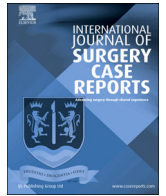




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Refractory shock during the anesthetic and surgical management of an intrahepatic tumor arising from the adrenal cortex: A case report

Philippe Hantson^{a,b,*}, Catherine Hubert^c, Audrey Dieu^d, Diego Castanares-Zapatero^a, Julie Lelotte^e, Pierre-François Laterre^a

^a Department of Intensive Care, Cliniques St-Luc, Université catholique de Louvain, 1200 Brussels, Belgium

^b Louvain Centre for Toxicology and Applied Pharmacology (LTAP), Université catholique de Louvain, 1200 Brussels, Belgium

^c Department of Abdominal Surgery and Transplantation, Unit of Hepato-biliary and Pancreatic Surgery, Cliniques St-Luc, Université catholique de Louvain, 1200 Brussels, Belgium

^d Department of Anesthesiology, Cliniques St-Luc, Université catholique de Louvain, 1200 Brussels, Belgium

^e Department of Pathology, Cliniques St-Luc, Université catholique de Louvain, 1200 Brussels, Belgium

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ABSTRACT

INTRODUCTION: Adrenocortical carcinoma is a rare type of malignant adrenal tumor with a possibility of delayed metastases. Diagnosis may be delayed with a non-secreting tumor or metastasis, and even in this case, surgical management may be complicate.

PRESENTATION OF CASE: A 55-year-old man underwent elective surgery for the resection of a large intra-hepatic mass from an undetermined type according to a recent liver biopsy. He had a previous history of a non-secreting adrenal tumor that was operated ten years before. Pre-operatively, he was poorly symptomatic, with a normal arterial blood pressure. Anesthesia induction was uneventful, but at the time of tumor resection and removal, he developed extreme vasoplegia and shock with anuric renal failure, lactic acidosis, four-limb and abdominal compartment syndrome. The patient died on day 9 from delayed septic complications. According to the pathological findings, the tumor was a non-secreting adrenocortical carcinoma.

DISCUSSION: Adrenocortical carcinoma (ACC) is rare condition with diverse clinical manifestations due to excessive hormonal production when the tumor is secreting and mimicking pheochromocytoma. Our patient underwent the resection a large intrahepatic non-secreting metastasis more than ten years after the initial lesion. Peri-operative and post-operative management was complicated by a refractory shock with the characteristics of a secondary systemic capillary leak syndrome. The role of endothelial lesions may be discussed.

CONCLUSION: Surgery of metastatic adrenocortical carcinoma may be complicated by severe hemodynamic complications, even in the absence of hormonal secretion.

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1. Introduction

Adrenocortical carcinoma (ACC) is a rare type of malignant adrenal tumor that may produce various types of steroids [1]. When the tumor is not secreting, the diagnosis may be delayed and large tumors are occasionally found in poorly symptomatic patients [2]. Very rarely, ACC may present as pheochromocytoma [2–5]. We present an unusual observation in an academic hospital of a large intra-hepatic mass occurring ten years after the resection of a non-secreting adrenal mass of an unidentified type. The anesthetic management was complicated by a refractory vasoplegic

shock allowing a discussion about the possible pathophysiological mechanisms. The work has been reported in line with the SCARE criteria [6].

2. Presentation of case

A 55-year-old man had a previous history of resection of a right adrenal tumor 10 years ago. At that time, the exact nature of the tumor was undetermined. There was no documented evidence for an excessive secretion of aldosterone, cortisol, catecholamines or sexual hormones at endocrine work-up, neither for monoclonal gammopathy. The mass (diameter 10.6 cm) had been found after that the patient had presented post-traumatic hematuria. He was poorly symptomatic, with a normal blood pressure. According to the staging system, the tumor was classified as stage II (> 5 cm). The anesthetic and surgical procedure was unevent-

* Corresponding author at: Department of Intensive Care, Cliniques St-Luc, Avenue Hippocrate, 10, 1200 Brussels, Belgium.

E-mail address: philippe.hantson@uclouvain.be (P. Hantson).

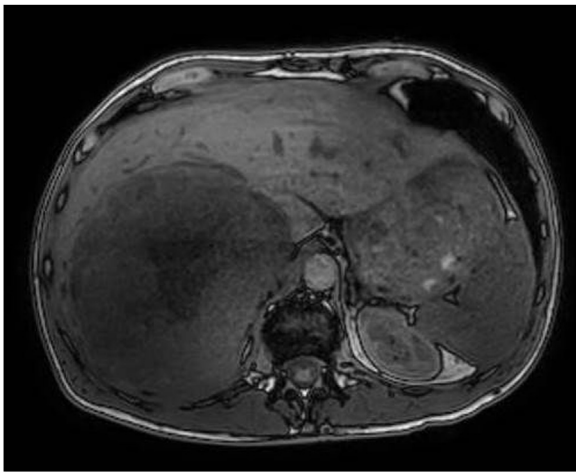


Fig. 1. Pre-operative magnetic resonance imaging (MRI) demonstrating a large (14.4 × 12.6 cm) intra-hepatic mass.

ful. A follow-up (computed tomography and positron emission tomography (PET)) was proposed on an annual basis for at least five years. The patient remained asymptomatic until January 2019 when liver enzymes disturbances were found at routine laboratory investigations. The abdomen computed tomography and magnetic resonance imaging revealed the presence of a large (14.4 × 12.6 cm) intrahepatic mass (Fig. 1). No other localization was found at PET-scan (FDG-18) and the tumor appeared metabolically active. A liver biopsy was proposed. The results were not conclusive. A molecular research assay for the identification of single nucleotide variants in 26 frequently mutated genes in solid tumors (Tumor Hotspot MASTR Plus » (Multiplicom)) was negative. The surgical resection of the intrahepatic tumor was planned. At the pre-anesthetic visit, the patient was asymptomatic, with a normal arterial blood pressure (133/73 mmHg) and heart rate (58/min) and did not take any medication. Again, laboratory investigations for abnormal endocrine hormonal secretion (cortisol, aldosterone, testosterone, catecholamines) and biomarkers of liver cancer were negative. The induction of anesthesia was uneventful and maintenance was achieved with sevoflurane. The major difficulty of the surgical procedure was the mobilization of the right liver according to the previous operation of right adrenalectomy and severe adhesions between the posterior part of the liver and the vena cava responsible of bleeding at the level of hepato-caval small vessels. The patient became hypotensive and required blood transfusions (1347 mL) and increasing doses of norepinephrine infusion (up to 0.65 µg/kg/min) to maintain blood pressure. Once the right liver had been mobilized, the parenchymal transection was easy and bleeding free. No portal nor hepatic vein was opened and there was no residual bleeding at the end of the operation. Additionally, the patient received per-operatively 6000 mL of cristalloids and 2000 mL of colloids. No changes were noted in oxygen saturation and end-tidal carbon dioxide during surgery, and the hypothesis of air embolism appeared unlikely. On arrival in the intensive care unit (ICU), norepinephrine infusion rate was 2 µg/kg/min and arterial blood pressure was strictly dependent from major fluid replacement therapy. While the patient had received an additional volume of 16000 mL of cristalloids over 8 h, hemoglobin concentration rose from 8.4 g/dL to 11.5 g/dL within the same interval. Total plasma protein concentration was only 14 g/L at the end of surgery. Further evolution was characterized by refractory vasoplegic shock. The patient was repeatedly investigated by transthoracic echocardiography from ICU admission. At any time, there was a well preserved left ventricular function, with low filling pressures. On the whole, the patient

received 47000 mL of fluids (cristalloids, albumin, and fresh frozen plasma) over the first postoperative day, high dose of vasopressors (norepinephrine up to 5 µg/kg/min) and methylprednisolone. He was ventilated with 1.0 FiO₂. He developed generalized oedema, anuric renal failure, lactic acidosis, four-limb ischemia and rhabdomyolysis. The diagnosis of abdominal compartment syndrome (ACS) was made by the determination of bladder pressure that was higher than 20 mm Hg (normal range <12) with signs of multiple organ dysfunction. At the second laparotomy for decompression of ACS, there was no evidence for an acute liver failure or for intestinal ischemia. On postoperative day 7, while some hemodynamic improvement had been noted with a decrease of vasopressors and of lactic acidosis, blood cultures returned positive for *Escherichia coli* without evidence of intestinal ischemia or perforation on the abdomen computed tomography. This last complication resulted in a refractory septic shock with acute respiratory distress syndrome and the patient died on postoperative day 9. The determination of catecholamines or cortisol concentration was impossible as the patient was anuric and had also received huge amounts of catecholamines during resuscitation. The morphological and immunohistochemical features of the intrahepatic tumor were similar to these described in the primary adrenal tumor (synaptophysin +, MART1 +, alpha-inhibin +, CKA61/AE3 -, chromogranin -), but with a higher Ki67 index (>30%). The diagnosis of metastatic adrenocortical carcinoma was affirmed. At postmortem examination, the main findings were acute tubular necrosis in the kidneys, foci of centrilobular liver necrosis, hemorrhagic necrosis of the spleen, lung congestion with diffuse intra-alveolar hemorrhage and inflammatory cell infiltration. By contrast, coronary arteries were normal, and no signs of inflammatory or ischemic injury were found in the myocardium.

