

CASE REPORT

Early pregnancy-associated ischemic stroke during first trimester in a young woman: A case report

Asma Ouerdiene  | Mariem Messelmani | Malek Mansour | Jamel Zaouali |
Ridha Mrissa

Department of Neurology, Military Hospital of Instruction of Tunis, Tunis, Tunisia

Correspondence

Asma Ouerdiene, Department of Neurology, Military Hospital of Instruction of Tunis, Montfleury 1008 Tunis, Tunisia.
Email: ouerdiene.asma@gmail.com

Funding information

None

Abstract

Pregnancy-associated ischemic stroke is rare. The degree of the risk is the highest in the third trimester, but clinicians should be also wary from the beginning of the pregnancy as the risk still exists like demonstrated by our case.

KEYWORDS

acute ischemic stroke, first trimester pregnancy, pregnancy

1 | INTRODUCTION

Ischemic stroke during pregnancy is rare but constitutes a disastrous disease during a crucial period in life responsible of a significant mortality and a high morbidity. It is responsible of one eighth of deaths during pregnancy. Physiological changes during pregnancy and puerperium, in coagulability, circulatory dynamics, immune system, and connective tissue structure, confer an increased risk for ischemic as well as hemorrhagic stroke. This risk is especially the highest during the third trimester until 6 weeks postpartum, which coincide with the highest rates of hypertensive disorders of pregnancy and gestational hypercoagulability. Thus, stroke can occur earlier in pregnancy and the pathophysiological mechanism is still not fully understood until now. We report herein a rare case of stroke in a young woman into the first trimester pregnancy with a negative exhaustive etiological workup.

Stroke is the fourth main cause of women's death and accounts for one eighth of all pregnancy-associated deaths.¹ Incidence of pregnancy-associated stroke ranges from 3.8 to 34.2 per 100,000 births.^{1,2} Pregnancy and puerperium

confer a threefold higher risk for ischemic and hemorrhagic stroke, compared with nonpregnant women.³ This risk varies depending on the stage of pregnancy, and it is the most elevated from the third trimester until 6 weeks postpartum, coinciding with the highest rates of hypertensive disorders of pregnancy and gestational hypercoagulability.³ Most pregnancy-associated strokes appear to result from some pathological conditions overlaid by the physiological changes of pregnancy, delivery, and the postpartum period, but others remain unexplained.⁴

2 | CASE REPORT

A 34-year-old woman presented to our department of neurology in the military hospital. She was 9 weeks pregnant. It was her 5th pregnancy with three healthy kids and one spontaneous abortion in the second month of pregnancy 3 years ago. She had no remarkable past medical history or any vascular risk factor. The patient presented a sudden onset of a slurred speech, and a facial asymmetry, which spontaneously and partially regressed after 90 min. Initial neurological exam at admission showed a right

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2021 The Authors. *Clinical Case Reports* published by John Wiley & Sons Ltd.

central facial palsy and right hyperreflexia, scoring NIHSS to 1 controlled 0 with a complete regression of symptoms 5 h later. The cerebral magnetic resonance imaging (MRI) showed ischemic stroke in the territory of the left middle cerebral artery in the centrum semiovale. Time-of-Flight (TOF) angio-MRI and cervical FAT-Saturation sequences were normal. Blood pressure was normal. An extended blood panel workup revealed only a mild iron deficiency anemia (Hb 10.8 g/dl), without other relevant abnormalities. Serum markers for thrombophilia (Protein C, protein S, antithrombin III, factor II, factor V, methylenetetrahydrofolate reductase, and fibrinogen), autoimmune (antinuclear antibodies, anti-double stranded DNA, anti-neutrophil cytoplasmic antibodies, and antiphospholipid antibodies) and infectious diseases, were normal. Ultrasonography of supra-aortic trunks was normal, and ECG monitoring, transthoracic, and transesophageal echocardiography were also normal. Serial obstetric ultrasonography was unremarkable. She was put on low doses of aspirin (150 mg) and on prophylactic low molecular weight heparin (LMWH; enoxaparin 4000 anti-Xa IU) for the duration of her pregnancy. She remained neurologically stable and was discharged home 1 week after admission. She gave birth to a healthy full-term baby, by eutocic delivery. LMWH was stopped after postpartum, and no recurrence of stroke happened until this day.

3 | DISCUSSION

Stroke is infrequent during pregnancy and puerperium but constitutes a disastrous complication. The incidence of pregnancy-related stroke ranges from 3.8 to 34.2 per 100,000 maternities with the highest risk in the early postpartum period.¹ Identification of risk factors and underlying pathophysiological mechanisms is primordial for stroke prevention and management.

