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Concomitant Pituitary Apoplexy and Acute Fatty Liver of Pregnancy: About A Case with Review of the Literature

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Abstract **Case Report**

Pituitary complications during childbirth have become relatively rare in developed countries. In this case report, we report a case of panhypopituitarism complicating postpartum acute liver failure. We also review the current literature on cases of pituitary hormone deficiencies associated with acute statosis of pregnancy. 26-year-old patient, pregnant at 37 weeks of amenorrhea, admitted for jaundice with abolition of fetal movements, ultrasound showed a monofetal pregnancy corresponding to the gestational age with absence of any cardiac activity, the initial assessment showed a hepatic cytolysis, hepatic cholestasis, renal insufficiency and oliguria, hemostasis abnormalities, abdominal ultrasound had objectified a hyper echogenic liver suggesting fatty infiltration, After induction of labor and vaginal delivery of a stillborn, the postpartum was marked by the presence of uterine hemorrhage despite the presence of a good safety globe responsible for a state of shock with hypotension requiring the administration of vasoactive drugs, the patient had received several massive transfusions. evolution was marked by the improvement of the hemodynamic state, regression of hepatic cytolysis, improvement of hemostasis, Subsequently the patient reported headaches, abdominal pain, an absence of milky rise and a tendency to hypoglycemia, the hypophysiogram objectified a pituitary insufficiency raising suspicion of the diagnosis of pituitary necrosis which was confirmed by the realization of cerebral magnetic resonance imaging. The presence of risk factors such as peripartum bleeding and disseminated intravascular coagulation secondary to hepatic steatosis acute pregnancy seems to be a risk factor for the occurrence of pituitary apoplexy.

Keywords: Acute fatty liver of pregnancy, pituitary apoplexy, panhypopituitarism, deliverance hemorrhage.

INTRODUCTION

Pituitary complications of childbirth are relatively rare in developed countries. However, the presence of certain circumstances and risk factors can precipitate their occurrence. In our case, the presence of disseminated intravascular coagulation (DIC) in the context of acute fatty liver of pregnancy (AFLP), as well as a postpartum hemorrhage, favored the occurrence of pituitary apoplexy. We report a case of a young patient who developed pituitary apoplexy concomitant with AFLP.

CASE REPORT

The patient is a 26-year-old pregnant woman, G2P2, her first pregnancy was carried to term with a vaginal delivery of a healthy infant 4 years ago, the current pregnancy was estimated at 37 weeks gestation, monitored by a general practitioner, one week before her admission, the patient developed a subicterus and felt a decrease in fetal movements, her general practitioner examined and transferred her to the Military Hospital of Instruction Mohammed V of Rabat in the obstetric gynecology ward. On admission, the patient was found to be conscious and in a good general condition, with conjunctival jaundice, blood pressure at 160/90mmhg, apyretic, absence of edema of the lower limbs, presence of proteinuria in the labstix, absence of uterine contractions, absence of fetal heart sounds, Uterine height was consistent with gestational age, ultrasound showed a monofetal pregnancy consistent with gestational age with no cardiac activity, placenta in place with no detachment or retro-placental hematoma.

An initial blood test indicated a liver cytolysis: alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were increased more than 10 times the normal value , liver cholestasis with total bilirubin at 120 mg , alkaline phosphatase at 257 mg , Hemoglobin at 11.9 g/100ml, white blood cells at 21000, platelets at 191000, prothrombin time (PT) at 38%, activated thromboplastin time (ATT) at 64/36, fibrinogen at 0.54 with high di dimers, renal failure with urea at 0.50g /l, creatinine at 21mg with oliguria . Abdominal ultrasound showed a hyper echogenic liver suggesting a fatty infiltration without dilation of the intra and extra hepatic bile ducts After induction of labor and vaginal delivery of a stillborn baby, the postpartum period was marked by the presence of uterine bleeding despite the presence of a good safety globe. A second check-up was requested showing: a deglobulation with hemoglobin at 7.9, PT still low with high ATT and appearance of thrombocytopenia with a drop-in fibrinogen in favor of progressive disseminated intravascular coagulation (DIC), a slight initial improvement in liver cytolysis: ALT 134, AST 216 and cholestasis and worsening of renal function with oligo-anuria. The patient was transfused with 03 packed red blood cells (PRBCs), 06 fresh frozen plasma (FFPs), 10 platelets pellets (PPs) with filling and restarting of diuresis. In view of the persistence of the hemorrhage and hypotension at 90/40mmhg.the patient was transferred to the surgical intensive care unit (ICU) after ruling out any surgical indication. On admission to the ICU the patient was conscious, subicteric, hemodynamically: arterial hypotension with tachycardia corrected by fluid administration of saline, discolored conjunctiva The blood tests showed anemia at 5.7 g/dl hemoglobin, thrombocytopenia at 75.000, prothrombin time (PT) out of range, deterioration in renal function with urea at 0.60, creat at 20 , persistent hepatic cytolysis: AST at 111, ALT at 176 and cholestasis: Bilirubin at 95 mg, hyponatremia at 128 mmol/l and kalemia at 5.3 mmol/l, the patient received a massive transfusion with a total of: 09 (PRBC), 22 FFPs, 20 PPs With the following treatment: Tranexamic Acid , oxytocin ,antibiotic , With safety globe monitoring. The evolution was marked by Regression of hepatic cytolysis until normalization of renal function with resumption of good diuresis improvement of hemostasis: increase in PT, fibrinogen and cessation of uterine bleeding Persistence of deglobulation in relation to hemolysis. Persistence of thrombocytopenia with gradual improvement. The patient subsequently developed headaches with absence of milk production and a tendency to hyponatremia and hypoglycemia in the biological work-up. A cortisolaemia was then requested which revealed very collapsed values. A hypophysiogram was performed, which showed pituitary insufficiency with: luteinizing hormone (LH) at 0.00 IU, follicle-stimulating hormone (FSH) at 0.06 IU, prolactin at 12 IU. A cerebral Magnetic resonance imaging (MRI) was performed, which indicated a pituitary necrosis (Figure 1). The patient was then transferred to the gynecology ward and was put on hydrocortisone 40mg per day, levothyrox 25 ug per day, potassium supplementation and gastric protection by proton pump inhibitor (PPI), the symptoms improved in 48 hours and the patient was transferred to the endocrinology ward.

