

Hemorrhagic stroke complicating severe pre-eclampsia: A report of two cases

I. Baouch¹, M. Dridi¹, F. El Hilali¹, H. Moustaid¹, S. Benkirane¹

¹Department of Gynecology and Obstetrics
University hospital center Mohamed VI,
Abdelmalek Essadi university
Tanger, Morocco

Abstract: *Pregnancy is classically considered a risk factor for both ischemic and hemorrhagic strokes. The state of maximal hypercoagulability, increased cardiac output, total blood volume, and structural changes in arterial media are regarded as physiological modifications during pregnancy that may elevate the risk of vascular events. Hemorrhagic stroke can occur either spontaneously or as a result of the rupture of vascular lesions such as aneurysms and arteriovenous malformations. This complication only occurs in a small proportion of women with pre-eclampsia but is associated with high morbidity and mortality. The relationship between pre-eclampsia and the occurrence of non-traumatic hemorrhagic stroke involves risk factors, including endothelial damage secondary to pre-eclampsia, uncontrolled hypertension, and biological disorders such as thrombocytopenia in the context of HELLP Syndrome and coagulation disorders. It is important to consider the risk of stroke in women diagnosed with pre-eclampsia or eclampsia. Specifically, women experiencing neurological symptoms should undergo prompt evaluation, blood pressure management, and initiation of thromboprophylaxis. This case report's aim is to shed the light on the significance of conducting thorough neurological examinations for pregnant women who exhibit neurological symptoms. It also emphasizes the role of multidisciplinary management in severe, life-threatening conditions.*

Keywords: Severe pre-eclampsia, Hemorrhagic cerebrovascular incident

1. INTRODUCTION

The cerebrovascular accident is a very common neurological emergency, leading to significant morbidity and mortality. The term "stroke" is employed to denote brain damage arising from a vascular origin (1). In essence, an ischemic stroke transpires when there is a hindrance in blood flow to the brain, leading to tissue death. Various factors contribute to ischemic stroke, such as atherosclerotic disease, embolisms, thrombi, and hypotension. On the other hand, a hemorrhagic stroke occurs when a blood vessel ruptures, causing damage to the brain tissue as blood spreads into the parenchyma. Hypertension, aneurysms, and arteriovenous malformations are key factors that contribute to the occurrence of hemorrhagic strokes (2).

Stroke is a rare event during pregnancy, with an incidence ranging from 10 to 34/100,000 deliveries (3). The incidence of stroke during the antepartum period is relatively low, increasing by 9 times in the peripartum period, and 3 times in the early postpartum period. (4).

Pre-eclampsia and eclampsia stand out as among the most prevalent risk factors for stroke during pregnancy, especially in the postpartum phase (3,5). The shared characteristics and risk factors between pre-eclampsia and stroke offer valuable insights into the underlying pathophysiology, presenting

opportunities for developing preventive strategies addressing both conditions.

We report the cases of two patients treated in our establishment, who both experienced a stroke during the early peripartum period in the context of severe pre-eclampsia.

Our study aims to demonstrate that the incidence of stroke in the postpartum period should not be neglected and to emphasize the importance of thorough clinical, especially neurological examination in every pregnant woman, particularly those with pre-eclampsia.

2. CASES PRESENTATION

2.1 Case 1:

Our first patient is a 31-year-old with no specific medical history, 2nd Gravida, admitted to the maternity hospital during the active phase of labor at full-term pregnancy, without follow-up. Upon admission, the examination revealed a conscious patient with Glasgow Coma Scale (GCS) score of 15/15, high blood pressure at 170/100 mmHg, positive proteinuria at 3+ on urine dipstick, and lower extremity edema, without neurosensory signs of hypertension.

