



Cerebral pontine infarctions during pregnancy – A case report and review of the literature

Jenna Kaye Wildman^a, Bassam H. Rimawi^{a,b,*}

^a University of South Alabama, Children's and Women's Hospital, Department of Obstetrics and Gynecology, 251 Cox Street, Mobile, AL 36604, United States

^b Division of Maternal Fetal Medicine, United States

ARTICLE INFO

Article history:

Received 15 December 2018

Received in revised form 13 January 2019

Accepted 22 January 2019

Keywords:

Cerebral infarction

Pontine infarction

Pregnancy

Gestational

ABSTRACT

Cerebrovascular disease is not uncommon during pregnancy as a result of either venous or arterial occlusion, or a hemorrhagic event, resulting in ischemia. Pregnancy may alter the prognosis of these neurologic disorders, with increased risks of morbidity and mortality for the mother and the developing fetus. Etiologies of stroke during pregnancy and the postpartum period include preeclampsia, eclampsia, HELLP syndrome, posterior reversible encephalopathy syndrome (PRES), amniotic fluid embolism, postpartum angiopathy, postpartum cardiomyopathy, thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), cerebral venous thrombosis, CNS infections, and maternal thrombophilia.

Essentially any of the vessels in the brain can be involved in cerebral infarction; however, pontine infarctions are rare and are generally secondary to occlusive insults or after dissection of an aneurysm. Though not common, these conditions can result in devastating sequelae and significant disability. Scant literature is available regarding pontine infarctions during pregnancy. Here we present a rare case of a pregnant patient who presented with new-onset seizures and was found to have a cerebral pontine infarction on imaging. The purpose of this article is to summarize existing data regarding the incidence, risk factors, and potential etiologies, as well as treatment strategies for pontine infarctions during pregnancy.

© 2019 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Pregnant women are predisposed to cerebrovascular disease due to pathophysiologic processes associated with pregnancy. The incidence of stroke is approximately 11 to 34 per 100,000 deliveries [1]. While 40% of strokes occur around the time of delivery and 50% occur in the postpartum period, only 10% of strokes occur in the antepartum period [2]. Etiologies of stroke during pregnancy and the postpartum period include preeclampsia, eclampsia, HELLP syndrome, posterior reversible encephalopathy syndrome (PRES), amniotic fluid embolism, postpartum angiopathy, postpartum cardiomyopathy, thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), cerebral venous thrombosis, CNS infections, and maternal thrombophilia [2].

Not all medical providers may be familiar with some of the physiological neurological changes that occur during pregnancy, including the prevalence of certain nerve palsies (Table 1). As pregnancy progresses, pregnant women face challenges with fluid changes that ultimately disrupt the pre-pregnancy plasma volume and colloid oncotic

pressure. For example, pregnant women have decreases in systematic vascular resistance and colloid oncotic pressure, and these changes can account for some of these physiological changes. Lastly, in general, when medical providers are examining pregnant women with certain neurological disorders, there may not be many differences when compared with nonpregnant women [3]. The article will illustrate some of the management considerations for medical providers caring for pregnant women with such neurological disorders.

The cerebral pons is located close to the hindbrain and sits directly above the medulla, which serves as a major message station between several areas of the brain, specifically from the cortex to the cerebellum [4]. Pontine strokes account for a small percentage of all ischemic events but can be associated with significant disability [5]. These lesions may be missed on computed tomography and therefore magnetic resonance imaging is generally preferred for the assessment of brainstem strokes [6]. Progressive neurological deterioration is relatively common and has been associated with the extension of such lesions. Here we present a case of a pregnant patient who presented with new-onset seizures and was found to have cerebral pontine infarctions on imaging [6]. The purpose of this article is to summarize existing data regarding the incidence, risk factors and potential etiologies, as well as treatment strategies for pontine infarctions during pregnancy.

* Corresponding author at: University of South Alabama, Children's and Women's Hospital, Department of Obstetrics and Gynecology, 251 Cox Street, Mobile, AL 36604, United States.

E-mail address: bassamrimawi@yahoo.com (B.H. Rimawi).

Table 1
Normal maternal physiological neurological changes during pregnancy.

