Clinical case

Adrenal necrosis mimicking pheochromocytomas during acute pancreatitis

Une nécrose surrénalienne au cours d’une pancréatite aiguë mimant un phéochromocytome

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Résumé

Contexte. – L’association d’une hypertension artérielle et d’une augmentation de l’excrétion des catécholamines et des métanéphrines est fortement évocatrice de phéochromocytome. Cependant, toute libération massive de catécholamines et dérivés métoxylés n’est pas synonyme de phéochromocytome. Patients. – Nous rapportons deux cas de patients atteints de pancréatite aiguë ayant présenté des fluctuations tensionnelles avec poussées hypertensives et évaluations des catécholamines et métanéphrines dans les valeurs de celle d’un phéochromocytome. Résultats. – L’apparition au scanner d’une hétérogénéité d’une glande surrénale sans image tumoraire orienta vers une nécrose unilatérale de la glande associée à une libération concomitante et massive de catécholamines et dérivés métoxylés. Conclusion. – Au cours des atteintes multiviscérales associées aux pancréatites aiguës, le choc cardiogénique est fréquent. Cependant, les fluctuations tensionnelles peuvent aussi être en rapport avec des atteintes centrales (neurologiques) ou encore comme dans notre cas avec des atteintes nécrotiques des glandes surrénales. La prise en charge de ces fluctuations tensionnelles nécessite alors des thérapeutiques spécifiques.

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Abstract

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Keywords: Acute pancreatitis; Hypertension; Pheochromocytoma; Metanephrines

Mots clés : Pancréatite aiguë ; Hypertension ; Phéochromocytome ; Métanéphrines

1. Introduction

Acute pancreatitis is a severe disease often worsened by a systemic inflammatory response syndrome and septic shock [1]. During acute pancreatitis, many peptides are released by
the necrotic pancreas transforming a localized disease into a multisystem disease frequently including the cardiac muscle [2]. The hemodynamic features of cardiovascular depression or shock (e.g. reduced ejection fraction, decreased vascular systemic resistances) are thus often present. Conversely, hypertensive episodes are quite rare in this situation. Generally speaking, the association of hypertension and/or acute hypertensive crisis with catecholamine and metanephrine excretion above normal range and with adrenal gland radiological abnormalities strongly supports the diagnosis of pheochromocytoma [3].

We report here two cases of acute pancreatitis with hypertensive crisis and markedly elevated catecholamine and metanephrine excretion. The development over a few days of an adrenal mass rules out the preexistence of pheochromocytoma, but supports the diagnosis of necrosis of the adrenal gland.

2. Patients

2.1. Case 1

Mr S. (34-year-old) was admitted into an intensive care unit for a severe abdominal pain. He had no previous medical or surgical history. The physical examination was normal apart from abdominal pain. Blood pressure was 130/90 mmHg and heart rate was 100 beats/min. Laboratory data revealed an inflammatory syndrome, hypercalcemia and biochemical characteristics of acute pancreatitis including elevated serum amylase and lipase. Abdominal computed tomodensitometry (CT) scans showed normal adrenal glands, no adrenal tumor but a fluid collection in the right pararenal anterior space (Fig. 1A). The diagnosis was acute pancreatitis induced by hypercalcemia related to primary hyperparathyroidism (calcium 2.71 mmol/l, N [2.1–2.65], parathormone 131 pg/l, N [10–60]). Two parathyroid tumors were visible on the neck ultrasonography.

After 8 days, Mr S. developed a systemic inflammatory response syndrome (SIRS) with hyperthermia (40 °C), tachycardia (150 beats/min), elevated white blood cell count (28.6 10^9/L). Intravenous antibiotics (ofloxacin, piperacillin, tazobactam, netilmicin) were added to the ongoing antalgic drugs (acetaminophen, nefopam). Because of the development of adult respiratory distress syndrome (paO₂/FiO₂ < 150, bilateral pulmonary infiltrates), Mr S. needed sedation, intubation and ventilation.

Surprisingly, Mr S. developed a fluctuating hypertension (from 110/60 to 180/80 mmHg) and tachycardia (139 beats/min). These hypertensive crises which required intravenous antihypertensive drugs questioned the existence of a pheochromocytoma. In the context of hyperparathyroidism, the diagnosis of multiple endocrine neoplasia 2A (MEN2A; hyperparathyroidism, pheochromocytoma, medullary thyroid carcinoma) was challenged. Plasma catecholamines and urinary catecholamines and metanephrines (24h periods) collected before any antihypertensive treatment were elevated (Table 1). The third component of putative MEN2A, the medullary thyroid carcinoma, was ruled out because of a normal plasma calcitonin level (<3.0 pg/ml).

Because of the possible pheochromocytoma and as the pancreatitis was worsening, another abdominal CT-scan was performed. It showed an enlargement of the right adrenal gland and a more heterogeneous structure than the one described on the previous scan but no obvious tumor (Fig. 1B). The diagnosis of pheochromocytoma was then excluded. The etiological diagnosis of this hypertension with elevated catecholamines
and metabolites mimicking pheochromocytoma was likely a necrosis to the left adrenal gland. There was absolutely no clinical or unspecific biochemical features of adrenocortical insufficiency. No specific assay was performed for the diagnosis of adrenal insufficiency. Under invasive antihypertensive treatment (urapidil, clonidine and nicardipine), blood pressure returned to normal values (121/64 mmHg). The patient was also maintained on enoxaparin. A percutaneous drainage under imaging guidance was then attempted but Mr S. died a few days later because of severe hemorrhagic shock with liver and kidney failure. Because of the widespread abdominal necrosis, no autopsy for adrenal pathological analysis was performed.

