

## Case Report

# Aseptic Meningitis in Pregnancy – A Case Study Detailing Potential Diagnostic Dilemmas

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## Abstract

There are few reported cases of meningitis in pregnancy and presentation can be variable in each patient which may cause diagnostic challenges and potential delays in treatment. Here, we discuss a case of aseptic meningitis - a 36 years old Gravida 2 Para 1 pediatric physician with "the worst headache of her life" at 31+5 weeks of gestation. At presentation, she did not have any of the classic triads of meningitis (fever, neck stiffness, and/or a change in mental status) and did not report any neurological symptoms. In view of persistent headache, development of pyrexia, and evolving symptoms of photophobia, she was referred to a neurology specialist, and a lumbar puncture was performed. Findings were in line with meningitis and the polymerase chain reaction confirmed enterovirus meningitis. Although aseptic meningitis is rare, it should be considered as a differential diagnosis in patients with persistent complaints, development of associated symptoms of pyrexia, photophobia, and neck pain, as well as in patients with increased risk of exposure to viral illnesses.

## Introduction

Meningitis is the inflammation of the meninges, caused by bacterial or viral infection of the central nervous system. It can be associated with significant morbidity and mortality, which has been observed to be as high as 21% in bacterial meningitis [1].

Lumbar puncture and evaluation of the cerebral spinal fluid (CSF) are often required to confirm the diagnosis [2,3]. However, lumbar puncture is invasive and runs the risk of complications such as post-lumbar puncture headache, bleeding, infection, spinal hematoma, and cerebral herniation [4]. Hence, detailed clinical assessment, evaluation of the patient and associated risk factors, as well as a high index of clinical suspicion is crucial. Due to atypical clinical presentation in the early evolving disease, such invasive investigations may not be offered to the patient as first-line, and less invasive investigations such as magnetic resonance imaging (MRI) are often prioritized to rule out other possible differentials. These, however, may be of low yield and can potentially confound clinical judgment with non-specific findings. Early referral to a neurology specialist for multidisciplinary care is recommended when clinical suspicion is high.

## More Information

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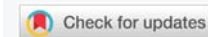
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## Case presentation

### Patient information and clinical findings

We describe a case of a 36 years old Gravida 2 Para 1 pediatric physician who presented with "the worst headache of her life" at 31+5 weeks of gestation. She had no significant past medical or surgical history of note. Her first pregnancy cumulated in a full-term normal vaginal delivery and she did not have any hypertension or gestational diabetes. For the current pregnancy, she had been on regular follow-up since the first trimester. It was an otherwise low-risk pregnancy with no prior issues.

At presentation, she did not complain of any symptoms related to the classic triad of meningitis (fever, neck stiffness, and/or a change in mental status) nor report any neurological symptoms. Physical examination findings including temperature, blood pressure, heart rate, and full neurological examination were normal. Differential diagnoses, in this case, included tension headache, migraines, cerebral venous thrombosis, tumors, hypertension, intracranial hemorrhages, iatrogenic causes, and meningitis.

### Diagnosis & treatment

Initial investigations revealed an abnormal white cell count



of  $9.47 \times 10^9/L$  with a mild neutrophilic shift of  $7.88 \times 10^9/L$ . C-reactive protein was elevated at 35.3 mg/L, and serum lactate levels were normal. She underwent an MRI of the brain which showed no evidence of cerebral venous thrombosis or any other pathology, but revealed a non-specific finding of a 2-centimeter arachnoid cyst. At this point, she was treated symptomatically with analgesia and intravenous hydration.

She turned pyretic several hours after admission where she spiked a temperature of 38.8 degrees Celsius. There were no other localizing sources of infection. In view of persistent headache, development of pyrexia, and evolving symptoms of photophobia, she was referred to a neurology specialist, and a lumbar puncture was performed. The CSF was turbid with an elevated white cell of 1030/uL, normal CSF to blood glucose ratio, and normal opening pressure. The lymphocyte differential count was raised to 75%. Empirical coverage with antibiotics (ceftriaxone) and antiviral (acyclovir) therapy was started in view of significant leucocytosis in her CSF full examination microscopic examination (FEME) while awaiting culture and polymerase chain reaction (PCR) results.

Repeated history taken by referred neurologist further revealed subjective neck pain and recent exposure to pediatric patients with viral infections. Her CSF PCR results later showed the detection of enterovirus ribonucleic acid.

### Follow-up and outcomes

By the third day of admission, the patient's fever lysed and she clinically improved. She was discharged well on the fourth day of admission and CSF culture results came out negative for bacteria growth on the following day. Her recovery thereafter was uncomplicated. Subsequently, she had routine antenatal visits and a normal vaginal delivery at 39 weeks without any adverse maternal or fetal outcomes. A standing appointment with the neurologist was also scheduled post-partum for a follow-up of the incidental finding of the arachnoid cyst on her MRI.

## Discussion

The most common causes of headaches in pregnancy are tension headaches and migraines [5]. However, secondary headaches such as cerebral venous thrombosis, tumors, hypertension (including pre-eclampsia, eclampsia, and associated syndromes such as Reversible Cerebral Vasoconstriction Syndrome, and Posterior Reversible Encephalopathy Syndrome), intracranial hemorrhages, iatrogenic cause, and meningitis need also be considered as differential diagnoses [5].

