CASE REPORT

Insulinoma with focal hepatic lesions: malignant insulinoma?

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SUMMARY

Insulinoma is a rare tumour that is malignant in only 10% of cases. We report a case of insulinoma in a 59-year-old woman, associated with focal liver lesions, which raised the suspicion of malignancy of a pancreatic tumour. Enucleation of the insulinoma was performed with wedge resection of one hepatic nodule. Pathological examination indicated that the pancreatic tumour was compatible with insulinoma whereas the hepatic lesion was related to focal nodular hyperplasia. This clinical case highlights the need for histopathological proof of malignancy before selecting therapeutic strategies for insulinomas.

BACKGROUND

Insulinoma is a rare tumour representing 1–2% of all pancreatic neoplasms.¹ It is malignant only in 10% of cases.² The malignancy can be stated only in the presence of locoregional invasion into the surrounding soft tissue, lymph node or liver metastases.³

We report a case of insulinoma associated with vaguely defined hepatic lesions. This clinical case highlights the need for definitive diagnosis of malignancy before selecting therapeutic strategies for insulinomas.

CASE PRESENTATION

A 59-year-old woman presented with symptoms of hypoglycaemia of 3 years duration including diaphoresis, headache and loss of consciousness occurring especially in the morning, and weight gain. At admission, her body mass index was 40 kg/m². The rest of the physical examination was unremarkable.

INVESTIGATIONS

Plasma glucose levels during symptoms varied between 30 and 40 mg/dL. The serum insulin level was 110.4 µU/mL (normal range 4–20 µU/mL) and serum C-peptide level 4.33 ng/mL (normal range 0.51–2.72 ng/mL), suggesting endogenous hyperinsulinism, in particular insulinoma. Endoscopic ultrasound showed a hypoechoic, homogenous and well-demarcated 14 mm tumour in the uncinate process of the pancreas (figure 1). MRI identified the insulinoma, which demonstrated low signal intensity on T1-weighted images and high signal intensity on T2-weighted images (figure 2). There were also three arterial phase-enhancing 3–5 mm hepatic lesions (figure 2).

DIFFERENTIAL DIAGNOSIS

The findings raised the problem of whether or not the hepatic lesions were metastatic in nature. Octreotide scintigraphy (Octreoscan) did not show any abnormal fixation in the liver or pancreas. Since the liver lesions were too small to be biopsied percutaneously, surgical exploration was performed.

TREATMENT

At laparotomy, the tumour in the uncinate process of the pancreas was easily detected (figure 3). No other pancreatic lesions were revealed by manual palpation and perioperative ultrasound. The subcapsular hepatic nodule in segment 8 was identified, but the other two liver lesions, even using perioperative ultrasound, were not found because they were intraparenchymal and too small. There were no enlarged lymph nodes in favour of malignancy around the pancreas. Wedge resection of the subcapsular hepatic nodule was performed. The frozen section examination showed no evidence of malignancy. Enucleation of the insulinoma was then performed (figure 4). The postoperative course was uneventful. The pathological examination indicated that the pancreatic tumour was of neuroendocrine origin, well differentiated and with low mitotic rate (<2 mitoses per 10 high-power fields) (figure 5). Immunohistochemical staining was positive for chromogranin and synaptophysin. The Ki-67 index was <2%. Regarding the hepatic lesion, the pathological conclusion was focal nodular hyperplasia (FNH) (figure 6).

OUTCOME AND FOLLOW-UP

Currently, the patient is fine and has not presented hypoglycaemia after 6 months of follow-up.

Figure 1 Endoscopic ultrasound showed a hypoechoic, homogenous and well-demarcated 14 mm tumour (black arrow) in the uncinate process of the pancreas.

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Figure 2 MRI showed (A) a solid 15 mm mass in the uncinate process of the pancreas (white arrow) with three arterial phase-enhancing 3–5 mm hepatic lesions (B) in segments VIII, (C) VII and (D) VI (white arrows).

DISCUSSION

We reported a new case focused on a probably coincidental association of insulinoma and FNH simulating a malignant insulinoma with liver metastasis. Insulinoma is a pancreatic neuroendocrine tumour that is usually benign.⁴ Indeed, malignancy was observed in only 10% of cases.² Therefore, the association of insulinoma with liver lesions raises the question of whether these liver lesions are benign or metastatic. Distinction is essential since there are no other specific morphological, biochemical or genetic features discerning benign from malignant insulinoma.² However, as seen in our case, this distinction may be difficult for focal arterial phase-enhancing hepatic lesions. In fact, metastases of insulinomas are primarily perfused through the hepatic artery, and demonstrate early and pronounced enhancement in the arterial phase of contrast-enhanced imaging. This enhancement pattern is also seen in primary liver tumours such as FNH, adenoma, large regenerative nodules and

most primary hepatocellular carcinomas.⁵ Among these lesions, FNH is the most common tumour, with prevalence estimated at 0.9%.⁶ MRI is valuable in diagnosing or at least narrowing the differential diagnosis for most of these lesions.⁷ More specifically, in patients with cancer, MRI is accurate for distinguishing benign lesions from malignant or high-risk lesions.⁸ Indeed, on delayed phase, malignant lesions tend to wash out contrast from the periphery and show a target appearance known as the 'peripheral washout sign', which is highly specific for hypervascular metastasis.⁹ Moreover, in the only two cases reported in the literature involving insulinoma and FNH,^{5 10} MRI has been decisive to exclude the hypothesis of hepatic metastasis. In the two cases,^{5 10} the diagnosis of FNH was provided by US-guided needle biopsy of the liver. The classic histopathological description of FNH is that of a non-encapsulated nodule with a central fibrous body from which there are radiating septa dividing nodules of hyperplastic hepatocytes. The central fibrous regions

Figure 3 Intraoperative findings showing the insulinoma in the uncinate process of the pancreas (black arrow).

Figure 4 Intraoperative image showing enucleation of the insulinoma.

Figure 5 Histological image of the insulinoma (H&E $\times 400$): well-differentiated neuroendocrine tumour with uniform epithelial cells separated by scant fibrovascular stroma.

usually contain abnormal vessels of different sizes, as well as proliferating bile ductules.¹¹

The association of insulinoma with FNH remains unclear and is probably coincidental. If the nature of the liver lesions remains uncertain preoperatively, as in our case, frozen section represents an accurate perioperative method in determining their malignancy status.¹² Indeed, the correct diagnosis was important to obtain because it allowed us to carry out conservative pancreatic surgery and avoid hepatic surgery.

Figure 6 Histological image of the focal nodular hyperplasia (H&E $\times 40$): hyperplastic nodules of hepatocytes separated by fibrous septa with thick-walled arteries and ductules within the septa.

Learning points

- ▶ Insulinoma is a rare tumour that is usually benign.
- ▶ Insulinoma with focal hepatic lesions requires a multidisciplinary team to support the patient.
- ▶ In case of insulinoma associated with hypervascular liver lesions, MRI is accurate for distinguishing benign hepatic lesions from metastatic lesions.
- ▶ If there is any doubt about the malignancy of an insulinoma, surgical exploration must be performed because medical treatment is often ineffective.

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