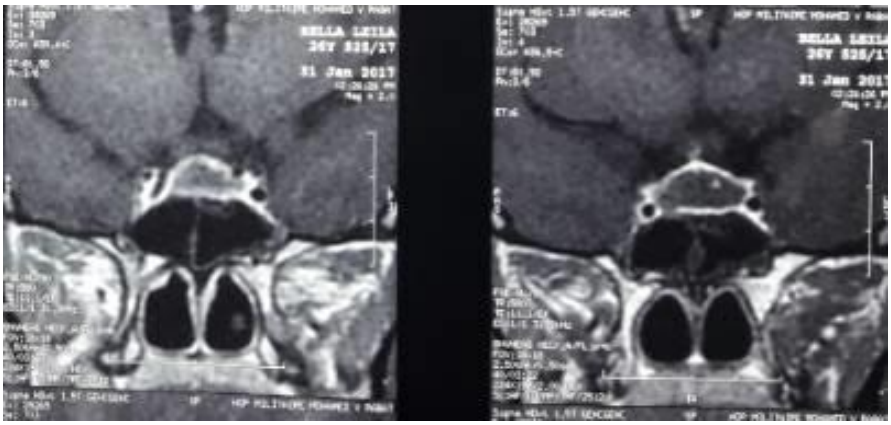

Figure 1: Enlarged pituitary gland with heterogeneous signal in T1 and T2, with peripheral contrast evoking pituitary necrosis with onset of apoplexy

DISCUSSION

We present here a case of acute fatty liver of pregnancy (AFLP) complicated by pituitary apoplexy. Our review of the literature suggests that this is the fourth case reported to describe the coexistence of these two rare and often fatal syndromes. Study of the circumstances surrounding this case and those reported in the literature suggest that coagulopathy and blood loss may be a risk factor for the co-occurrence of the 2 conditions during pregnancy.Acute fatty liver of pregnancy is a rare disease associated with high mortality that was first described by Sheehan in 1940[1] with many cases reported since. Mortality has decreased considerably with early diagnosis and advances in treatment in both intensive care and obstetrics but AFLP remains a clinical syndrome of relatively uncertain pathogenesis. Recent evidence suggests a fetal-maternal effect, related to a fetal defect in mitochondrial fatty acid oxidation due to a deficiency of (LCHAD: Long chain 3-hydroxyacyl CoA

dehydrogenase) [2]. Currently, the diagnosis of AFLP is based on clinical data and biological abnormalities such as uric acid, antithrombin III, white blood cells (WBC), creatinine, electrolytes, blood glucose, liver cytolysis, cholestasis and also by imaging in the form of ultrasound and/or computed tomography (CT). Liver biopsy, although fundamental to the diagnosis of certainty, is not usually performed because of the risks associated with pregnancy and coagulopathy [2]. The Swansea criteria [3] are used to make the diagnosis.Specifically, the presence of 6 or more of the following criteria are necessary to make the diagnosis in the absence of another cause: (1) vomiting, (2) abdominal pain (3) polydipsia/polyuria, (4) encephalopathy, (5) elevated bilirubin at 14 mmol / L, (6) hypoglycaemia with glucose < 70 mg / dL, (7) elevated uric acid > 5.7 mg / dL, (8) hight leukocytosis , (9) ascites or glowing liver on ultrasound, (10) elevated transaminases (AST or ALT) > 42 IU /L, (11) elevated blood glucose > 5.7 mg / dL , (12) elevated ammonia level at 47 mmol/L, (12) renal failure with creatinine > 1.7 mg/dL, (13) coagulopathy with prothrombin time at 14 s or Activated thromboplastin time (ATT) more than 3 times control, and (14) microvesicular steatosis on liverbiopsy . Our patient has more than 6 of these criteria, thus confirming the diagnosis. Some authors also propose to incorporate an antithrombin III activity at 65% in the early diagnosis of AFLP [4].