Few studies have investigated detailed causes in patients with pregnancy and puerperium-associated ischemic stroke. In fact, pregnancy is responsible of physiological changes in coagulability, circulatory system, connective tissue structure, and immune responses, in adaptation to childbearing's demands.⁴ Thus, these changes are responsible of an increased risk of ischemic and hemorrhagic stroke especially from the third trimester until 6 weeks after postpartum, coinciding with the highest rates of hypertensive disorders of pregnancy and gestational hypercoagulability,³ unlike our case who presented a stroke in the first trimester. Hemodynamic changes include an increase in cardiac output and blood volume beginning from the first weeks of pregnancy, and a cardiac remodeling with physiological ventricular hypertrophy.² This increase in blood volume can cause strain on the vessel walls. The

increased cardiac output may exacerbate or cause structural changes, resulting in turbulent blood flow around cardiac or major vessel abnormalities increasing the risk of formation of clots that can dislodge and cause ischemic strokes.⁵ A failure to adapt to all of these changes can result in cardiovascular complications in pregnant women with known cardiac disease, or even reveal an unknown underlying cardiac disease.² Hypercoagulability beginning at 11 weeks, results from an increase in coagulation factors VII, X, XII, fibrinogen and plasminogen activator inhibitors, and a decrease in anticoagulant factors protein C and antithrombin, especially during the third trimester and in early postpartum.¹ This hyper-coagulable state along with venous stasis is responsible of a higher risk of thromboembolic complications.¹ If a woman has a genetic predisposition for increased clotting or decreased fibrinolysis, her ability to form and maintain clots may be further enhanced. If she also has factors that contribute to clot formation, such as vascular defects or injuries, her risk of a thromboembolism is greatly increased.⁵

Ischemic stroke can thus be related to other conditions exclusively associated with pregnancy including preeclampsia, eclampsia with HELLP syndrome or posterior reversible encephalopathy syndrome, postpartum cardiomyopathy, cerebral angiopathy, choriocarcinoma with trophoblastic embolism or cerebral metastases with direct vascular damage, and amniotic fluid embolism,^{1,2} which were eliminated in our patient. However, up to 40% of ischemic strokes have no identifiable cause despite investigations and are regarded as cryptogenic similar to our case.¹

The understanding of the complex pathophysiological mechanisms underlying such pregnancy-related stroke remains unfortunately limited. Most reports seem to incriminate the hemodynamic changes brought about by elevated blood volume and cardiac flow during pregnancy, besides the prothrombotic state, but without convincing evidence.⁶

The clinical approach to the assessment and investigation of ischemic stroke during pregnancy is not different from that in nonpregnant women. In Tunisia, seen the rare occurrence of stroke during pregnancy, screening including serum markers for thrombophilia and autoimmune diseases are performed only in certain circumstances with high risk, like in case of the occurrence of two or more miscarriages, and in the presence of personal or family history of thrombotic events, outside these circumstances no special screening is done.

Regarding stroke management during pregnancy, there is still no consensus. The investigation and management of stroke in pregnancy should follow published guidelines like in nonpregnant women. Thus, treatment risk must be balanced against the potential of maternal

disability and death. Treatment with recombinant tissue plasminogen activator (rTPA) in ischemic stroke during pregnancy should be considered. In fact, rTPA does not cross the placenta and so does not have teratogenic or hemorrhagic risks to the fetus. The risk of rTPA in pregnant women is comparable to nonpregnant women⁷ but more studies need to be conducted to analyze the risk/benefit. Mechanical thrombectomy is an interesting approach in this population and may be preferable to intravenous thrombolysis seen the higher risk of maternal hemorrhage in late pregnancy using rTPA, but intraprocedural radiation risks should be considered.^{2,7} Aspirin was found to be safe for use in the second and third trimesters, and during lactation period in low daily doses (50–150 mg/day) without teratogenic effects. Thus, data on safety in the first trimester are limited, there are some but inconsistent reports of birth defects such as gastroschisis, but other studies and meta-analyses of aspirin use for prevention of preeclampsia even before 11 weeks do not support the same findings.^{2,3} Aspirin was used in our patient in low doses, and no noxious effects were noted. The impact of antiplatelet agents such as ticagrelor and clopidogrel on fetal development has not been well studied; therefore, these are not recommended for use during pregnancy, but rather should be considered on a case-by-case basis.⁷ Oral anticoagulants are contraindicated during pregnancy seen the demonstrated teratogenic effects. Low molecular weight heparins (LMWH) and unfractionated heparin (UFH) are the anticoagulants of choice during pregnancy, as they do not cross the placenta.⁷ Aspirin and anticoagulants should be withdrawn before delivery (1 week prior for aspirin and 24 h prior for heparin) in order to allay the postpartum bleeding risks.⁷ The choice between aspirin or heparin depends on the underlying stroke etiology like in nonpregnant patients. In the case of cryptogenic stroke like in our case, there is no benefit demonstrated between therapies.⁸ Several studies are currently underway to determine whether anticoagulation or antiplatelet therapy is the best preventive strategy in cases such as ours.⁶ In Tunisia, most of medical teams use aspirin in monotherapy in case of preeclampsia, and associate it with low molecular weight heparin (LMWH) in case of history of thrombotic events in pregnant women. For Zhu et al⁶ who described a similar case of cryptogenic stroke in a 28-year-old woman, 9 weeks pregnant, preferred prophylactic LMWH in monotherapy (enoxaparin 4000 anti-Xa IU) considering the possible implication of a prothrombotic state as suggested by literature, which was replaced by a daily dose of 160 mg of aspirin after postpartum. Peksa et al⁹ used the association between aspirin and prophylactic enoxaparin in a 35-year-old-woman who was also 9 weeks pregnant and presented a cryptogenic stroke like in our case.

