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POSTPARTUM CEREBRAL VENOUS THROMBOSIS: A CASE REPORT AND REVIEW OF THE LITERATURE

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INTRODUCTION

Cerebral venous thrombosis (CVT) is a cerebrovascular accident affecting the venous network, in particular the dura-merian sinuses. It is a neurological emergency that mainly affects young women[1] given the use of oral contraceptives, hormone replacement therapy, in vitro fertilization and mainly during pregnancy, and postpartum[2,3] Pregnancy considerably increases the occurrence of thrombosis explained by its state of hypercoagulability. This increased thrombotic risk increases further during the postpartum period, which is defined by the 6 weeks following childbirth[4] CVT presents with a very rich and varied picture depending on its topography, but the superior and lateral sinuses are frequently involved. Due to its wide clinical spectrum, its diagnosis becomes more or less difficult and late, it can manifest itself by an isolated intracranial hypertension syndrome (HTIC), by a focal deficit syndrome, or by an encephalopathy[5,6] L Imaging and in particular angio-MRI is the reference examination which allows early diagnosis and also to assess the severity and to decide on the prognosis. In most cases the evolution is favorable with a recovery without sequelae under a well conducted treatment[7,8] Here, we report a rare case of postpartum CVT which was initially confused with a post-dural puncture headache of spinal anesthesia, but was diagnosed in time and successfully managed with a favorable outcome.

OBSERVATION

30-year-old female patient with no known pathological history, having never taken estrogen-progestogen contraception, with a BMI of 25 kg/m2, primiparous primigravidae presenting with a surgical pelvis on scano-pelvimetry, having given birth by scheduled caesarean section

of a full-term pregnancy, under spinal anesthesia , of her first child with a PAN 3000g and an Apgar 10/10, without any noted complication either per or immediately postoperative and having been put on preventive anticoagulation, the next day the patient complained of isolated occipital headaches worsening in standing and sitting position but do not improve either when lying down, the patient was put on analgesic treatment and reported a slight improvement, at this time the headaches were correlated with the puncture of the spinal anesthesia. The following day at H48 the patient woke up with jet vomiting with accentuation of her headaches becoming resistant to analgesics also associated with behavioral disorders such as agitation and confusion, two hours later an alteration in her state of consciousness set in then the patient presented 2 episodes of tonic-clonic seizures lasting 60 seconds each, yielded under 10 mg of Valium, with post-ictal amnesia and without clear recovery of consciousness. The initial physical examination reveals anisocoria, a GSC 13/15, with temporal spatial disorientation, the patient is afebrile and remains hemodynamically and respiratory stable with no neurological deficit or meningeal stiffness observed. An initial assessment was carried out with an hb of 11g/dl, a platelet rate of 500,000, fibrinemia at 6.7, a d-dimer rate of 2,000, the rest is without abnormality. Cerebral CT done in an emergency returned to normal. The evolution was marked by the persistence of tonic seizures despite the anticonvulsant treatment, which required her rapid transfer to an intensive care unit where the patient was put on mechanical ventilation with deep sedation. A cerebral MRI was subsequently requested, revealing cerebral thrombophlebitis at the expense of the superior longitudinal sinus with hemorrhagic softening of a right posterior parietal venous infarction. Intravenous curative heparin therapy based on unfractionated heparin (UFH) was started, thus allowing ventilation weaning and extubation of the patient after 3 days of mechanical ventilation, with an overlap with antivitamins K (AVK) which was started on the 6th day. The evolution is marked by the improvement of the neurological state, conscious patient, Glasgow score at 15/15, the patient left the intensive care unit on D10 without sequelae with an INR at 2.3. In addition, a thrombophilia assessment (protein S, protein C, antithrombin III test for a mutation in the factor V Leiden gene) was carried out, which returned without abnormality. VKAs were continued for 3 months afterwards with an INR targeted between 2 and 3. Monitoring lasted 6 months afterwards with good control.

