



## Scientific letter

# Ampullar Metastasis of a Breast Lobulillar Carcinoma <sup>☆,☆☆</sup>



## Metástasis ampular por carcinoma lobulillar de mama

Although breast cancer is the cancer with the greatest incidence among women, the appearance of ampullary metastasis of a breast carcinoma is a rare finding as it usually occurs in the context of advanced systemic disease.<sup>1</sup>

We present the case of a sexagenarian female patient who had undergone left segmentectomy with homolateral axillary dissection 4 years earlier for multifocal pleomorphic lobular carcinoma of the left breast. At that time, the diagnosis was established with a core needle biopsy (CNB), which determined the following characteristics: histological grade III (tubule formation, 3; nuclear grade, 3; number of mitoses, 2), triple negative (oestrogen, progesterone and HER2 negative [Herceptest<sup>®</sup> immunohistochemistry: 2+ with negative FISH]). The initial clinical stage was cIIIA (cT3, cN1, Mx), but there was complete pathological response in the surgical specimen and partial pathological response of the lymph nodes after receiving neoadjuvant chemotherapy with TXT-A (6 cycles).

Currently, the patient presented non-painful jaundice, and lab work confirmed altered liver function (total bilirubin, 10 mg/dL; GGT/FA, 1379/846 U/L; and GOT/GPT, 338/266 U/L). Abdominal-pelvic computed tomography (CT), magnetic resonance cholangiopancreatography, endoscopic retrograde cholangiopancreatography and endoscopic ultrasound showed marked dilatation of the intrahepatic bile duct, a common bile duct that was 2 cm in diameter and dilatation of the Wirsung duct. Both were amputated at the level of the ampullary region, where a hypoattenuated mass was observed, measuring 2.8 cm × 1.5 cm. It was not possible to canalise the bile duct, but a biopsy was taken of the ampullary mass and, using a right transhepatic approach, a catheter was inserted for internal-external bile drainage.

The patient developed symptoms of intracranial hypertension and diplopia, and cranial CT demonstrated the

existence of cerebral lesions. Treatment was administered with holocranial radiotherapy, pending assessment for palliative chemotherapy, but the patient died one month later.

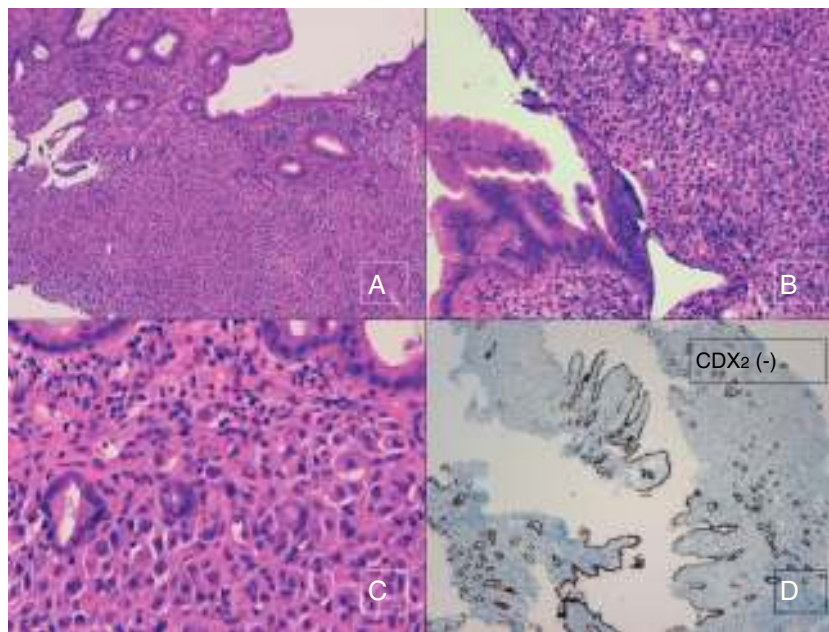
The histological study of the biopsy identified a solid-growing invasive epithelial neoplasm of non-cohesive cells with abundant cytoplasm and variable nuclear pleomorphism, some signet cell, which invaded the periampullary mucosa (Fig. 1A–C). Given the pathological history, a comparative histopathological study was conducted of the ampullary neoplasm and the primary breast tumour, which demonstrated morphological similarity. This study was complemented with immunohistochemistry techniques that showed coinciding and conclusive results (positive CK7, p53, mammaglobin and GCDFP15; negative E-cadherin, CK20, CDX2, HER2, oestrogen and progesterone) (Figs. 1D and 2A–D), which established the definitive diagnosis of a metastasis versus a poorly differentiated primary ampullary carcinoma.