The patient's evolving symptoms posed a diagnostic challenge due to equivocal clinical findings. Her initial presenting complaint was that of a headache. While she had subjective neck stiffness, she was initially afebrile and clinically well, and her physical examination findings were otherwise unremarkable. It has been shown that the classic

triad of fever, neck stiffness, and change in mental status may be present in less than half of adults with meningitis [6]. However, there should be a high index of suspicion for meningitis where one presents with a headache in addition to at least one other symptom from the classical triad [6].

In cases of a new onset headache and/or differs from baseline, or the presence of neurological deficits, or where the headache is persistent, imaging should be considered early to rule out secondary headaches. Hormone changes and hypercoagulability in pregnancy can increase the risk of vascular causes of headaches [7]. Imaging options include MRI, with or without arteriography and venography, and non-contrast head computed tomography (CT) [8]. MRI is safe in pregnancy as it involves no radiation. Hence, it should be considered over CT in cases in which they are equivalent for the required diagnosis, and if it is accessible without delay [9]. However, gadolinium contrast should be avoided unless absolutely necessary due to the theoretical risks of teratogenicity [9].

Lumbar puncture to obtain and assess the CSF should also be considered if imaging studies are inconclusive for diagnosis. The opening pressure of a lumbar puncture is a surrogate measurement for intracranial pressure [10] and high opening pressure can indicate cerebral edema from infections, idiopathic intracranial hypertension, cerebral venous thrombosis, and mass effect from tumors or hemorrhage [11]. The CSF can be examined for cell counts and CSF to blood glucose ratio – in the presence of pleocytosis, the infection should be suspected [3]. Mononuclear pleocytosis is classical to viral meningitis but there may be a neutrophilic predominance in the first 24 hours of the disease [12]. CSF to blood glucose ratio is often lowered in bacterial meningitis [3,13]. The CSF should also be sent for gram stain and culture, as well as polymerase chain reaction (if available) to further differentiate between bacterial and viral meningitis. Examination of the CSF for xanthochromia [8] can also be useful in excluding minor intracranial hemorrhage and sentinel bleeding from an aneurysm or arterial-venous malformation which may not be apparent on imaging. This is important as a sentinel bleed can precede a life-threatening rupture.

Altered immunity in pregnancy can affect a pregnant women's susceptibility to infections. They may be at increased risk depending on the placental immune response toward specific viruses and pathogens [14]. While pregnancy alone is not a risk factor, it should be considered when evaluating infective aetiologies for a patient's symptoms due to potential differences in immune response compared to a non-pregnant adult.

While meningitis is a rare occurrence, especially in adults, the most common infectious aetiologies of meningitis are viruses, with a large majority of cases attributable to



enterovirus. Other common causes include arboviruses, influenza, and other respiratory viruses, as well as herpes viruses (such as herpes simplex virus (HSV) and varicella-zoster virus (VZV)) [1,15]. Enteroviral meningitis in pregnancy has also been described in other centers [16].

Important factors that should be taken into consideration when evaluating a patient include potential exposures to sources of infection. In this case, the patient works as a pediatrician with significant exposure to children with viral infections. Enterovirus infection is a common virus affecting children, commonly presenting as herpangina, hand-foot-mouth disease, and gastrointestinal infections. It has the propensity to cause significant neurological diseases including but not limited to aseptic meningitis, acute flaccid paralysis, brainstem encephalitis, and Guillan-Barre syndrome [17].

Meningitis in pregnancy can potentially result in further complications. Bacterial meningitis in pregnancy can cause septic shock and significant mortality risks [1]. It can also result in fetal loss, as well as neonatal infection and death [18]. Even in cases of aseptic meningitis, in one report relating to HSV meningitis in pregnancy, the disease evolved and resulted in encephalitis - this patient required hemodialysis and underwent emergency cesarean section at 33 weeks of gestation. HSV and VZV meningitis can potentially be treated with antiviral therapy, with evidenced benefits in immunocompromised patients [19]. This underlines the importance of early diagnosis and treatment with antibiotics and antivirals where appropriate. Nonetheless, with regard to enterovirus infection and meningitis, the prognosis has been good. There have been no clear causal links with adverse fetal or neonatal outcomes [20].

## Conclusion

Headache is a common symptom presented in pregnancy. Although aseptic meningitis is rare, it should be considered as a differential diagnosis in patients with persistent symptoms, the development of related symptoms including but not limited to pyrexia, nuchal stiffness, and photophobia, as well as in patients with increased risk of exposure to viral illnesses. In addition, in patients with a non-specific and atypical presentation, the early involvement of a multi-disciplinary team can reduce diagnostic delay and expedite treatment.

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## Author's contributions

YSN and MSSMG conceptualized the study, collected data, and drafted, reviewed, and revised the manuscript. Both authors take full responsibility for the accuracy and integrity of the study and approve the final manuscript submission. MM supervised the above.

## Data availability

All data in our report was obtained from the patient's hospitalization. Any inquiries regarding supporting data availability of this study should be directed to the corresponding author.

## References

- Bamberger DM. Diagnosis, initial management, and prevention of meningitis. *Am Fam Physician*. 2010 Dec 15;82(12):1491-8. PMID: 21166369.
- Attia J, Hatala R, Cook DJ, Wong JG. The rational clinical examination. Does this adult patient have acute meningitis? *JAMA*. 1999 Jul 14;282(2):175-81. doi: 10.1001/jama.282.2.175. PMID: 10411200.
- Straus SE, Thorpe KE, