Endocrinología, Diabetes y Nutrición 71 (2024) 221–225

Endocrinología, Diabetes y Nutrición

www.elsevier.es/endo

SCIENTIFIC LETTER

Pheochromocytoma-induced acute pancreatitis: A rare presentation

Pancreatitis aguda inducida por feocromocitoma: una presentación poco frecuente

Introduction

Acute pancreatitis, characterised by pancreatic inflammation, usually stems from well-documented causes like gallstone disease, excessive alcohol consumption, and trauma. However, in rare cases, it can be the initial manifestation of a pheochromocytoma, an adrenal tumour releasing excessive catecholamines. This unexpected link can puzzle clinicians due to the absence of typical pheochromocytoma symptoms. Recognising this interplay and understanding the complex pathophysiological mechanisms is challenging. Pheochromocytomas often mimic other conditions, but there are few reports of pheochromocytoma-induced pancreatitis in the medical literature.[1] The absence of usual pheochromocytoma symptoms, such as sustained hypertension, complicates timely diagnosis when presenting as acute pancreatitis. This case report highlights a unique scenario where acute pancreatitis was the first sign of an underlying pheochromocytoma, underlining the importance of early identification and accurate diagnosis in managing this uncommon but potentially life-threatening association.

Case report

This was a 51-year-old male referred to the Endocrinology Department after the incidental discovery of a left adrenal mass on a CT scan performed for acute pancreatitis. His previous medical history included a history of hypomania, renal microlithiasis and cholecystectomy. He was not on any regular medication. He had been admitted two days prior to the Endocrinology consultation due to acute pancreatitis, diagnosed by typical abdominal pain with amylase and lipase levels three times above the upper limit of normal (amylase 1184 IU/l, lipase 936 IU/l), with a CT scan revealing a 38-mm lesion in his left adrenal gland (Fig. 1). Once in hospital, potential triggers such us gallstones, alcohol intake, other toxins or drugs, hyperlipidaemia and hypercalcaemia were ruled out. Additionally, the patient had no history of recent surgery, ERCP, trauma, anatomical abnormalities in the pancreas or gastrointestinal tract or infectious symptoms.

During the initial examination, he reported colicky abdominal pain for weeks, as well as palpitations occurring once or twice a month. A pre-admission episode of elevated blood pressure and glucose levels was noted. However, 24-h ambulatory blood pressure monitoring (ABPM) did not show sustained hypertension. He had no associated headache or diaphoresis.

Analysis carried out after the acute episode of pancreatitis revealed plasma metanephrines of 582 mg/dl (normal <90) and 24-h urine metanephrines of 1820 μg/24 h (normal <341). Plasma cortisol, aldosterone and renin were within normal limits. Electrocardiogram and transthoracic echocardiography ruled out the presence of heart disease.

Given the probable diagnosis of pheochromocytoma, the patient was started on medical treatment, the alpha-blocker doxazosin 1 mg per day, with a progressive increase to 2 mg per day, for the two weeks prior to surgery. During follow-up, the patient responded well to doxazosin treatment, maintaining blood pressure at 115–125 mmHg systolic and 80–85 mmHg diastolic, with heart rate in the range of 65–75 beats per minute. Notably, beta-blockers were not added due to the patient's tendency to hypotension with low doses of doxazosin and to maintain heart rate within the target control range. Finally, a laparoscopic total left adrenalectomy was performed with no postoperative complications.

Pathology examination confirmed a pheochromocytoma. There was no infiltration of capsular venous spaces and no infiltration of the capsule. The Ki67 staining index was 5%. Post-surgery, the patient's abdominal pain resolved and his urine metanephrine levels returned to normal, with no recurrence of hypertension or hyperglycaemia.

Discussion

Acute pancreatitis as a form of presentation of pheochromocytoma, although uncommon, has been described in several previous cases in the literature.[2–5] In these cases, the main challenge is to recognise the relationship between two apparently unrelated diseases in order to avoid misdiagnosis or delayed diagnosis. These cases often have common features. Patients usually present with the clinical features of acute pancreatitis, such as severe abdominal pain, nausea, vomiting and elevated pancreatic enzymes. A thorough evaluation, including imaging studies, is then performed to determine the aetiology of the pancreatitis, leading to the incidental discovery of a pheochromocytoma.