Symptoms	Pregnancy
Nerve Palsies	Slightly increased risk of carpel tunnel syndrome
Swallowing	Increased risk of gastrointestinal reflux disease secondary to progesterone effects
Neurological examination	No change when compared to nonpregnant women

2. Case Report

A 16-year-old nulliparous female presented to the emergency department at 31 weeks of gestation with complaints of dyspnea, chest pain, and new-onset seizure activity that began two days earlier. Her medical history was significant for asthma and chronic anemia. She was evaluated at two different hospitals and was diagnosed with an upper respiratory tract infection and anxiety, and was given an inhaler and steroids and discharged home. A CT angiogram of the chest and a chest x-ray both showed no acute pathology, and an EKG showed sinus tachycardia. She returned to the second hospital the following day and was again discharged home with the diagnosis of anxiety. She then presented to our hospital complaining of shortness of breath and blurred vision after seizure-like activity and loss of consciousness.

She was found to be posturing upon arrival at the emergency department. She was awake but in initially unresponsive, although she became responsive after 3–4 min. She was admitted to the labor and delivery department for continuous monitoring and was started on magnesium sulfate and received a course of antenatal corticosteroids. The differential diagnosis included eclamptic seizures, a seizure disorder, and pseudoseizures. Her vital signs were stable, and her blood pressure was within normal limits. To rule out preeclampsia, laboratory investigations included a complete blood count, comprehensive metabolic panel, lactate dehydrogenase, uric acid, and a urine spot protein-to = creatinine ratio; these were all within normal limits. She had normal lactate levels, including normal routine hemostasis lab results, and a urine drug screen was negative. She admitted experiencing occasional headaches but denied vision changes or right upper-quadrant pain. She had no obstetrical complaints. It was noted that she had staring spells when staff members were talking to her, and so the neurology department was consulted.

The neurologic exam was significant for left-eye extropia but was otherwise within normal limits. A non-contrast CT scan of the brain showed no acute intracranial pathology. An MRI scan of the brain showed a focal area of restricted diffusion within the central pons demonstrating T2 and FLAIR hyperintensity, which suggested a differential diagnosis of subacute ischemic pons infarct (Fig. 1). A MRA/MRV of the head and neck, an EEG, and a transthoracic echocardiogram were all within normal limits. She was started on aspirin 81 mg daily. A lumbar puncture was performed, and the cerebrospinal fluid was sent for analysis to rule out an infectious etiology. The cerebrospinal fluid was negative for cryptococcal antigen, herpes simplex virus (HSV) types 1 and 2, mumps, rubella, varicella, and West Nile disease. The cerebrospinal fluid gram stain was negative, and the cultures had no growth. The patient was stable, did not have any further seizure activity during hospitalization, and was discharged home on hospital day 7. Throughout her admission, fetal monitoring remained reassuring, including reactive fetal heart rate monitoring, and a fetal anatomy scan was normal. Given this reassurance, she was not subjected to delivery and close outpatient follow-up visits in the high-risk obstetrical clinic were made. She was also followed up at the neurology department as an outpatient and remained stable without any progression of her initial symptoms and disabilities.

3. Discussion

Infarctions of the cerebral pontine are rare in both pregnant and nonpregnant women, but medical providers should consider these conditions in their differential diagnosis when women present with CNS symptoms that raise the suspicion of a cerebral vascular accident [5]. In the general population, the clinical presentation of cerebral pontine infarcts varies with the extent and specific location of the infarct; however, typical mild features include vertigo, ataxia, dysphagia, dizziness, facial palsy, ophthalmoplegia, aphonia, horizontal gaze paresis, hearing loss and dysarthria [7]. In more severe cases, patients may have motor hemiparesis involving the face, as well as upper and lower limb brachio-crural ataxia [7]. These signs and symptoms are no different in pregnant and non-pregnant women, and so their management is similar [8].

