Case report: Cerebral vein thrombosis after subarachnoid analgesia for labour

[Thrombose veineuse cérébrale à la suite d'une analgésie sous-arachnoïdienne pour le travail obstétrical]

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Purpose: We report a case of sagittal sinus thrombosis occurring after spinal analgesia for labour to highlight the difficulty of such diagnosis in the presence of postpartum atypical headache following regional anesthesia/analgesia.

Clinical features: A previously healthy 21-yr-old, primiparous, preeclamptic parturient was admitted to the hospital at 37 weeks gestation for uterine contractions. Before pregnancy she was taking no medication other than oral contraceptives and was a non-smoker. Spinal analgesia was established on the first attempt at 8 cm of cervical dilation, in the setting of rapid progression of labour. Following an uneventful delivery, on the third day postpartum, the patient experienced gradual onset of an atypical headache with unclear postural character, followed by focal neurological signs five days later. Emergency neuroimaging revealed direct evidence of thrombosis in the posterior sagittal venous sinus. Anticoagulation was initiated with *iv* heparin (500 UI·kg^{-1}·day^{-1}). The patient's headache decreased progressively and full motor recovery was noted by day 14 postpartum. After 24 days, the patient was discharged without any neurological disability. Common inherited thrombophilic dispositions were absent, with the exception of a decrease in protein S level.

Conclusion: Central venous thrombosis, while rare, is a recognized cause of puerperium stroke. The present case highlights the importance of considering the diagnosis in the presence of postpartum atypical headache following spinal anesthesia/analgesia. Early intervention with systemic heparinization is critical when the diagnosis is confirmed.

Objectif *: Présenter un cas de thrombose du sinus longitudinal, survenue après une rachianalgésie de fin de travail obstétrical, pour illustrer la difficulté d'établir ce diagnostic en présence de céphalées atypiques du postpartum.*

Éléments cliniques *: Une parturiente primipare de 21 ans, prééclamptique, antérieurement en bonne santé, est admise à l'hôpital à 37 semaines de grossesse pour contractions utérines. Avant la grossesse, elle prenait des contraceptifs oraux et ne fumait pas. La rachianalgésie est réalisée sans difficulté au premier essai, au moment où la dilatation cervicale est de 8 cm et le travail en progression rapide. Après un accouchement sans incident, au troisième jour du postpartum, la patiente présente des céphalées atypiques d'apparition graduelle à caractère postural mal défini, suivies de signes neurologiques focaux cinq jours plus tard. Un scanner cérébral et une résonance magnétique en urgence révèlent une thrombose du sinus veineux longitudinal postérieur. L'anticoagulation par héparine iv (500 UI·kg^{-1}·jour^{-1}) est instaurée. Les céphalées diminuent progressivement et la récupération motrice complète est établie au 14e jour du postpartum. La patiente quitte l'hôpital après 24 jours sans séquelles neurologiques. Le bilan de thrombophilie héréditaire s'est avéré négatif, à l'exception d'une baisse du niveau de protéine S.*

Conclusion *: La thrombose veineuse centrale, bien que rare, est une cause connue d'accident vasculaire puerpéral. Il est important de tenir compte du diagnostic en présence de céphalées atypiques du postpartum après une anesthésie/analgésie rachidienne. L'intervention précoce par une héparinisation complète est cruciale pour la confirmation du diagnostic.*

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CENTRAL venous thrombosis (CVT) accounts for less than 1% of all strokes.[1] The disease occurs in all age groups with a peak incidence in neonates and in adults in the third decade with a female:male ratio of 1.5 to 5.[2] The association of CVT with pregnancy and puerperium remains a recognized cause of maternal mortality and morbidity in developing countries.[3,4]

In occidental countries, CVT is an unusual complication of pregnancy with an incidence of 1:10,000 to 1:20,000 deliveries, mainly observed during the postpartum period, and represents the main cause of puerperium stroke.[1,4,5] Some case reports have associated postpartum CVT with accidental postdural puncture due to epidural analgesia.[6–9] Until now, only one case report mentions CVT after spinal anesthesia for Cesarean delivery.[10] We report a case of sagittal sinus thrombosis occurring after spinal analgesia for labour. The diagnosis was initially misled due to the atypical nature of the headache. Institutional approval was obtained for the publication of the personal health information in this report.