2.2. Case 2

Mr U. (43-year-old) was admitted into an intensive unit care for acute pancreatitis. He had a history of moderate hypertension treated with angiotensin-converting enzyme inhibitors. Mr U. underwent coelioscopy for a puncture of a pancreatitis nodules thought to be a pancreatic cancer. On D+2, Mr U. developed a bilateral adrenal hemorrhage with adrenal insufficiency. No specific assay was performed for the diagnosis of adrenocortical insufficiency. Under intravenous antihypertensive treatment (urapidil, clonidine and nicardipine), blood pressure returned to normal values (121/64 mmHg). The patient was also maintained on enoxaparin. A percutaneous drainage under imaging guidance was then attempted but Mr U. died a few days later because of severe hemorrhagic shock with liver and kidney failure. Because of the widespread abdominal necrosis, no autopsy for adrenal pathological analysis was performed.

### Table 1

Catecholamine and metanephrine levels in patients S and U compared to values from (i) hospitalised subjects, (ii) patients in an intensive care unit and (iii) patients with a proven pheochromocytoma median [range] [14].

<table>
<thead>
<tr>
<th></th>
<th>Patient S</th>
<th>Patient U</th>
<th>Normal range</th>
<th>Intensive care unit</th>
<th>Pheochromocytomas</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 1</td>
<td>Day 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urines (nmol/ld)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Metanephrine</td>
<td>1900</td>
<td>2125</td>
<td>1498</td>
<td>445 [25–2500]</td>
<td>966 [76–1765]</td>
</tr>
<tr>
<td>Noradrenalin</td>
<td>514</td>
<td>602</td>
<td>2783</td>
<td>265 [17–2682]</td>
<td>304 [79–930]</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>188 [20–1638]</td>
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<td></td>
<td></td>
<td></td>
<td>7047 [1158–102,221]</td>
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<td></td>
<td></td>
<td>2431 [451–43,733]</td>
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<td></td>
<td>818 [73–14,704]</td>
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<td></td>
<td></td>
<td></td>
<td>188 [20–1638]</td>
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<tr>
<td>Plasma (pmol/l)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adrenalin</td>
<td>936</td>
<td>&lt;1000</td>
<td>33</td>
<td>343 [250–13,895]</td>
<td>691 [250–124,974]</td>
</tr>
</tbody>
</table>

\[ a \text{ } n=32, \quad b \text{ } n=24, \quad c \text{ } n=15, \quad d \text{ } n=21.\]

3. Discussion

Pheochromocytomas are rare hypertensive diseases with multiple clinical presentations. To confirm the diagnosis of pheochromocytoma both biology (catecholamines metabolites i.e. metanephrines overexcretion) and imaging (adrenal imaging by CT or MRI or isotopic MIBG scans) are mandatory [3]. Indeed, in some situations such as intense stress, catecholamines and metanephrines can rise in the range of pheochromocytomas; imaging is of course normal confirming the functional nature of the catecholamine and metanephrine overexcretion [4]. We report here two cases of acute pancreatitis associated with hypertensive crisis leading to the discovery of markedly elevated catecholamine and metanephrine excretion raising the suspicion of pheochromocytoma. In this context, abdominal imaging (repeated CT-scans) displayed the development of an adrenal enlargement related to adrenal necrosis rather than to a pheochromocytoma. The catecholamine-induced hypertension was then related to a non-functional, non-neoplastic adrenal lesion.

Bilateral adrenal hemorrhages, generally due to sepsis or coagulopathy, are associated with adrenocortical insufficiencies but do not mimic pheochromocytoma. Adrenal hemorrhage with adrenal insufficiency has also been described in patients with severe acute pancreatitis [5–7]. Very rare cases of unilateral adrenal hemorrhage have been reported to mimic pheochromocytomas [8–10]. Our patients had unilateral adrenal enlargements and no adrenal insufficiency suggesting that the process was indeed restricted to a single gland. The adrenal necrotic process could have been promoted by the anticoagulant therapy although no evidence of hemorrhage was visible on the CT-scans. Furthermore, at the time, there was neither hepatic insufficiency nor abnormal coagulation.

Intensive care unit hospitalization per se can induce stress-related intense catecholamine and metabolite secretion [4]. A brief study in our department indicated that the levels of metanephrines excreted by patients could reach the range of

pheochromocytoma because of the very wide range of values. This was achieved in the absence of acute blood pressure fluctuations such as the one reported in our cases. In this context of acute pancreatitis, SIRS is a frequent and serious complication usually associated with hemodynamic disorders such as low blood pressure, low systemic vascular resistances and requires the use of vasopressive drugs. In our reports, the criteria for the diagnosis of SIRS were all present but there was a paradoxical hypertension. The latter could be attributed to recurrent massive release of catecholamines (adrenal gland necrosis). The unexpected fluctuating hypertension occurring during acute pancreatitis and SIRS may be misunderstood if catecholamines and metanephrines are not studied. Adrenal medulla lesions have been reported in animals after acute pancreatitis with shock [11]. Conversely, acute pancreatitis has been reported in malignant hypertension [12] that could possibly be secondary to a pheochromocytoma. Clinicians must be aware of this complication and adrenal gland lesions must be suspected in these circumstances. While elevated excretion of catecholamines and metanephrines could be ambiguous especially in the context of intensive care, radiological examinations can effectively establish this diagnosis while ruling out a pheochromocytoma [13].

References