DISCUSSION

Cerebral venous thrombosis is a rare entity, but always serious and urgent, with different predisposing conditions and the causes involved in its occurrence[9,10] pregnancy and

especially postpartum are the main risk factors because the average incidence of thrombophlebitis (CVT) during pregnancy and postpartum is 15 to 20 per 100,000 deliveries, which represents 10 to 20% of CVT[11 Pregnant or postpartum women have a risk of CVT 3, 5 times higher compared to non-pregnant or postpartum women of the same age. This risk is multiplied by 10 during the postpartum period compared to during pregnancy. The risk of occurrence of CVT postpartum was highest, especially during the first 6 weeks after delivery; or patients had an almost 19-fold increased risk of having CVT[[12,13] Pregnant patients have this increased risk of CVT because of normal pregnancy-related alterations in the coagulation process, these hematological changes preventing bleeding at the time of delivery, and persist even several weeks later, postpartum. Levels of fibrinogen, platelets and most factors (VII, VIII, IX, X and XII) are elevated while fibrinolytic activity is decreased (5) Other conditions may be added, such as venous stasis , increased venous capacity, multiparity, and advanced age, and combine to produce prime conditions for clot formation during the puerperium. This state of hypercoagulability predisposes pregnant patients and new mothers to CVT.[14] The other risk factors for thrombosis include age over 40, chronic hypertension, obesity, smoking, use of oral contraceptives, associated malignancy, anemia (< 9.9 g/dL) and infections such as sinusitis otitis mastoiditis or meningitis an increased thrombotic tendency due to an inherited or acquired coagulation disorder, such as the factor V Leiden gene or antiphospholipid syndrome. Those related to pregnancy such as a history of thromboembolic disease in a subsequent pregnancy, preeclampsia, placental abruption, postpartum hemorrhage, varicose veins, cesarean section or sepsis.[15–19]

Based on these studies, the predisposing risk factors in our patient seem to be cesarean section, in addition to the postpartum period that she was running. The clinical picture of PCT is very polymorphic, depends on the location of the thrombosis, the presence of cortical lesions, the age of the patients and the time between the onset of symptoms and admission to hospital (3) However, the interindividual variation of the cerebral venous anatomy as well as the frequent association of thrombosis of several sinuses and veins at the same time make a precise clinico-topographical correlation difficult. Involvement of the superior sagittal sinus (70%) and lateral sinus (70%) is the most common, followed by involvement of the right sinus (15%) then that of the cavernous sinus (3%). SSS and/or LS or cavernous sinus thrombosis is usually accompanied by a variable combination of symptoms.[20] Consideration is most important for early diagnosis. The onset of symptoms can be acute (less than 48 hours

from delivery) in 28% of cases, subacute (between 48 hours and 30 days) in 47% of cases or late (more than 30 days) in 25% of cases.[7.21]

A CPT must be suspected in the presence of symptoms grouped together to varying degrees intracranial hypertension (headache, vomiting, papilledema, impaired consciousness) and/or a focal neurological deficit linked to a hemorrhagic or ischemic cerebrovascular accident and/or a subacute encephalopathy made up of seizures[22]

Headaches are the most common and often the earliest symptom, found in 75% of cases, they have no specific characteristics or evolutionary profile but present as a recent headache, global, persistent, generally severe, which is rapidly getting worse. Focal or generalized convulsive seizures are also present in 20 to 57% of cases, papilledema in 50% of cases with nerve damage, neurological deficit in 34 to 70% of cases, consciousness disorders in 34 to 70% of cases may progress to coma, associated with vegetative disorders in severe forms.[23.24]

However, other slightly more unusual presentations exist such as transient ischemic attacks, subarachnoid hemorrhages, isolated psychiatric disorders which are sometimes in the foreground and mark the rest of the symptomatology or isolated headaches in the absence from any other neurological signs, making it difficult to initially differentiate CVT from several common diagnoses such as severe pre-eclampsia, stroke, migraine, tension headache, meningitis, posterior reversible encephalopathy (PRES), reversible cerebral vasoconstriction syndrome (CRVS), cervical artery dissection or post-dural puncture headache.[25,26] The incidence of CVT is much lower than post-dural puncture headache. Yet patients who report postpartum headache are more likely to be diagnosed with post-dural puncture headache even if they have CVT, as our patient did during her first 24 hours. While recognizing that early diagnosis is important in the prognosis of CVT, and any delay may be fatal.[9] Therefore, close observation of other symptoms is essential in patients who complain of headache postpartum like the present case.

Since the differential diagnosis is broad, neuroradiological examinations must be carried out quickly to establish an early diagnosis of a CVT which is made by highlighting the thrombotic occlusion of the cerebral veins or sinuses. This can be objectified in the form of a spontaneous hyperdensity at the site of the thrombosed vein as a direct sign of a fresh thrombus, but only in less than 20% of cases, by a simple cerebral CT scan which remains the

examination carried out in first intention. The typical appearance is the presence of a delta sign, which appears as a hypo-dense area surrounded by contrast enhancement. The indirect signs visible on the cerebral scanner are essentially venous infarctions but also the existence of cerebral edema.[22,27] In our case, brain CT was normal.