Case report

A previously healthy 21-yr-old, ASA I, gravida 1, para 0 parturient was admitted to the hospital at 37 weeks gestation for gestational hypertension associated with uterine contractions. Her medical history was significant for a previous appendectomy and latex allergy. Before pregnancy she was taking no medication other than oral contraceptives and she was a non-smoker. During pregnancy the patient suffered from a pyelonephritis and presented with an episode of threatened preterm labour at 32 weeks gestation. Initial physical examination revealed cervical effacement. Her blood pressure was 145/95 mmHg and urinalysis showed 2+ proteinuria, raising the diagnosis of mild preeclampsia. Routine blood tests were non-contributory.

Acceleration of labour with oxytocin was initiated 12 hr after spontaneous rupture of membranes. Her cervical dilation was 8 cm when regional analgesia was requested, three hours later. The patient did not receive any antihypertensive medication until this time, in the absence of progressive hypertension.

Considering the rapid progression of labour, a spinal analgesia technique was chosen and performed successfully on the first attempt under aseptic conditions. A 27G Whitacre spinal needle (Becton Dickinson SA, Erembodegem, Belgium) was introduced into the L3–L4 interspace and 0.5 mL of 0.5% hyperbaric bupivacaine mixed with 2.5 μg sufentanil was administered. No parenteral analgesics were added. There was no hemodynamic compromise and the patient spontaneously delivered a healthy infant 30 min later. Apgar scores were 9/10/10.

During the next three days, the patient's arterial blood pressure varied between 120/60 mmHg and 140/90 mmHg. On the third day postpartum, the patient experienced the gradual onset of a dull throbbing frontal headache and neck pain, which were not completely relieved by recumbency. Pain was accentuated on day five postpartum, associated with dizziness in the upright position and slight photophobia. The patient was apyrexial, normotensive and had no abnormal neurological signs. Interpretation of the headache was challenging because of the unclear postural character. The diagnosis of postdural puncture headache (PDPH) was considered doubtful.

Treatment with oral analgesics, caffeine, rehydration and rest relieved the headache over the ensuing 48 hr. However, on the eighth postpartum day, the patient's headache returned with similar intensity and localization. She developed paresthesia progressing from the left hand to the face over the distribution of the facial nerve, associated with acute left hemiparesis, blurred vision, and somnolence. The patient was not nauseated and she remained apyrexial. Fundoscopic examination revealed mild bilateral papilledema.

Cranial computed tomography (CCT) after contrast injection; revealed direct signs (empty triangle sign) of thrombosis in the posterior sagittal venous sinus, and secondary cortical venous infarctions into the left frontal and the right posterior parietal territories. Brain magnetic resonance imaging (MRI) confirmed these findings (Figure).

Anticoagulation was initiated with heparin (500 $UI \cdot kg^{-1} \cdot day^{-1}$ *iv*). During the evening, the patient complained of an intense headache associated with nausea and vomiting and she developed two generalized grand mal seizures. Convulsions stopped after administration of valproic acid 400 mg *iv* and the patient was transferred to the intensive care unit. Treatment there consisted of valproic acid, methylprednisolone, paracetamol, ranitidine and heparin.

On day 11 postpartum, neurological evolution was marked by the appearance of Bravais-Jacksonian type focal seizures. Epilepsy was controlled by the addition of carbamazepine 300 mg *po* every eight hours. The patient's headache resided gradually thereafter, to the point where it was managed by paracetamol on a *prn* basis. Full motor recovery was gained on day 14, despite persisting slow cortical activity on the electroencephalogram (EEG). After 24 days, the patient was discharged without any neurological deficit. Of note, an EEG performed eight weeks after onset was normal. The patient was advised to avoid oral contraceptives