The fetal heart rate monitoring was normal. Obstetric ultrasound showed a monofetal pregnancy with positive cardiac activity and an anterofundal placenta with a normal quantity of amniotic fluid, the estimation of fetal weight was 3200 g. The diagnosis of pre-eclampsia was established. The blood pressure was controlled by antihypertensive medication, and all blood investigations returned normal. Vaginal delivery was accepted giving birth one hour after

admission to a newborn female; Apgar 10/10 at 1st and 5th min, birth weight at 3350 g

The immediate postpartum period was uneventful. However, six hours later, the patient abruptly experienced a generalized tonic-clonic seizure, rapidly worsening into a post-critical coma. Despite the administration of anticonvulsants and initiation of resuscitation measures, the GCS score dropped to 3/15, with bilaterally unresponsive mydriasis and blood pressure at 180/120 mmHg.

In the intensive care unit, the patient was intubated based on neurological criteria and underwent a cerebral computed tomography (CT) scan, revealing a massive cerebral-meningeal hemorrhage with a mesencephalic and pontine hematoma leading to amygdala herniation (Figure 1).

The course of the patient was marked by the onset of hemodynamic instability which ultimately resulted in an unrecoverable cardiorespiratory arrest.

2.2 Case 2:

Our second patient is 41 years old, G3P3 (gravid 3, para 3), with no specific medical history and no follow-up, admitted to the emergency department due to altered consciousness in the context of a generalized tonic-clonic seizure after four hours of a vaginal delivery of full-term pregnancy at home. Upon admission, the examination revealed an unconscious patient with a blood pressure of 170/100 mmHg and a positive proteinuria at 2+ on urine dipstick. The uterus was firm, with minimal lochia. The patient stayed in the intensive care unit to stabilize, correct blood pressure, and administer anticonvulsant treatment. Blood investigations, revealed a HELLP Syndrome with thrombocytopenia at 30,000 platelets/ μ L, hepatic cytolysis with AST at 611 U/L, and ALT at 308 U/L. An abdominal pelvic ultrasound was performed, revealing a moderate peritoneal effusion and an empty uterus. After resuscitation measures, the patient regained normal consciousness. Twenty-four hours later, the patient experienced confusion with a GCS score of 14/15 and signs of meningism, prompting a cerebral CT scan that showed a cerebro-meningeal hemorrhage with ventricular flooding (Figure 2). The patient was transferred to the neurosurgery department, where she received symptomatic treatment with mannitol to reduce intracranial pressure. The patient's evolution was favorable, with significant clinical and laboratory improvement.

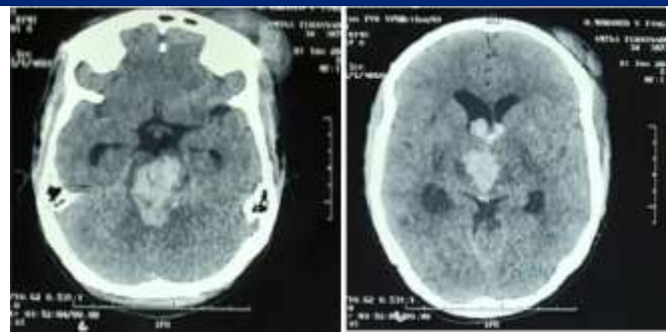


Figure.1 : Transverse section cerebral CT scan showing a massive cerebro-meningeal hemorrhage with a mesencephalic and pontine hematoma.

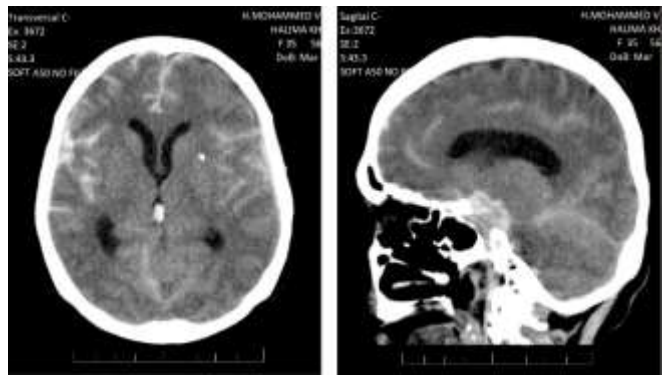


Figure.2 : Cerebral CT scan in transverse section (a) and sagittal section (b) showing a cerebro-meningeal hemorrhage with ventricular flooding.