### Discussion

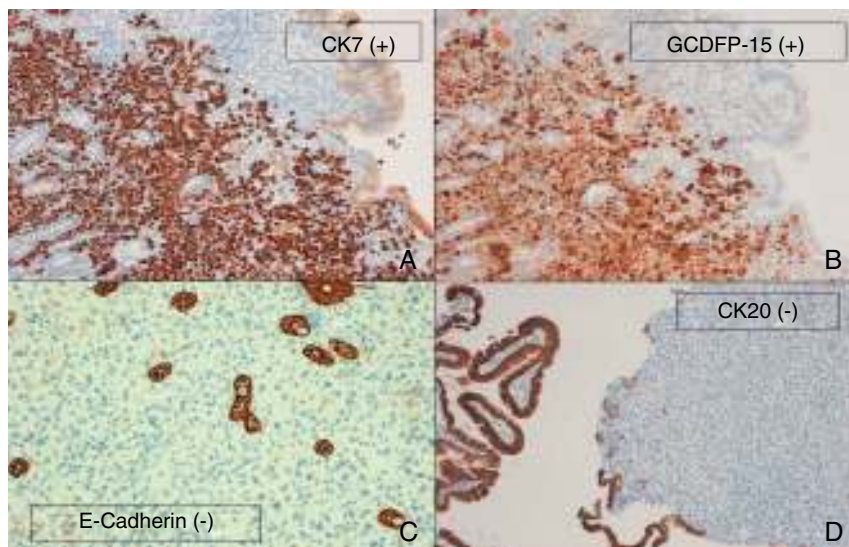
Tumours that metastasise to the pancreas are rare, as shown in a series of 1000 autopsies with malignant neoplasias, with only 3% pancreatic metastases,<sup>1</sup> and the breast as the primary origin is unusual.<sup>2</sup> The incidence of pancreatic metastases due to breast cancer is around 5%–13%.<sup>3</sup> Lobular carcinoma of the breast metastasises to the CNS, leptomeninges, peritoneum, ovaries, uterus and gastrointestinal system; metastases have also been described in the lungs, bones and liver, but the ampullary/pancreatic location is uncommon.<sup>4</sup> The disease-free interval varies from 1 to 182 months, and a synchronous presentation is considered an extremely rare finding.<sup>4,5</sup> The disease-free interval in our patient was 44 months.

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**Fig. 1 – Microscopic image with haematoxylin–eosin stain of the metastasis of lobular carcinoma of the breast showing cells with variable pleomorphism and signet ring behaviour (A–C) (H–E  $\times 10$  [A], H–E  $\times 20$  [B] and H–E  $\times 40$  [C]), and metastatic tumour cells with negative immunoexpression for CDX2 (gastrointestinal organ-specific marker) in the neoplastic component (see positivity in the intestinal epithelium and normal glandular) (D) (CDX2  $\times 4$ ).**



**Fig. 2 – Metastatic tumour cells with positive immunoexpression for CK7 (A) (CK7  $\times 10$ ) and GCDFP15 (B) (GCDFP15  $\times 10$ ), and negative immunoexpression for E-cadherin (C) (E-cadherin  $\times 20$ ) and CK20 (D) (CK20  $\times 10$ ).**

The appearance of metastatic breast lesions occurs prematurely in the majority of cases, although cases have been described of solitary gastric metastases 30 years after mastectomy.<sup>6</sup> The clinical manifestations of this type of metastasis are not necessarily distinguishable from other types of pancreatic cancer. Most patients do not present symptoms, and the lesion is detected on routine radiological

exams, during surgery or on autopsy.<sup>1,7,8</sup> In our case, the patient debuted with frank jaundice 4 years after a quadrantectomy that improved after the placement of an internal-external biliary catheter.

It is complex to determine whether a pancreatic-ampullary carcinoma is primary or metastatic, but it is even more difficult to consider that it may be metastasis of breast cancer.

Imaging tests are of help in patients with multiple pancreatic nodules and a known primary tumour, but a solitary mass may be indistinguishable from a primary carcinoma of the pancreas, especially if it affects the head of the pancreas. An imaging-guided biopsy can establish the pathological diagnosis and avoid laparotomy, as in our patient.<sup>9</sup>

Unfortunately, the diagnosis of metastasis of lobular carcinoma of the breast is occasionally made when studying surgical resection specimens from a Whipple procedure after the diagnosis of ampullary carcinoma in a previous endoscopic biopsy. This can occur because the primary breast tumour has not been identified, the diagnosis of a multiple primary tumour is assumed, or the biopsy has not undergone an immunohistochemistry panel for the detection of metastatic neoplasms. In our patient, the use of immunohistochemistry studies, some of which are organ-specific (GCDFP-15, mammaglobin and CDX2), together with the history of lobular carcinoma of the breast 4 years earlier, were decisive. Hormone receptors, in addition to the HER2 study, were also negative in the metastasis. The triple negativity of the breast cancer and the metastasis likely provided a less favourable prognosis and limited the therapeutic strategies.

In conclusion, when a pancreatic tumour develops in a patient with a previous neoplasm in another location, the hypothesis of a metastasis in the pancreas should be considered. The clinical history should be thoroughly analysed, and all possibilities should be included in the diagnostic process. Therapeutic decision-making requires a multidisciplinary team. Treatment should be individualised and take into account the location and histology of the primary tumour and metastasis, interval from the first treatment until the time of metastasis, and the clinical-pathological manifestations caused by the metastasis.

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## Authorship

All the authors have read and approved this manuscript, and the requirements for authorship have been met. The patient gave informed consent for the publication of these data.

## Conflict of Interests

The authors declare no conflict of interests.

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