Intracranial Venous Thrombosis in the Parturient

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Intracranial venous thrombosis is a rare but potentially fatal complication of pregnancy and the postpartum period. The presenting symptoms can mimic those of a postdural puncture headache and are easily misdiagnosed, especially in a parturient who has undergone regional anesthesia. The incidence of 10–20 per 100,000 is likely higher than reported. The etiology, clinical presentation and course, risk factors, management, and relation of intracranial venous thrombosis to pregnancy are presented. Published case reports and series of intracranial venous thrombosis that have either occurred during the puerperium or involved women of childbearing age after dural puncture are summarizes. Finally, the diagnosis and management of intracranial venous thrombosis in parturients, focusing on parturients who have undergone regional anesthesia, is discussed. When intracranial venous thrombosis occurs in a parturient after regional anesthesia, it is often treated as a postdural puncture headache.

INTRACRANIAL venous thrombosis (ICVT) is a rare but potentially fatal complication of pregnancy. The headache symptoms of this disorder often mimic those of postdural puncture headache (PDPH). This often leads to misdiagnosis after regional anesthesia performed for vaginal delivery or cesarean delivery and epidural blood patch (EBP) placement in the presence of intracranial pathology. We review the incidence, presentation, and clinical course of ICVT in general terms and then specifically as it relates to pregnancy. We then focus on clinical aspects of ICVT that may help to differentiate it from PDPH.

Incidence

When first described, peripartum ICVT was thought to be very rare and uniformly fatal, but it is now recognized to occur uncommonly, with a relatively good prognosis when treated. Case series from North America and Western Europe report an average of 10–20 cases per 100,000 deliveries with a range of 2–60 per 100,000 deliveries. The reported incidence is much higher in developing countries. One review of 135 cases from India reports an average incidence of 450 per 100,000 deliveries. Mas and Lamy postulate that puerperal infection and dehydration contribute to the higher frequency of the disorder in developing countries. It is difficult to ascertain the true incidence because of its widely varying presentation and the need for neuroimaging or postmortem examination to confirm a diagnosis. It is likely that peripartum ICVT is underdiagnosed and has a higher incidence than reported.

Presentation and Clinical Course

Intracranial venous thrombosis presents with a wide and remarkably varying scope of nonspecific symptoms. Headache is the most frequent symptom and can simulate PDPH, subarachnoid hemorrhage, or migraine headache. ICVT is more common in women in the 20- to 35-yr age group, and there seems to be no racial predilection. Symptoms may include a constant or positional headache, dizziness, nausea, vomiting, blurred vision, lateralizing neurologic signs, lethargy, seizures, and coma. The specific presentation depends on the location and extent of thrombosis, the degree of venous collateral circulation around the thrombosis, and the presence of associated cortical lesions. An isolated cortical vein thrombosis may create focal symptoms of motor and sensory deficit, whereas extensive thrombus in a large sinus will lead to more generalized symptoms such as headache, signs of increased intracranial pressure, seizures, or coma. In addition, symptoms may fluctuate as thrombosis and fibrinolysis occur simultaneously, leading to fluctuations in surrounding blood flow and intracranial pressure. In the nonpregnant patient, the onset may be subacute or protracted; however, it is usually acute in onset during pregnancy and most often occurs postpartum.

Neuroimaging is required to confirm the diagnosis of ICVT. Computed tomography will be diagnostic in only one third of cases. Magnetic resonance imaging (MRI) with associated venography has become the standard for diagnosis of ICVT.
The treatment of ICVT is primarily supportive, although endovascular thrombolysis and surgical thrombectomy are considered in severe cases.\textsuperscript{15,16} Anticoagulation seems to be the treatment of choice worldwide, but the indications for its use remain somewhat controversial, given that approximately 50% of cases are associated with hemorrhagic cerebral infarcts.\textsuperscript{17} In a study that combined a retrospective review of 102 patients (with and without hemorrhagic infarction), both anticoagulated and not, and a prospective randomized trial of anticoagulation in 20 patients (all without hemorrhagic infarction), Einhaupl \textit{et al.}\textsuperscript{18} demonstrated a reduction in mortality and improved neurologic recovery in anticoagulated patients regardless of the presence of cerebral hemorrhage. An additional prospective, double-blind, randomized, multicenter trial of low-molecular-weight heparin \textit{versus} placebo in 59 patients demonstrated a trend toward better outcomes when anticoagulants were used.\textsuperscript{17} Canhao \textit{et al.}\textsuperscript{19} recommend anticoagulation only in presence of factors associated with poor prognosis.

