.

Treatment of multiple synchronous primary cancers is generally based on surgery or chemotherapy, but in the case of surgically unresectable tumours, chemotherapy targeting both tumours appears to be the most reasonable treatment [9].

Currently, the prognosis for patients with Krukenberg tumours is poor, with a mean survival of between 3 and 10 months; only 10% of these patients survive more than 2 years after diagnosis.

CONCLUSION

Krukenberg tumours are rare malignant tumours with a poor prognosis. Their association with multiple primary cancers is an exceptional situation, posing a real challenge for the physician and requiring multidisciplinary management in view of the difficulty of the therapeutic decision.

Competing Interests: The authors declare no competing interests.

Authors' Contributions: All the authors have read and agreed to the final manuscript.

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