Our patient underwent imaging of her brain, which helped establish the diagnosis of her pontine infarction. Computed tomography (CT) scans and magnetic resonance imaging (MRI) of the central nervous system are acceptable options during pregnancy. The American College of Obstetricians and Gynecologists (ACOG) gives guidance on the use of contrast with these modalities, and according to the literature there is no proven harm from contrast with CT and the data on gadolinium are also very inconclusive [9]. In fact, the ACOG suggests that contrast be used if it is likely to be of clear diagnostic benefit [9]. Our patient underwent a lumbar puncture during her admission and the cerebrospinal fluid (CSF) was negative for cryptococcal antigen, herpes simplex virus (HSV) types 1 and 2, mumps, rubella, varicella, and West Nile disease. The CSF gram stain was negative, and the cultures had no growth. The technique utilized to perform CSF testing during pregnancy is no different than the technique used in nonpregnant women; in addition, the literature has not shown any major differences in the laboratory results for the CSF, including but not limited to differences in opening pressure, white and red blood cell counts, and the protein concentration between pregnant and nonpregnant women [3,10].

Treatment of acute pontine infarctions during pregnancy involves a multidisciplinary team approach involving obstetricians, perinatologists, neurologists and neurocritical care specialists. The choice of which agent(s) or interventions to use during pregnancy is controversial and therefore prior to choosing a treatment option medical providers caring for these pregnant women should weigh the risks and benefits. More importantly, the treatment selected may depend on the specific location of the pontine infarction; this is why a multidisciplinary team approach is critical. One of the treatment options available is recombinant tissue plasminogen activator (rtPA). The literature classifies the safety profile of rtPA during pregnancy as category C; it does not cross the placenta and result in teratogenicity [11,12]. In addition, timing of administration should not differ when compared with that for non-pregnant women and therefore rtPA should be administered within 3 h of the ischemic stroke to achieve the highest rate of efficacy [13].

Another treatment modality used to treat pontine infarctions in non-pregnant women is mechanical thrombectomy and embolectomy; however, we were not able to find any reports of the use of these treatment modalities during pregnancy [14]. Further studies are needed to assess the safety and efficacy of other commonly used drugs to treat pontine ischemic infarctions during pregnancy, such as aspirin/extended-release dipyridamole, and clopidogrel. Based on experimental animal studies, the use of anti-platelet therapy (eg. clopidogrel) during pregnancy is not expected to increase the risk of congenital anomalies [15]. Low-dose aspirin (81 mg/day) is currently recommended by ACOG and the Society of Maternal-Fetal Medicine (SMFM) for a number of conditions to reduce the risk of preeclampsia, such as a prior pregnancy complicated by preeclampsia, multifetal gestation, renal disease, autoimmune disease, type 1 or type 2 diabetes, and chronic hypertension [16]. This recommendation was also supported by the U.S.