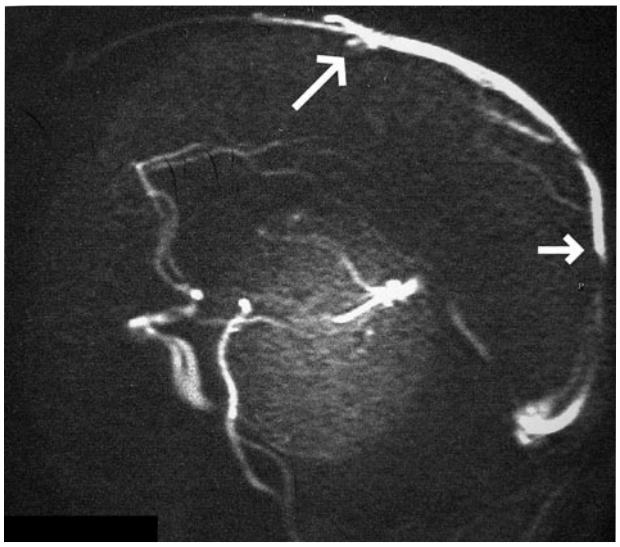

FIGURE Brain magnetic resonance imaging providing a hyperintense signal in the thrombosed posterior sagittal venous sinus and showing secondary cortical venous infarctions into the left frontal and the right posterior parietal territories (arrows).

and continue her antiepileptic medications and oral anticoagulants until the three-month follow-up visit.

During hospital stay, a complete screen was performed to exclude hereditary thrombophilia. Common inherited thrombophilic dispositions such as the factor V Leiden mutation, and the 20210 G to A mutation of the prothrombin gene were absent. Antithrombin III and protein C levels were normal. However, her protein S level was 48% of the normal value. Neither hyperhomocysteinemia nor any anticardiolipin and antiphospholipid antibodies were detected.

Discussion

This report highlights the diagnostic challenge and management of a CVT presenting in the postpartum period. Following an uneventful delivery facilitated with spinal analgesia, the patient experienced on day three postpartum the gradual onset of an atypical headache with an unclear postural character. Five days later, the headache was associated with focal neurological signs including left arm and face paresthesia, acute left hemiparesis, blurred vision, altered consciousness, and generalized grand mal seizures. The initial diagnosis was elusive according to current descriptions in the literature.[1,11] In fact, the wide spectrum of clinical symptoms and the often subacute or lingering onset frequently delay diagnosis. The diagnostic dilemma posed by the inaugural postpartum headache in our case was challenging. Headache is a common symptom during pregnancy and puerperium, affecting 30–40% of women.[12] The differential diagnoses of persistent headache in the puerperium includes spinal headache after regional anesthesia, migraine, pregnancy induced hypertension, meningitis, cerebral tumour, subarachnoid hemorrhage, subdural hematoma, CVT, and non-specific stress- induced pain.[7,9] Goldszmidt *et al.*; in a cohort study, observed that the majority of postpartum headaches are primary in nature, (i.e., migraine, tension-type, cervicogenic and cluster headaches). Furthermore, many primary headaches may have postdural puncture features, and up to 50 % of PDPH occur without a recognized dural puncture.[13]

In current practice, spinal anesthesia is rarely identified as a cause of PDPH. The incidence of spinal headache is decreasing with improved needle technology, although data on low-frequency events such as PDPH are difficult to ascertain through randomized clinical trials because of constraints of sample size.[14]

In this patient, the diagnosis of spinal headache was doubtful. The puncture of the subarachnoid space was uneventful and no postdural worsening of headache occurred.

Also, preeclampsia-related headache was excluded since the patient remained normotensive after delivery. Conventional analgesic treatment and caffeine, during the next 48 hr, relieved the patient's symptoms, but left the diagnosis in doubt. No blood patch was attempted, and the patient was kept under routine clinical follow up, without further investigations. The diagnosis was established on day eight postpartum with the appearance of a focal neurological deficit associated with seizure activity, and a diagnostic MRI.

Another reported case of CVT has been observed during the first week after normal delivery.[6] Headache is the most frequent symptom encountered, and tends to be unilateral, limited to the forehead, temple, or occiput, with subacute onset.[2,10] However, it can be particularly misleading when it simulates conditions such as PDPH, subarachnoid hemorrhage (thunderclap headache) or even migraine.[11,15] Subsequent neurological signs vary from focal deficits and Jacksonian type seizures, as experienced by our patient and described in 76% of peripartum CVT, to coma.[1,16] Therefore, in the absence of seizures or other neurological signs in the puerperium, it is difficult to distinguish CVT-induced headache from spinal headache associated with regional anesthesia.