3.1 EPIDEMIOLOGY

Recent data indicates a rising incidence of strokes during pregnancy. According to Kuklina et Al, there has been a notable increase in the rate of hospital admissions for stroke during both the antenatal and postnatal periods, rising from 47% to 83% (5).

The factors contributing to this observed trend remain unclear, but it is postulated that the increasing age of mothers and a higher prevalence of hypertensive disorders could be contributing factors.

A meta-analysis made in 2017 by Swartz et Al, which included 11 studies published from 1990 to 2017, has revealed that the incidence of hemorrhagic strokes is 30 cases per 100,000 pregnancies, which is approximately threefold greater than the rate seen in the general population of young adults (6).

3.2 Risk factors

Various conditions related to pregnancy can contribute to this elevated risk, notably pre-eclampsia and its associated complications, including eclampsia, HELLP syndrome, and disseminated intravascular coagulation. In a particular study done by James et Al, risk factors associated with strokes

during pregnancy were identified. These included sociodemographic elements such as age ≥ 35 years. Medical and obstetric determinants contributing to the risk included migraine headache (with an odds ratio OR of 16.9), thrombophilia (OR of 16.0), systemic lupus erythematosus (OR of 15.2), heart disease (OR of 13.2), sickle cell disease (OR of 9.1), hypertension (OR of 6.1), thrombocytopenia (OR of 6.0), postpartum hemorrhage (OR of 1.8), and preeclampsia/gestational hypertension (OR of 4.4) (7).

Hypertensive disorders constitute approximately 44% of the causative factors for cerebral-meningeal hemorrhages in pregnant and postpartum women, it remains a primary and readily reversible risk factor and a key focal point for the treatment of strokes during pregnancy. In comparison to normotensive women, those experiencing a hypertensive disorder during pregnancy face a six- to nine-fold higher likelihood of developing a stroke during this period (7).

The link between pre-eclampsia and stroke was previously explored in a 2013 review by Corvetto et AL, revealing that pre-eclampsia/eclampsia is typically linked to approximately 30% of stroke cases in pregnancy (8). Hemorrhagic stroke is identified as the most common type linked to pre-eclampsia/eclampsia. Specifically, within a study by Martin Jr et AL, exclusively involving women affected by pre-eclampsia/eclampsia, the incidence of hemorrhagic stroke was determined to be 89%, reinforcing the indication that hemorrhagic stroke is closely associated with pre-eclampsia (9).

3.3 Physiopathology

The precise pathophysiology of stroke in pre-eclampsia remains incompletely understood, encompassing various mechanisms, with endothelial dysfunction emerging as a central element. This dysfunction is predominantly linked to placental ischemia, triggering the release of inflammatory cytokines, fatty acids, and free radicals, all of which exert toxicity on the endothelium. Consequently, vessel permeability increases, leading to vasogenic edema. Pregnancy induces a disturbance in the physiological regulation of mean arterial pressure in the brain, primarily due to chronic hyperventilation (10).

The identified association between pre-eclampsia and altered autoregulation may result in vascular damage at the cerebral level (11).

Arteriovenous malformations (AVMs) dominate among other etiologies, with an incidence ranging from 15 to 18 cases per 100,000. The question of whether pregnancy itself raises the risk of AVM rupture remains contentious, old studies suggest no. Nevertheless, a new study in 2018 by Zhu Zhu et al. revealed an annual bleeding rate of 5.59% during pregnancy—a figure approximately 2.5 times higher than in non-pregnant contexts (12).

3.4 Diagnosis

Regarding the diagnosis, the signs of stroke during pregnancy are not specific. In our cases, the patients presented an altered consciousness and seizures. Other signs have been described in the literature such as persistent headaches, dizziness, vision disturbances, facial paralysis, neck stiffness, nausea and vomiting, or focal neurological abnormalities.

Severe headaches emerged as the predominant symptom, as reported in most studies. Its frequency ranged from 31% to 77% (13), being more prominent in the context of hemorrhagic stroke, particularly associated with pre-eclampsia/eclampsia (14).

In the study by Martin et al., 96% of preeclamptic women experienced headaches, and a majority of them (89%) went on to develop a hemorrhagic stroke (9).