Brain MRI is currently the reference method for the early diagnosis of CVT. The usual sequences are the echo and spin sequences weighted in T1 and T2, the FLAIR sequences for the study of the parenchyma. The T2* sequence is more sensitive to the presence of blood, especially in the very first days when the T1 hyper signal may still be lacking, and more recently the diffusion and perfusion weighted sequences. The signal of the thrombus depends on its seniority on the various sequences which thus make it possible not only to visualize but also to date the thrombus and to follow its evolution. Magnetic resonance angiography is a complement to cerebral MRI which allows the visualization of venous circulation and thrombosis.[28,29]

Our patient underwent a cerebral MRI allowing the diagnosis of cerebral thrombophlebitis in the superior longitudinal sinus. Thrombosis at this level results in a variety of symptoms ranging from headaches, seizures, disturbances of consciousness and mental status which occurred in this case. Sometimes a temporo-parietal hemorrhagic infarction (due to the obstruction of the vein of Labbé) is objectified as this case which illustrated a hemorrhagic softening of an associated right posterior parietal venous infarction.[30,31]

The D-dimer assay can be useful, but it does not have the same high negative predictive value as for deep vein thrombosis of the legs. In patients with recent CVT with symptoms such as seizures, focal deficits, or impaired consciousness, D-Dimers are normal in only 4% of cases[32] Our patient is among the majority of cases in this group with a high dosage of D-dimers. Yet in patients with only isolated headaches, the rate remains normal in a quarter of these patients. A negative D-dimer assay cannot therefore exclude a CVT in the context of a recent isolated headache, a very frequent practical situation in which the decision to perform an MRI is the most debated.[32]

Thrombophilia is systematically sought to identify a possible deficiency in antithrombin III, responsible for 20 to 40% of thrombosis during pregnancy[24] or a deficiency in protein C or S responsible respectively for 7 to 22%. postpartum thrombosis.[23,33] In our patient, the thrombophilia assessment returned to normal.

Treatment and Prognosis

The majority of patients improve with adequate management. The current treatment for CVT is anticoagulation in therapeutic doses combined with symptomatic treatment including control of seizures and elevated intracranial pressure to prevent life-threatening complications in most cases.[34] To combat intracranial hypertension, drug treatments such as corticosteroids, mannitol, deep sedation are used and sometimes surgical treatment, in particular decompressive craniotomy, which can be discussed in the event of major edema. Antiepileptics are also systematic in case of epileptic seizures[21] which is the case of our patient who received anticonvulsant treatment and also sedation.

The objective of anticoagulation is to prevent the extension of thrombosis and to allow an improvement of the occlusion lesion by ensuring the development of collateral circulation and the prevention of venous infarction, based on heparin unfractionated (UFH) or low molecular weight heparin, followed by vitamin K antagonists for 3 to 12 months with a target INR of 2.0 to 3.0. Once recognized, CVT should, urgently and even in the presence of intracerebral or subarachnoid hemorrhage, be anticoagulated with subcutaneous low molecular weight heparin adjusted to body weight (LMWH) which seems to have a better efficacy and safety profile than unfractionated heparin (UFH).[35] The European Stroke Organization guideline published in 2017 also prefers LMWH over UFH due to more predictable pharmacokinetics and better outcomes[36] For long-term anticoagulation, only antagonists of vitamin K or LMWH are recommended the most. New non-vitamin K antagonists are used in some cases of CVT; however, there is a randomized trial published in 2019 that demonstrated the efficacy and safety of dabigatran indicated for CVT.[37] Treatment with fibrinolytics is difficult to recommend in the absence of randomized studies that allow comparison of the risk-benefit ratio.[20] The benefit of using local thrombotics has not been demonstrated, even in the most acute forms.[11]

Our patient showed a significant clinical improvement with recovery without sequelae following the administration of UFH and the continuation of oral anticoagulation based on VKAs at home for the following 3 months. The outcome of postpartum-related CVTs is generally good, with mortality being less than 10%.[38,39] In case of suspension of the use of anticoagulants, there is a 3% chance of reappearance of CVT.[40,41], which was not the case here during 6 months of follow-up.

CONCLUSION

Here we have presented an extremely rare case of postpartum cerebral venous thrombosis. CVT is a diagnostic and therapeutic emergency. However, it is difficult at first to differentiate this rare entity from several common postpartum differential diagnoses, especially in the face of the broad, variable and non-specific clinical picture that it can take. It is necessary to think about it even in the face of isolated headaches. However, rapid recognition of this problem by keeping a high index of suspicion and early initiation of well-conducted treatment lead to favorable results with complete cure in 80% of cases.

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