Intracerebral hemorrhage during pregnancy

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Intracranial hemorrhage during pregnancy is rare catastrophic event which has a poor prognosis and can contribute to maternal death, fetal death or both.
Case

- 28-year-old G1P0 pregnant woman at her third trimester (35+4 wks) suddenly had severe bursting headache and altered level of consciousness since 2 days, not associated with nausea, vomiting, fever, dyspnea, and seizure. She didn’t have the history of hypertension and diabetes.
- She was symptomatically treated in the local hospital, but the headache was progressively increasing, hence, transferred to our hospital. On arrival, her vitals were in normal range; GCS 14/15; Pupil B/L 2.5 mm, equal and reactive to light.
- On abdominal examination, the uterus was of 34 wks gestation in size on palpation, and fetal heart sound was 140 bpm on auscultation. Cranial nerves examination, sensory & motor power, reflexes were all normal.
The routine blood examination including coagulation profile were within normal range.

T2W1 MRI showed heterogenous lesion at the left temporal lobe, features suggesting hemorrhage with surrounding brain edema. MRA and MRV showed normal cerebral vessels and sinuses. The patient was conservatively treated with analgesics, proton pump inhibitor and mannitol.

On the 5th day of admission, patient had increased blood pressure and multiple facial twiching. Antiepileptic drug levetriacetam was started and obstetric consultation was done.

Thereafter, she was transferred to the obstetric department where she underwent emergency cesarean section. After 2 weeks postdelivery she was discharged with GOS 4.
**Epidemiology**

The incidence of intracerebral hemorrhage in pregnant woman varies from region to region with the highest being reported from China and Taiwan. A study from America reported 6.1 ICH/100000 deliveries. A French study reported 4.6/100 000 deliveries. A population-based cohort study from Taiwan which was performed on 1,132,019 parturients found the incidence of intracranial hemorrhage was 12.27 cases per 100,000 deliveries. Recently, a single centre study in China reported incidence rate of 53/100 000 deliveries. The peripartum period carries the highest risk and most studies have reported an increased incidence of intracerebral haemorrhages in this period.
Etiology

Etiologic causes of ICH during pregnancy include preeclampsia/eclampsia, aneurysmal rupture, bleeding from AVMs or cavernomas, and cortical venous thrombosis.
Pathophysiology

The precise pathophysiology that accounts for this increased risk in not entirely clear. However, the physiologic changes that accompany the state of pregnancy may largely account for this elevated risk. Physiological changes during pregnancy predispose to a state of hypervolemia, increased circulatory demands, decreased blood pressure, and increased venous stasis, hypercoagulability thereby changing the hemodynamic landscape. Pregnancy is also associated with hyperplasia of arterial wall smooth muscle and loss of the normal elastic fibre alignment contributing to weakness of the vessel wall. Several studies in animal models have suggested that cerebral arterial architecture changes during pregnancy leading to decreased collagen, elasticity, and distensibility. Cerebral autoregulation is usually maintained over a mean arterial pressure range of 60–150 mm Hg, which may be altered in pregnancy as a result of chronic hyperventilation. Disturbance of cerebral autoregulation resulting in higher cerebral perfusion pressures has been reported in association with pre-eclampsia and eclampsia, which may result in barotrauma and vessel damage. Anatomical changes in pregnancy lead to venous stasis, which is likely to be a consequence of iliac vein compression by the gravid uterus. Risk of intracerebral hemorrhage increases as the cerebral arteries not be able to compensate with the changing physiological environment.
Clinical presentation

The Clinical features of pregnancy-related ICH consist of sudden onset headache, vomiting, blurred vision, focal neurological deficits (motor and sensory), seizures, and altered sensorium. The characteristic of the headache may point towards the underlying aetiology, with sudden severe onset seen in subarachnoid haemorrhage, and a more diffuse and gradual onset in venous thrombosis. Parenchymal haemorrhages may have variable severity of headache depending on the size and site of bleed.
Diagnosis

The brain needs to be imaged to determine the cause of focal deficits and severe headaches. Computerized tomography (CT) is often the first investigation in these cases. Although several concerns about fetal exposure to radiation arise, there is no major reported harmful effects so far. Fetal exposure to ionizing radiation from CT of the maternal head is extremely low and potential risks of fetus malformations are limited to the first few weeks. MRI is safe imaging modality. Ionizing contrast materials crosses placenta and may affect the fetal thyroid gland. MR contrast agents cross the blood–placenta barrier easily, and no data exist to assess the rate of clearance of contrast agents from the amniotic fluid cycle, or the potentially toxic effects to the fetus. Hence, the use of contrast agent should be avoided unless overwhelming potential benefit to the patient or fetus that outweighs the theoretical risks can be demonstrated. When aneurysms, vascular malformations and cerebral vascular thrombosis are a concern, MRA and MRV four-vessel cerebral angiography (DSA) may be warranted.
Treatment