The diagnosis of sagittal sinus thrombosis was disclosed by radiological investigation. Diagnosis of CVT is based on neuroimaging. Cranial computed tomography is usually the first technique performed

in this setting, but findings are normal in 25 to 30% of patients. The main value of CCT is to exclude hemorrhagic stroke. Direct signs of CVT, rarely seen on unenhanced CCT, include the cord sign and the dense triangle sign. However, after contrast injection, the appearance of the empty triangle or delta sign (25–30% of cases), as observed in our patient, confirms the diagnosis.[1] Magnetic resonance imaging and magnetic resonance angiography are considered the most sensitive diagnostic tests, disclosing the diagnosis in 90% of cases.

Treatment with heparin must begin immediately upon confirmation of the diagnosis, even in the presence of a hemorrhagic infarct.[1,11] Intravenous anticoagulation should be continued until remission of the acute stage of the disease, i.e., normal consciousness, improvement of headache and resolution of focal neurological deficits. Subsequent therapy should be converted from parenteral to oral anticoagulation for a period of three to six months. Patients with hereditary thrombophilia should be treated for a longer period (6–12 months).

Women who have suffered from a CVT while taking oral contraceptives should be counselled about alternative methods of contraception.[1] Long-term follow-up of patients who have experienced pregnancy-related CVT is important, since recurrence, although rare, is possible within the first 12 months.[1,19] Subsequent pregnancy is not contraindicated, although prophylactic low-dose anticoagulation should be considered, while recognizing that the risk-benefits of this therapy during pregnancy have not been established. Counselling about symptoms suggestive of CVT recurrence and neurological surveillance during pregnancy are strongly recommended. Regional anesthesia or analgesia for labour or Cesarean delivery in women with a history of CVT history is not contraindicated, while prophylactic anticoagulation is recommended in the postpartum period.[1]

While the pathogenesis of puerperal CVT has not been clearly elucidated, it may be related to three aspects characterizing Virchow's classic triad: 1) stasis of intracerebral blood flow (especially in the valveless sagittal sinus); 2) vascular endothelial damage due to fluctuations in intracranial pressure (especially during delivery); and 3) the hypercoagulable state associated with dehydration and physiologic anemia of pregnancy.[20]

The complex etiology may be associated with the following factors: hereditary thrombophilia, anticardiolipin antibodies, hyperhomocysteinemia, Cesarean delivery, pregnancy-related hypertension, and the use of oral contraceptives which may present a risk factor in 10% of cases.[1,11,21,22] Common inherited dispositions of thrombophilia include mainly the factor V Leiden mutation (15–17% of cases) and the prothrombin-gene-mutation 20210GA (10–12% of cases), whereas antithrombin III-, protein C- and protein S-deficiency are found in only 2–6% of cases.[1] In this patient, preeclampsia, decrease in protein S (even though commonly observed during pregnancy), and the use of oral contraceptives, were possible CVT-triggering factors.[23]

Implications of spinal anesthesia in the pathogenesis of this entity were considered in two previous case reports, but remain controversial. One report by Schou *et al.*,[24] described the appearance of postoperative sagittal sinus thrombosis after spinal anesthesia for hemorrhoidectomy in a 35-yr-old man. Suggested mechanisms included chemical arachnoiditis and changes in intracranial pressure. A second report described a case of cortical venous thrombosis after spinal anesthesia for Cesarean delivery. Direct implications of the anesthetic technique were considered doubtful.[10]

Neurological complications reported after spinal anesthesia (i.e., headache and subdural hematoma) have been related to cerebrospinal fluid (CSF) leakage, leading to intracranial hypotension with subsequent venodilatation and venous stasis.[25] In our case, considering the rapid progression of labour, a spinal analgesia technique was chosen and performed uneventfully. No significant hemodynamic disorders were observed after anesthesia or during delivery. Furthermore, the postpartum headache was atypical, with an unclear postural character. Therefore, leakage of CSF and important changes in intracranial pressure seem unlikely contributing factors. However, a cause-effect association is difficult to demonstrate in rare events such as CVT concomitant with spinal anesthesia, and the question is still under debate.

In summary, the present case highlights the importance of establishing a comprehensive differential diagnosis in the presence of postpartum atypical headache following spinal anesthesia/analgesia. The patient should remain under clinical follow-up and the diagnosis of CVT has to be considered. Early intervention with systemic heparinization is critical when this diagnosis is confirmed.

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