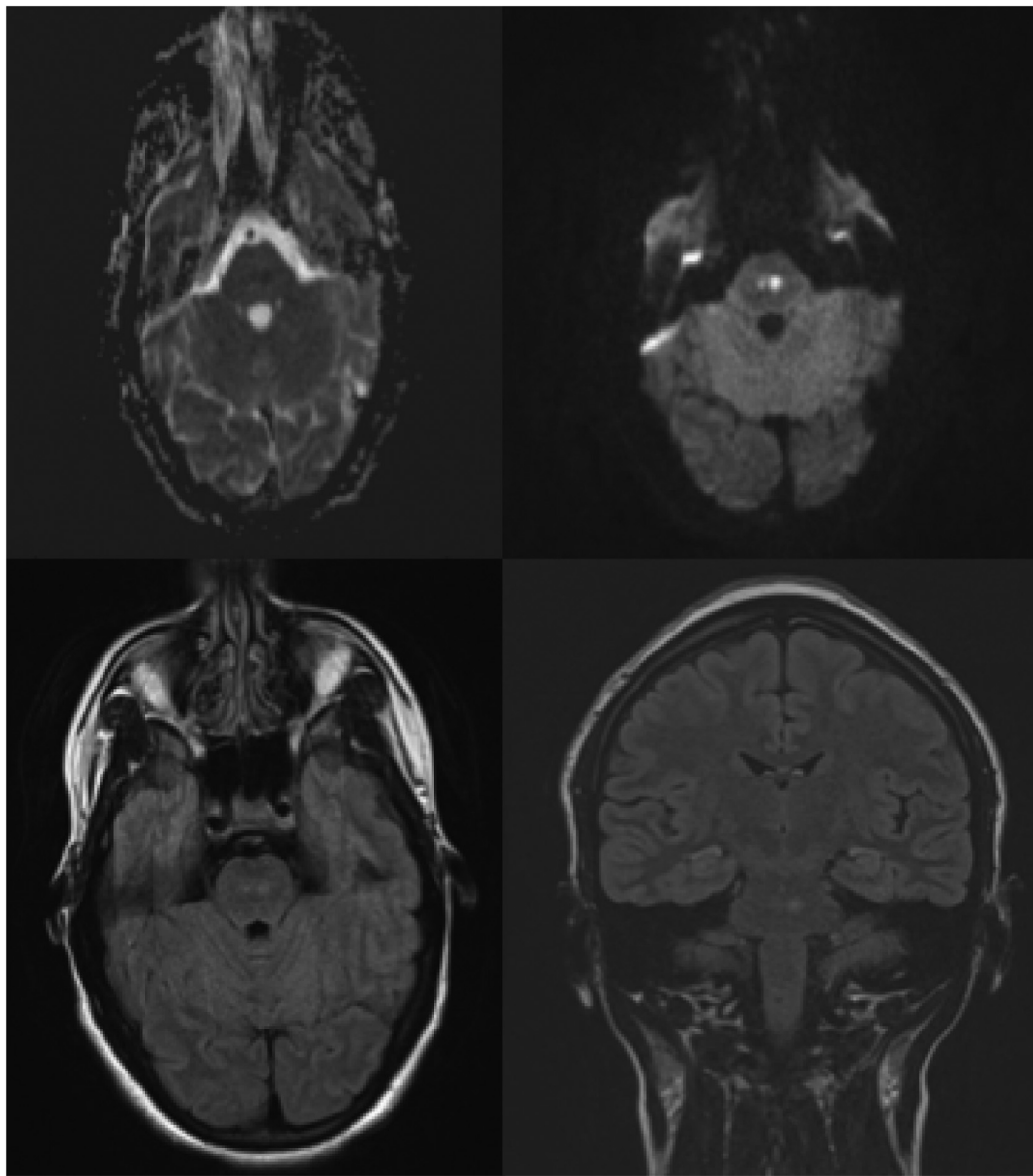


Fig. 1. Magnetic resonance imaging of brain. T2 weighted MRI – Depicts focal areas of restricted diffusion within the central pons demonstrating T2 and FLAIR hyperintensity – consistent with a diagnosis of subacute ischemic pons infarct.

Preventive Services Task Force [17]. Given the safety profile of low-dose aspirin, this can be considered an acceptable treatment modality. Higher doses should be avoided, as this can lead to teratogenic adverse pregnancy outcomes.

Immediate delivery of a pregnant woman with a vascular cerebral injury is not always indicated, especially if fetal monitoring has been reassuring. In these circumstances, delivery may be delayed during the maternal resuscitative and recovery periods, and therefore these patients should be managed on a patient-by-patient basis, as for any other neurological condition encountered during pregnancy [3]. In addition, as with other neurological disorders encountered during pregnancy, vaginal delivery should be considered the safest route of delivery for these women, unless there are other obstetrical indications [3]. Cesarean delivery is best reserved for routine obstetrical indications. Assistance of the second stage of labor with operative vaginal delivery (eg, vacuum and forceps extractors) may be considered in pregnant women in whom valsalva maneuvers should be avoided.

Lastly, when counseling these pregnant women on future pregnancies, we believe that they should have a preconception consultation

with a perinatologist to review not only their current medications and safety profiles, but also to assess their overall well-being and discuss timing of their next pregnancy. The risk of recurrence is likely to be low, and thus should not impact on mode of delivery. Patients using anti-platelet agents, such as clopidogrel, may continue this agent during pregnancy [15]. Low-dose aspirin (81 mg/day) can also be safely continued during pregnancy and can be initiated between 12 weeks and 28 weeks of gestation (optimally before 16 weeks) and continued daily until delivery [16].

Contributors

The two authors contributed equally to the preparation of this case report and saw and approved the final manuscript.