The precise pathophysiological mechanisms underlying pheochromocytoma-induced pancreatitis are not fully understood, but have been the subject of debate. It is known that pheochromocytomas release excess catecholamines,

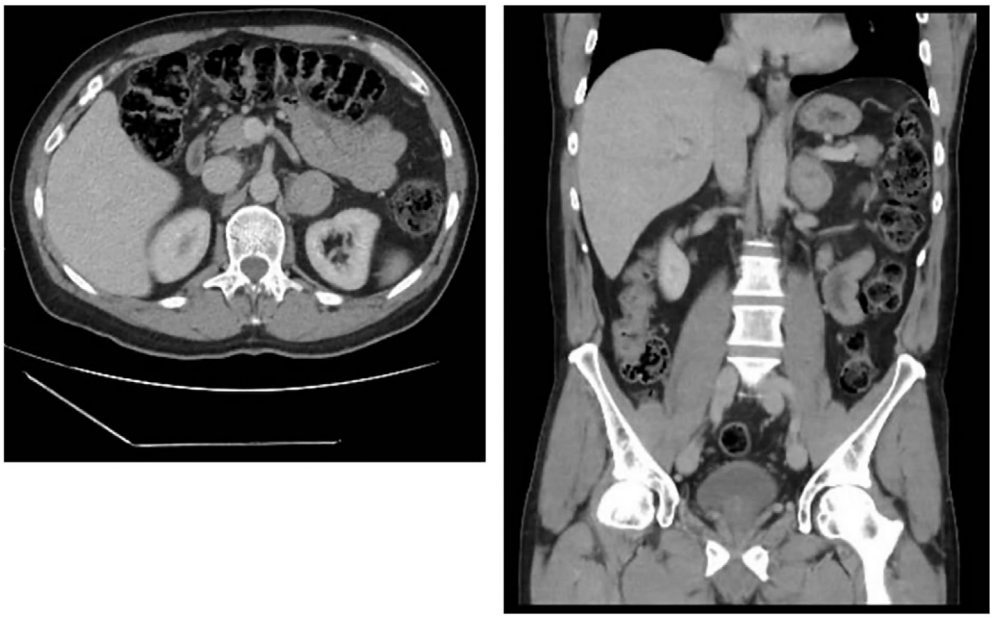

Figure 1 CT scan of abdomen and pelvis. Left adrenal nodule measuring 36 mm × 38 mm with regular contours, showing an average density of 43 HU.

in particular epinephrine and norepinephrine, which can cause a range of cardiovascular and systemic effects. One proposed mechanism is the vasoconstrictive action of catecholamines on the splanchnic arteries, reducing blood flow to the pancreas.[3] This can lead to pancreatic ischaemia, cell injury and ultimately acute pancreatitis. In addition, catecholamines can stimulate the release of inflammatory mediators, such as cytokines and chemokines, which can further aggravate pancreatic injury. This combination of processes results in a vasoconstriction/inflammation syndrome, which is the most recognised pathophysiological explanation in the literature.[4]

Another plausible explanation revolves around a mechanical cause, specifically a dysfunction of the sphincter of Oddi.[3,6] In this hypothesis, the adrenergic action of catecholamines triggers the contraction of the sphincter of Oddi, leading to increased resistance in both the biliary and pancreatic ducts. This can result in elevated intrapancreatic pressure, causing biliary reflux into the pancreatic duct and, ultimately, pancreatitis. Sphincter of Oddi dysfunction can disrupt the normal flow of pancreatic juices and bile, contributing to tissue damage and inflammation. These diverse mechanisms highlight the complexity of this presentation.