The clinical course of ICVT is unpredictable, and often the clinical picture worsens after diagnosis. Alterations in consciousness, coma, and intracranial hemorrhage are strong predictors for poor outcome.\textsuperscript{14} To look for specific causes and predictors of death, Canhao \textit{et al.}\textsuperscript{19} noted that reported mortality rates from ICVT in the general population varied from 4% to 33% and performed a multinational, prospective, observational study of 624 patients during a 3-yr period. The overall death rates were 4.3% in the acute phase and 3.4% within 30 days after symptom onset. Independent predictors for death were coma, right intercerebral hemorrhage, mental disturbance, deep cerebral vein thrombosis, and posterior fossa lesions. Worsening of previous or new onset focal deficits also increased the risk of death. Given the wide range of clinical presentation, delays in diagnosis are common. Although there seems to be no convincing evidence in the general population that delay in diagnosis or treatment influences clinical outcome,\textsuperscript{20} patients with symptoms suggestive of more progressive disease or poor outcome must be identified early so that appropriate therapy can be instituted.

\textbf{ICVT and Pregnancy}

It is widely accepted that the rate of ICVT in parturients is higher than in the general population\textsuperscript{21-23} and accounts for 34% of cases of all ICVTs in data reported from individual medical centers.\textsuperscript{24} Cantu and Barinagarrementeria\textsuperscript{13} retrospectively reviewed 113 cases of CVT in women of childbearing age seen at their institution in Mexico City from 1973 to 1993. Sixty-seven cases of documented pregnancy-associated ICVT (group 1) were compared with 46 cases that were unrelated to pregnancy (group 2). Of the patients in group 1, 34\% occurred during the first week after delivery, and 59\% occurred during weeks 2 and 3. Sixty-four percent of the patients in group 1 were multiparous, 54\% were from low-socioeconomic backgrounds, and 31\% had home deliveries with inadequate prenatal care. Only 3 of the 67 patients in group 1 had risk factor for ICVT other than being in the peripartum period. Peripartum patients (group 1) more often had an acute (<=48 h) onset, had a more progressive course but a quicker resolution of symptoms, were more likely to have an additional extraneural thrombosis, had much better outcomes, and had a lower mortality rate (9.7\% vs. 32.6\%).

For women with a previously diagnosed ICVT, counseling and management of subsequent pregnancies are a concern. In one retrospective review, Mehrain \textit{et al.}\textsuperscript{26} identified 30 women with a previous diagnosis of peripartum ICVT to determine the incidence of recurrence of ICVT during subsequent pregnancies. Twenty-two pregnancies occurred in 14 women during the 10-yr follow-up period, 19 children were born, and the mean interval between ICVT and the subsequent pregnancy was 5.3 yr. Low-dose heparin was given during 5 pregnancies, none during the remaining 14. There were no recurrences of ICVT, and no extracranial thrombotic complications were noted. In a similar study, Lamy \textit{et al.}\textsuperscript{27} noted no recurrences in the 68 cases reviewed. These and other published reports suggest that systemic heparin treatment for ICVT prevention during repeat pregnancy is not warranted unless there are other identified risk factors.\textsuperscript{28} One may consider prophylactic anticoagulation during the immediate postpartum period because this is a time of greater relative risk.\textsuperscript{28}

Traumatic injury to the dura is thought by some to be a risk factor for ICVT,\textsuperscript{1} although others state that dural puncture with an epidural or spinal needle constitutes an injury insufficient to increase the risk for ICVT.\textsuperscript{29} Aidi \textit{et al.}\textsuperscript{30} and Pannullo \textit{et al.}\textsuperscript{31} theorize that venous dilatation and stasis, shown in MRI studies of patients who have intracranial hypotension, increase the risk of ICVT in patients with low cerebrospinal fluid (CSF) pressure. They also suggest that the positional headache due to CSF leak after dural puncture becomes nonpositional when thrombosis leads to decreased CSF absorption and
increase CSF pressure. One retrospective review of ICVT notes that dural puncture is a risk factor in 8% of ICVT cases.20

We identified 13 published case reports of ICVT after regional anesthesia in parturients. Cases 1–3 represent previously unpublished cases that occurred at our institution. All cases are summarized in tables 1 and 2. Of the 16 pregnancy-related cases, all of the patients were noted to have a positional headache, 10 of which occurred on the first postpartum day, with a range of 1 day to 4 weeks. In 4 of the cases, the headache did not lose its positional character, although symptoms were progressive. Eleven of the 16 pregnant patients received an autologous EBP, and 4 of those had a second blood patch. Nine patients were anticoagulated after diagnosis, 13 had full recovery, and 2 had residual lower extremity weakness.