The general management of ICH during pregnancy follows the same principles as management in nonpregnant individuals. Additionally, immediate obstetric evaluation is necessary to ascertain fetal viability and gestational age.
**General & Supportive Management**

Patients need to be admitted to intensive care units. **Specific measures to reduce intracranial pressure may be necessary to salvage life.** These include use of osmotic diuretics, the safety of which is not completely established in pregnant females, and surgical measures like placement of external ventricular drains. Depending on the site, haematoma evacuation may be warranted. Seizures can raise the ICP and endanger the life of both the mother and the fetus. Newer antiepileptics Seizures therefore need to be treated with intravenous antiepileptics. However, given the potential teratogenic effects of most anticonvulsants, prophylactic use of these agents is not recommended. Study from Denmark reports no increased risk of major birth defects with first-trimester exposure to newer anti-epileptics like lamotrigine, gabapentin, levetiracetam, oxcarbazepine, and topiramate.

* The issue of blood pressure control should be managed with ICP monitoring, as lowering blood pressures in the setting of elevated ICP may decrease the cerebral perfusion pressure leading to brain ischaemia. As per the latest guidelines on spontaneous ICH management, pressures of 200 systolic and mean arterial pressure of 150 and above need to be brought down aggressively with the use of intravenous infusions. Systolic blood pressure (SBP) >180 and mean arterial pressure (MAP) >130 in the absence of raised ICP may be managed with intermittent boluses of antihypertensive to achieve a target of 160/90 and a MAP of 110. Labetalol and hydralazine are safer choices in pregnant individuals. Blood pressures need to be strictly monitored and medicines used for controlling them may differ slightly due to teratogenic effects.
In those patients with high operative risk or inoperable lesions, a conservative management course should be adopted during the pregnancy allowing stereotactic radiosurgery or embolisation options to be pursued after delivery.

For cortical venous thrombosis, low-molecular-weight heparin is the preferred agent. Aneurysms and vascular malformations need to be definitively treated to prevent re-bleed and this can be achieved through surgical or endovascular procedures. The timing of surgery depends on neurosurgical considerations.
Delivery

- The mode of delivery should be decided solely on obstetric indications. Historically, cesarean delivery has been recommended for women with hemorrhagic stroke, particularly recent SAH, untreated ruptured AVM, or unclipped ruptured aneurysm, to circumvent potential risks during labor and delivery.

- Delivery needs to be expedited in case of severe preeclampsia and eclampsia. Most clinicians favour vaginal delivery unless the aneurysm is diagnosed at term, there has been neurosurgical intervention within the week before delivery, or other maternal factors indicate caesarean delivery. For aneurysms and AVMs, if the source of bleeding has been secured, patients may undergo labour and delivery. However, studies suggest that outcomes of vaginal and cesarean delivery are probably equivalent after ICH. Therefore, the general trend is to reserve Caesarean delivery for the usual obstetric indications only.
Prognosis – intracerebral rebleeding

Intracranial haemorrhage in pregnancy carries a high morbidity and mortality. The largest reported series on pregnancy related ICH reports a 20% maternal mortality. Fetal mortality is also quoted between 7 and 25% and is more for ICH related to AVM. A recent report from China describes a fetal mortality of 37.5% associated with all forms of maternal ICH. Eclampsia complicated by intracranial haemorrhage has worst prognosis. The rate of recurrence of ICH in subsequent pregnancies depends on the underlying aetiology. Aneurysms once secured, and AVMs once taken care of, do not recur. However, untreated lesions are prone to re-bleeding, irrespective of whether the patient becomes pregnant again or not. They should, therefore, be definitively treated. Cortical venous thrombosis associated with pregnancy also has a chance of recurrence, but this is quite minimal. AVMs, CVT are not a contraindication for future pregnancies.
Prevention and management

Identification of risk factors for stroke during pregnancy is critical in order to prevent this rare and often devastating condition. Hypertension is a major risk factor of ICH, that is more frequent in the presence of pre-eclampsia/eclampsia, and early identification is needed for prevention. A combined therapy for hypertension and a prophylaxis for eclampsia should be adopted for all women with severe pre-eclampsia. **Other risk factors** associated with pregnancy-related stroke include, diabetes, valvular heart disease, hypercoagulable disorders, sickle cell disease, lupus, abuse of tobacco and other substances, and migraines.
Thanks