3. Discussion

Adrenocortical carcinoma (ACC) is rare condition (1–2 cases per million per year in adults) with diverse clinical manifestations due to excessive hormonal production when the tumor is secreting (25–75% of ACC). Features of virilisation or Cushing syndrome are then observed. Exceptionally, ACC may present clinically as pheochromocytoma [4,5]. In our patient, the primary adrenal tumor in 2009 was not secreting. No further endocrine work-up was performed between 2009 and 2019 as the patient was strictly asymptomatic. No hepatic mass was found between 2009 and 2014, and the present tumor was diagnosed on the basis of liver test disturbances. Logically, this intrahepatic mass should be considered as a metastatic localization of the first tumor. There was no paroxysmal hypertensive crisis during the surgical manipulation of the tumor. In contrast, the resection of the tumor was immediately followed by a major hypotension with vasoplegic shock. It is known that tumors producing epinephrine alone cause hypotension rather than hypertension [7]. In addition, during the anesthetic management of pheochromocytoma, the manipulation of the tumor is usually causing paroxysmal hypertension followed by hypotension after tumor removal [8]. In the present observation, it could not be documented, either preoperatively or peri-operatively, that the tumor was secreting cortisol, epinephrine or norepinephrine. Huge amounts of fluids, norepinephrine and methylprednisolone were required during resuscitation. At that time, there was no evidence for hemorrhagic, septic or cardiogenic shock. The shock shared most of the characteristics of an acquired systemic capillary leak syndrome [9,10]. This syndrome presents with a characteristic triad of hypotension, hemoconcentration and hypoalbuminemia [10]. The etiologies and triggering factors remain uncertain. It may be considered either as idiopathic (Clarkson's disease) or secondary to infections, chemotherapy, drugs, malignancy or even anesthesia

and surgery [10]. The underlying mechanism is a transient dysfunction of the endothelium, with up to 70% of the plasma shifting from the intravascular to the interstitial space. By contrast to cardiopulmonary bypass surgery, abdominal surgery is a condition that has been exceptionally associated with systemic capillary leak syndrome [11–15]. In all the reported cases after abdominal surgery, the diagnosis was based on the triad of hypotension, hemoconcentration and hypoalbuminemia, after reasonable exclusion of other etiologies of shock. Several reports support an immunologic basis for this syndrome. Among the potential mediators, vascular endothelial growth factor (VEGF) expression is increased in a number of tumor types including ACC and elevated levels of circulating VEGF have been found in some patients with systemic capillary leak syndrome [16,17]. Despite of aggressive resuscitation with fluids and vasopressors, the prognosis is usually very poor. Compartment syndrome involving the limbs or the abdomen is a frequent complication requiring urgent surgery [18,19]. Several pharmacological interventions (steroids, immunoglobulins, . . .) have been proposed, but there is no validated protocol [10].

4. Conclusion

Patients with a history of an adrenal mass of a poorly identified histological type should certainly be investigated for excessive hormonal production when there is evidence for a delayed extra-adrenal localization. With non-secreting ACC as with other tumors, there is still the possibility of vasoplegic shock during surgery due to non-hormonal mechanisms. Systemic capillary leak syndrome is a rare complication of abdominal surgery and may be related to endothelial injury.

Conflicts of interest

No conflict of interest to declare.

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Ethical approval

Not required for single case report according to our institution.

Consent

A written consent was obtained from the relatives.

Author contribution

Dr Philippe Hantson: ICU management, conceptualization, writing original draft, review and editing.

Dr Catherine Hubert: Surgical management.

Dr Audrey Dieu: Anesthetic management, review.

Dr Pierre-François Laterre, Dr Diego Castanares-Zapatero: ICU supervision, review and editing.

Dr Julie Lelotte: Analysis and interpretation of pathological data.

Registration of research studies

NA.

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