4 | CONCLUSION

Pregnancy-related ischemic stroke is rare but its risk is high seeing the countless physiological changes during pregnancy. The degree of the risk is the highest in the third trimester, but clinicians should be also wary from the beginning of the pregnancy as the risk still exists, which was demonstrated by our case. Early detection and intervention prevent long-term morbidity and mortality. Fortunately, this patient's prognosis was excellent. A preliminary risk assessment for stroke needs to be considered and be included as a part of routine antenatal care protocol and patient stratification can be done accordingly for a better and aggressive management.

ACKNOWLEDGEMENTS

We thank the patient and all clinicians who participated in this study.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Ouerdiene Asma involved in investigation, formal analysis, data curation, wrote the review and edited the manuscript, original draft, and visualization. Messelmani Mariem involved in conceptualization, resources, investigation, methodology, validation, visualization, and supervision. Mansour Malek involved in formal analysis, visualization, and supervision. Zaouali Jamel and Mrissa Ridha involved in validation, project administration, and supervision.

ETHICAL APPROVAL

This article does not contain any studies with human participants or animals performed by any of the authors. Informed consent was obtained from our patient.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Asma Ouerdiene  <https://orcid.org/0000-0003-3557-9916>

REFERENCES

1. Ubaid MF, Salim A, Faiz SA, Azeem Z, Abid R, Shakeel M. Stroke in early postpartum period in a young woman: a case study. *J Clin Case Rep*. 2019;09:1205. <https://doi.org/10.4172/2165-7920.10001205>
2. van Alebeek ME, de Heus R, Tuladhar AM, de Leeuw F-E. Pregnancy and ischemic stroke: a practical guide to

- management. *Curr Opin Neurol*. 2018;31:44-51. <https://doi.org/10.1097/WCO.0000000000000522>
3. Camargo EC, Feske SK, Singhal AB. Stroke in pregnancy. *Neurol Clin*. 2019;37:131-148. <https://doi.org/10.1016/j.ncl.2018.09.010>
 4. O'Neal MA, Feske SK. Stroke in pregnancy: a case-oriented review. *Pract Neurol*. 2016;16:23-34. <https://doi.org/10.1136/practneurol-2015-001217>
 5. Sanders BD, Davis MG, Holley SL, Phillippi JC. Pregnancy-associated stroke. *J Midwifery Womens Health*. 2018;63:23-32. <https://doi.org/10.1111/jmwh.12720>
 6. Zhu F, Gory B, Mione G, Humbertjean L, Derelle A-L, Richard S. Combined reperfusion therapy to treat cryptogenic acute ischemic stroke during the first trimester of pregnancy: case report and literature review. *TCRM*. 2018;14:1677-1683. <https://doi.org/10.2147/TCRM.S166289>
 7. Terón I, Eng MS, Katz JM. Causes and treatment of acute ischemic stroke during pregnancy. *Curr Treat Options Neurol*. 2018;20:21. <https://doi.org/10.1007/s11940-018-0506-5>
 8. Orchard EA, Wilson N, Ormerod OJM. The management of cryptogenic stroke in pregnancy. *Obstet Med*. 2011;4:2-6. <https://doi.org/10.1258/om.2010.100027>
 9. Peksa GD, Ostrem J, Davis T. Intravenous tissue plasminogen activator for ischemic stroke in early pregnancy dosed by actual body weight. *SAGE Open Med Case Rep*. 2019;7:2050313X1982824. <https://doi.org/10.1177/2050313X19828247>

How to cite this article: Ouerdiene A, Messelmani M, Mansour M, Zaouali J, Mrissa R. Early pregnancy-associated ischemic stroke during first trimester in a young woman: A case report. *Clin Case Rep*. 2021;00:e04736. <https://doi.org/10.1002/ccr3.4736>