Five cases of ICVT after dural puncture in nonpregnant women of childbearing age are also summarized so as to include all case reports of ICVT in association with demonstrated or potential dural puncture in women of child bearing age. Four occurred after diagnostic lumbar puncture, and another occurred after an uneventful lumbar epidural anesthetic placed for knee surgery. All of these presented with a positional headache, three on the first day, with a range of 1–4 days. Only one of the nonpregnant patients received an EBP. All five of these were anticoagulated, and there was one death.

### Discussion

Reported cases of ICVT after regional anesthesia in parturients are rare; however, the clinician faces a common diagnostic dilemma when presented with a positional headache after regional anesthesia in a postpartum patient. ICVT occurs most commonly postpartum. This is also the time period when it can easily be misdiagnosed as a PDPH in a patient after regional anesthesia. The management options are quite different because ICVT may require anticoagulation and PDPH may require...
an EBP, which cannot be performed in the presence of anticoagulation.

When considering the association of ICVT and a positional headache in a parturient after regional anesthesia, two possible relations exist. First, a patient may have both an ICVT and a PDPH. As was previously discussed, either low CSF pressure from a dural puncture predisposes patients to developing ICVT or the two are entirely coincidental. Using the algorithm suggested by Borum et al., if the unintentional dural puncture rate with a Tuohy needle averages 2% and there is an 80% PDPH rate, the incidence of coincidental ICVT and PDPH is approximately 4 persons per year among the 52% of yearly US deliveries who receive analgesia. The unintentional dural puncture rate with a Tuohy needle was 1 of the nonpregnant cases cited in tables 1 and 2 who had dural punctures with large-bore needles may fall into this category. Approximately 20% of patients will not develop a PDPH after a large-bore dural puncture. A positional headache in this subset of patients may easily be attributed to their dural puncture in the presence of an undiagnosed ICVT.

A second and, based on our review, probably more common scenario is that parturients who are at low risk for PDPH (uncomplicated epidural, small-bore puncture, and multiple attempts) have an ICVT that is attributed to PDPH and are treated as such, most commonly with hydration, caffeine, or EBP. If the symptoms do not completely resolve, but are not progressive, patients may be thought to have experienced a less than complete response to therapy for PDPH and are then expected to resolve over time. After delivery, the hypercoagulable state returns to normal by 2 weeks postpartum, and this may explain why the symptoms in these women improve without specific therapy for ICVT. Patients who have progressive symptoms are more likely to return for follow-up and are eventually diagnosed after neuroimaging. For example, patient 3 from our institution had an antepartum nonpositional occipital headache. After labor, uneventful lumbar epidural, and cesarean delivery, her headache became bilateral and significantly positional. The patient was treated with caffeine, with initial resolution, though her headache returned within 24 h with associated nausea, vomiting,
photophobia, and phonophobia. Although this patient’s ICVT may have begun in the antepartum period, it was the progression of symptoms that led to further evaluation.

The changing nature of the headache associated with ICVT over time and the fact that it often presents as a positional headache that overlaps the usual timing of and treatment of PDPH in the parturient likely contribute to the confusing clinical picture. In a patient who has had regional anesthesia, a positional headache is often treated as a PDPH. This treatment, as noted in table 1, often occurs before the symptoms that signal a postpartum ICVT become apparent. Of the pregnancy-related cases reviewed in tables 1 and 2, 1 of the 16 patients had no neuraxial procedure or known dural trauma, and another 7 had low risk factors for dural puncture headache (dural puncture with small-bore conical needles, uneventful epidural anesthetic, multiple epidural attempts without obvious dural puncture); however, all presented with positional headache consistent with low intracranial pressure. In 12 of the reviewed patients (11 postpartum and 1 nonpregnant), none of whom had evidence of more serious intracranial pathology, EBP placement occurred in the presence of an undiagnosed ICVT. Four of the 12 received blood patches despite symptoms that suggested that the postural component of their headache was no longer significant. No complications were noted, and all of these 12 patients recovered fully.

All but 1 of the 12 patients (11 postpartum and 1 nonpregnant) reviewed in tables 1 and 2 who received EBP experienced absent, partial, or short-lived (hours) initial relief. Studies of EBP report that 75% to 90% of patients have an excellent initial response, although long-term follow-up of EBP suggest that 60% or fewer patients receive lasting and complete relief. Initial failure of an EBP is certainly not diagnostic but should at least raise suspicion for an undiagnosed ICVT.