Pituitary apoplexy is a rare clinical syndrome due to haemorrhage and/or sudden infarction of the pituitary gland [5]. Ischaemic necrosis of the pituitary gland due to low blood flow, also known as Sheehan's syndrome, is the oldest known cause of pituitary insufficiency, described in 1939 by Sheehan [6]. It classically occurs in the aftermath of haemorrhagic childbirth with cardiovascular collapse. The diagnosis of anteropituitary insufficiency can be quickly evoked with symptoms such as: headaches, visual disorders, diplopia due to compression of the oculomotor nerves and signs of hypopituitarism, notably the absence of milk production and return from childbirth with hypoglycaemic crises [7-9]. However, hypopituitarism is most often dissociated and the clinical signs, which are usually discreet, lead to the diagnosis being overlooked. Some partial pituitary necroses are manifested by frustrated forms, dissociated endocrine manifestations and make the diagnosis difficult [10]. Hormonal investigations are of major importance and allow the confirmation of anteropituitary insufficiency and are based on the exploration of the 5 axes: corticotropic, lactotropic, thyroid, gonadotropic and somatotropic. MRI has an important role to play in the positive diagnosis of pituitary apoplexy, given its sensitivity in exploring the hypothalamic-pituitary region [11]. Although the pathophysiology of pituitary insufficiency is not fully understood, the basic process is known. Actually, it is an infarction secondary to a cessation of blood flow to the anterior lobe of the pituitary, which may be due to vasospasm, thrombosis or vascular compression [12]. It is well known that the pituitary gland is physiologically enlarged during pregnancy due to nodular hyperplasia, which may be responsible for a 30-100 per cent increase in pituitary gland weight [12]. The size of the sella turcica may also play a role in the pathogenesis of pituitary necrosis. A relatively small size has even been suggested as a risk factor [13].

Pituitary apoplexy with concomitant AFLP is rare .Until this day, only 3 cases have been reported in the literature. In the case described by Piech et al, the patient developed concomitant diabetes insipidus and the diagnosis was made 3 weeks after delivery. DIC and massive haemorrhage during delivery were reported in this case, which contributed to the pituitary insufficiency [14]. Yamauchi et al have highlighted the involvement of DIC and delivery stress in ante-pituitary necrosis and have published a case of a patient with acute gravidic hepatic steatosis complicated by hypercoagulability due to DIC who developed postpartum ante-pituitary failure without massive haemorrhage or hypovolaemia [15]. The third case was reported by Barvalia in the United States in 2015. The case reported a 29-year-old woman at 25 weeks gestation who presented with subacute onset of headache accompanied by nausea and vomiting. The diagnosis of acute liver failure was made in view of the clinicobiological signs associated with coagulopathy secondary to hidden intravascular coagulation . The paraclinical workup revealed a deficiency of all anterior pituitary hormones and brain magnetic resonance imaging (MRI) was compatible with pituitary apoplexy [16].

In our patient, the presence of DIC in the setting of AFLP and the subsequent delivery haemorrhage and massive transfusion precipitated the onset of pituitary failure. As there is limited data on the association between AFLP and hypopituitarism, it is difficult to discern the exact pathophysiology leading to this event. It is possible that in the 4 clinical cases including our case, DIC is an independent risk factor in pregnant women. A previous study concluded that the presence of DIC and AFLP was not significantly associated with maternal outcomes except in patients with a genital injury that resulted in excessive bleeding [17]. The latter, however, is not uncommon in patients with AFLP who frequently have hemostasis disorders with massive bleeding and fluctuating blood pressure during the peripartum period, potentially increasing the risk of pituitary apoplexy. Further noting that many reported cases of pituitary apoplexy have been associated with thrombocytopenia independently of DIC [18].

In conclusion, fluctuations in blood pressure during peripartum, massive haemorrhage, stress and coagulopathy secondary to acute liver failure may all contribute to an increased risk of pituitary apoplexy in

an already oedematous gland. Hypopituitarism is usually treated with resuscitative measures including vascular filling, monitoring of electrolyte disturbances, and replacement of deficient pituitary hormones. In our patient, the symptoms of headache and generalized weakness improved within 24 hours of initiation of glucocorticoids and levothyroxine. Early neurosurgical intervention is often not necessary, as the risk of surgery in the context of thrombocytopenia would outweigh the benefit [19]. We could not find any randomised prospective studies and recommendations in the literature on the surgical management of acute cases of pituitary apoplexy. However, surgery may be considered in cases of Neuro-ophthalmic symptoms and vision loss [20]. In our patient, there was no surgical indication because of the absence of severe ophthalmic signs.

CONCLUSION

Our case report as well as 3 others presented in the literature suggest that patients with acute fatty liver of pregnancy, particularly if associated with disseminated intravascular coagulation, may develop pituitary apoplexy or even panhypopituitarism. Therefore, these high-risk patients should receive a complete peripartum hemodynamic monitoring.

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