The second most common symptom is the impairment of consciousness, with the frequency ranging from 30% in the case of ischemic stroke to 73% for hemorrhagic stroke (14).

All individuals suspected of having a stroke should undergo brain imaging. In most instances, a non-contrast computed tomography (CT) scan will furnish the necessary information for making decisions regarding acute management.

The positive diagnosis is made using a non-contrast cerebral CT scan by visualizing the blood that appears hyperdense in the case of hemorrhagic stroke (15).

Contrary to popular belief, a CT scan is not contraindicated during pregnancy because the radiation doses are very low compared to the teratogenic threshold for the fetus (16).

When dealing with an ischemic stroke, an MRI is more effective and should be preferred over a CT scan.

In our cases, the CT scans showed a massive cerebral-meningeal hemorrhage with a mesencephalic and pontine hematoma in our first patient and a cerebro-meningeal hemorrhage with ventricular flooding in our second patient.

3.5 MANAGEMENT

Upon establishing the diagnosis, crucial measures involve blood pressure control and addressing other risk factors. Controlling intracranial pressure becomes paramount to prevent worsening hemorrhage and cerebral involvement.

The most important aspect of the treatment is to ensure adequate cerebral perfusion to counteract secondary brain injury (17). Blood pressure should be reduced judiciously during the acute phase, with a target blood pressure below 160/110 (18). Intravenous labetalol is commonly employed as the initial choice for blood pressure reduction in pregnant individuals experiencing a stroke (8).

Additionally, magnesium sulfate ($MgSO_4$) should be incorporated into acute management for prophylaxis against eclampsia.

Surgical intervention for AVMs may be considered to halt bleeding and forestall recurrence. Swift deterioration in neurological status requires admission to the intensive care unit with appropriate interventions.

The definitive management of pre-eclampsia centers around the extraction of the fetus. The determination of the delivery date and method is largely contingent on the severity of pre-eclampsia and the gestational age. Presently, there is no evidence from studies indicating that opting for a cesarean delivery yields a better prognosis or reduced morbidity compared to vaginal delivery post-cerebrovascular accident. The decision-making process should be personalized and involve a multidisciplinary team. In many instances, early administration of epidural anesthesia is advised to mitigate blood pressure fluctuations and abbreviate the active phase of delivery.

3.6 Prognosis

The outlook primarily hinges on the duration between the commencement of hemorrhage and the commencement of treatment.

In comparison to the general population, the prognosis seems to be bleaker for pregnant women (19). This could be linked to the physiological hemodynamic alterations induced by pregnancy, as well as the hesitancy to administer specialized stroke treatments due to pregnancy-related concerns.

Moreover, the postpartum period is identified as the most precarious phase for cerebral events. Kittner et al. (13) revealed an increased risk of stroke during the postpartum period, particularly for hemorrhagic stroke. Subsequent studies have supported and validated this observation.

3.7 Prevention

Presently, there is evidence that the occurrence of pre-eclampsia can be halved by implementing a preventive approach. This approach entails identifying individuals at high risk and commencing preventive treatment with acetylsalicylic acid at a dosage of 100 mg per day before the 16th week of gestation. (20).

Aspirin also plays a crucial role in preventing ischemic stroke in women. Therefore, the preventive use of aspirin signifies a significant overlap between these two conditions. While there is no effective prophylactic therapy for hemorrhagic stroke during pregnancy, it is essential to prevent and manage severe pre-eclampsia and high blood pressure, especially as discussed earlier.

4 Conclusion

The incidence of stroke during the postpartum period is on the rise. Several risk factors during pregnancy can contribute to it, including advanced age and pre-eclampsia. The association with the latter has been demonstrated.

During the acute phase, healthcare personnel must be vigilant in the presence of clinical signs suggestive of a stroke, especially headaches or altered consciousness.

Suspicion should lead to imaging exploration to confirm the diagnosis, with non-contrast cerebral CT as the first-line approach.

The correct and early management of hypertensive pathology remains the best means of prevention.

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6 COMPETING INTERESTS

Authors have declared that no competing interests exist.

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