Wilder-Smith et al. suggest that EBP placement might actually help to protect against ICVT formation in patients who have low CSF pressure headache. It is interesting that none of the patients, pregnant or nonpregnant, who experienced lasting neurologic sequelae had an EBP. Low CSF pressure may allow sagging of intracranial contents, which promotes intracranial vessel damage and venous stasis thought to be necessary for ICVT formation. EBP raises CSF pressure and thus might prevent vessel damage and venous stasis. Turnbull and Shepherd and Zeidan et al. suggest that untreated dural puncture headache may lead to an increased risk of subdural hematoma and intracranial hemorrhage through the above mechanisms, and suggest that early rather than later blood patch use might prevent some cases of ICVT, subdural hematoma, and cerebral hemorrhage. This reasoning is speculative, however, and decisions about when to perform an EBP must be weighed against other published clinical data and experience.

Cases 1 and 2 can be used to illustrate diagnostic difficulties when dealing with a postpartum patient with positional headaches after regional anesthesia. The decision to perform a diagnostic MRI, especially before EBP, is challenging given the low incidence of ICVT. Case 1 had an uncomplicated combined spinal–epidural technique for labor analgesia with an 18-gauge Tuohy/27-gauge Whitacre needle. The risk of PDPH with a 27-gauge Whitacre needle is reported to be less than 1%. However, this patient was postpartum and had a previous history of deep venous thrombosis with a pulmonary embolus, both of which increase risk for ICVT. One should at least consider MRI imaging in such a patient before EBP even though the risk of ICVT is smaller than that of PDPH, especially given that her anticoagulation was held to perform an EBP. When her EBP did not provide complete relief, the indication for imaging was even more compelling.

The indication for MRI imaging is not compelling in patient 2 (fig. 1) because she was at lower risk for ICVT than patient 1. She had uneventful lumbar epidural analgesia for labor without recognized dural puncture. The incidence of PDPH after unrecognized dural puncture and uneventful epidural analgesia in parturients is 0.6% or less, and lower than that after dural puncture with a small-gauge Whitacre needle.
In addition, she had no previous history of venous thrombosis, and her headache never lost its postural component. The subsequent increase in headache severity with progressive nausea and vomiting after EBP suggested more serious intracranial pathology, for which she received a diagnostic MRI.

A brief neurologic examination should be performed on all patients before EBP is performed, including those at high risk for PDPH. This examination should include ocular and facial movements and gross motor and sensory examinations and be targeted at eliciting symptoms of more severe intracranial pathology. The more extensive exam suggested by Martin and Hauser\(^4\) (evaluation of: pupils, ocular movements, optic fundus, facial movements, speech, arm and leg strength, reflexes, and sensation to pinprick and vibration bilaterally in hands and feet) should be considered on patients who fail EBP and in those who are at low risk for PDPH (i.e., patients with dural puncture with small-bore needles, or epidural placement without obvious dural puncture). The majority of patients in our review experienced a change in the headache pattern over time representing a progression of intracranial pathology (table 1). The average time that the change in headache was noted was approximately 4 days, with a range of 1.5–10 days. Neuroimaging should be performed if abnormality on examination is noted or if the patient’s symptoms change over time.\(^5\,\,\,6\)

Summary and Specific Recommendations

The complete differential diagnosis of the postpartum headache is extensive and beyond the scope of this review. ICVT must be considered in differential diagnosis of the parturient with a headache after regional anesthesia. After reviewing the literature and the published case reports, several themes emerge. ICVT in this population often presents with or is associated with a positional headache which is often attributed to PDPH. The character of the headache associated with ICVT most often changes over time. EBP often does not provide initial relief, although it seems to have little sequelae if performed in patients who have a subsequent diagnosis of ICVT. Published reviews of this disorder consist of small numbers, the mechanism of ICVT formation remains unclear, and the true incidence in this population remains ill defined because there are likely cases that are never diagnosed. Heightened awareness of ICVT may lead to earlier diagnosis, more information about the clinical course, and better identification of patients at higher risk. Although most pregnant patients do well, severe neurologic morbidity can occur if ICVT is unrecognized.

Based on our review, we offer the following specific recommendations:

- ICVT should be included in the differential diagnosis of all postpartum headaches, particularly after a regional anesthetic in which there is no recognized dural puncture or one with a small-bore needle.
- A brief neurologic examination should be performed on all patients before EBP is performed, including those at high risk for dural puncture headache.
- Focal deficits and mental status changes point toward more detailed neurologic examination and imaging before consideration of an EBP.

Consider imaging if:

- character of the headache changes
- EBP does not provide initial improvement or relief of short duration
- there are additional risk factors for ICVT
- examination results are suggestive of more severe intracranial pathology

References