In fact, cases of pheochromocytoma associated with hyperamylasaemia have been described without evidence of pancreatic involvement.[2,7,8] In general, it is thought that the origin of hyperamylasaemia in these cases may be pulmonary. Ischaemic damage to amylase-containing tissues can lead to release of the enzyme. Amylase is present in both diseased lung tissue and normal tissue. Thus, when pulmonary endothelial cells are subjected to hypoxia due to the potent vasoconstrictor action of circulating catecholamines, amylase levels may increase in the absence of pancreatitis or salivary disease. In the cases described, most patients had associated cardiomyopathy and acute pulmonary oedema, explaining the pulmonary hypoxia.[8,9] Therefore, in a patient with pheochromocytoma and hyperamylasaemia, not only acute pancreatitis should be considered as a differential diagnosis. This suggests the need to perform amylase isoenzyme analysis to differentiate its origin, and to add the determination of serum lipase to guide the diagnosis.[10]

In conclusion, acute pancreatitis as a presentation of pheochromocytoma is an uncommon but important phenomenon to consider in clinical practice. Patients with acute pancreatitis of unclear aetiology should undergo a thorough evaluation, including imaging studies, to detect the presence of a pheochromocytoma. Pathophysiological mechanisms underlying this unusual presentation include catecholamine-induced vasoconstriction and possible sphincter of Oddi dysfunction. In addition, cases of hyperamylasaemia have been documented in patients with pheochromocytoma, underscoring the importance of differentiating the origin of the amylase for accurate diagnosis. Early diagnosis and treatment can lead to successful recovery and avoid serious complications in these cases.

Patient consent

Written consent was obtained from the patient after full explanation of the purpose and nature of all procedures used.

Funding

None declared.

Conflicts of interest

None declared.

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The importance of MLPA technique in the diagnosis of multiple endocrine neoplasia type 1

La importancia de la técnica MLPA en el diagnóstico de neoplasia endocrina múltiple tipo 1

Multiple endocrine neoplasia type 1 (MEN1), or Wermer syndrome, is a rare entity with an autosomal dominant inheritance pattern with high penetrance due to pathogenic variants in the germ line of the MEN1 tumor suppressor gene, which encodes a protein called menin1. Its estimated prevalence is 2 cases per 100,000 inhabitants and is characterized by a predisposition to primarily endocrine neoplasms (most commonly parathyroid, enteropancreatic, and pituitary). The diagnosis of MEN1 in a patient has relevant implications for family members, as first-degree relatives have a 50% chance of inheriting the pathogenic variant and can be identified through MEN1 sequential analysis.[1,2]

We present the case of a patient with a personal history of several neoplasms and initial negative genetic study by MEN1 gene sequencing, but with subsequent detection of a heterozygous deletion using multiplex ligation-dependent probe amplification (MLPA), which eventually confirmed the diagnosis.

A 65-year-old woman with a personal history of essential hypertension, type 2 diabetes mellitus with good metabolic control, and several previous neoplasms. At the age of 45, she underwent surgery for primary hyperparathyroidism through right hemithyroidectomy and multiple parathyroidectomy (3 and a half glands), with pathological anatomy consistent with adenoma in the right inferior gland and hyperplasia in the right superior gland. Two years later, she underwent cephalic duodenopancreatectomy due to the finding of one mass in the head of the pancreas after significant unintentional weight loss, which was both analytically and histologically consistent with pancreatic glucagonoma (2 tumors) and subsequently left adrenal adenoma treated with left adrenalectomy. At age 59, she underwent right hemicolectomy for moderately differentiated adenocarcinoma of the colon pT2N0. She has currently been referred to for hereditary cancer screening and for a left breast nodule incidentally detected on follow-up computed tomography one month earlier. Further study was completed with mammography (BI-RADS 3–4A) and biopsy, which were consistent with the presence of intraductal carcinoma with estrogen receptor expression. A multidisciplinary team decided to perform seed-guided tumorectomy along with radiotherapy and hormonal treatment with anastrozole. Given the clinical phenotype of MEN1, genetic testing was performed 4 years earlier using polymerase chain reaction (PCR) amplification of the coding exons and splicing regions of the MEN1 gene and subsequent analytical sequencing, with no pathological findings. Given the personal history of multiple neoplasms, genetic sequencing of genes related to breast, ovarian, and colorectal cancer (BRCA1, BRCA2, CDH1, STK11, TP53, ATM, BRIP1, CHEK2, PALB2, MSH6, RAD51D, MSH2, MLH1, APC, MUTYH, EPCAM, and PMS2) was performed, with no