Conflict of interest

The authors declare that they have no conflicts of interest.

Funding

No funding was sought or secured in relation to this case report.

Patient consent

Obtained from the patient's mother, as the patient was a minor and was not able to consent on her own account.

Provenance and peer review

This case report was peer reviewed.

References

- [1] D.B. Petitti, S. Sidney, C.P. Quesenberry Jr., A. Bernstein, Incidence of stroke and myocardial infarction in women of reproductive age, *Stroke J. Cereb. Circ.* 28 (2) (1997) 280.
- [2] Andra H. James, Cheryl D. Bushnell, Margaret G. Jamison, Evan R. Myers, Incidence and risk factors for stroke in pregnancy and the puerperium, *Obstet. Gynecol.* 106 (3) (2005) 509.
- [3] B.H. Rimawi, Botulism in pregnancy – a clinical approach to diagnosis and management, *J. Matern. Fetal Neonatal Med.* (2018 Apr 6) 1–8.
- [4] A. Fernandez-Gil, R. Palacios-Bote, M. Leo-barahona, J.P. Mora-Encinas, Anatomy of the brainstem: a gaze into the stem of life, *Semin Ultrasound CT MR* 31 (3) (2010 Jun) 196–219.
- [5] A. Silverstein, Acute infarctions of the brain stem in the distribution of the basilar artery, *Confin. Neurol.* 24 (1964) 37–61.
- [6] L. Ling, L. Zhu, J. Zeng, S. Liao, S. Zhang, J. Yu, Z. Yang, Pontine infarction with pure motor hemiparesis or hemiplegia: a prospective study, *BMC Neurol.* 9 (2009) 25.
- [7] C. Bassetti, J. Bogousslavsky, A. Barth, F. Regli, Isolated infarcts of the pons, *Neurology* 46 (1996) 165–175.
- [8] K.E. Grear, C.D. Bushnell, Stroke and pregnancy: clinical presentation, evaluation, treatment and epidemiology, *Clin. Obstet. Gynecol.* 56 (2) (2013 Jun) 350–359.
- [9] Guidelines for diagnostic imaging during pregnancy and lactation. Committee Opinion No. 723, American College of Obstetricians and Gynecologists, *Obstet. Gynecol.* 130 (2017) e210–e216.
- [10] L.E. Davis, Normal laboratory values of CSF during pregnancy, *Arch. Neurol.* 36 (7) (1979 Jul) 443.
- [11] J. DeKeyser, Z. Gdovinova, M. Uyttenboogaart, P. Vroomen, G. Jan Luijckx, Intravenous alteplase for stroke. Beyond the guidelines and in particular clinical situations, *Stroke* 38 (2007) 2612–2618.
- [12] K. Wiese, A. Talkad, M. Mathews, D. Wang, Intravenous recombinant tissue plasminogen activator in a pregnant woman with cardioembolic stroke, *Stroke* 37 (2006) 2168–2169.
- [13] The National Institute of Neurological Disorders, Stroke rt-PA Stroke Study Group tissue plasminogen activator for acute ischemic stroke, *N. Engl. J. Med.* 333 (1995) 1581–1587.
- [14] W.S. Smith, G. Sung, J. Saver, et al., For the multi MERCI investigators: mechanical thrombectomy for acute ischemic stroke. Final results of the multi MERCI trial, *Stroke* 39 (2008) 1205–1212.
- [15] M. De Santis, C. De Luca, I. Mappa, E. Cesari, A. Mazza, et al., Clopidogrel treatment during pregnancy: a case report and review of literature, *Intern. Med.* 50 (16) (2011) 1769–1773.
- [16] Low-Dose Aspirin Use During Pregnancy, Committee Opinion No. 743. American College of Obstetricians and Gynecologists, *Obstet. Gynecol.* 132 (1) (2018 Jul) e44–e52.
- [17] M.L. Lefevre, Low-dose aspirin use for the prevention of morbidity and mortality from preeclampsia: U.S. Preventive Services Task Force recommendation statement. U.S. Preventive Services Task Force, *Ann. Intern. Med.* 161 (2014) 819–826.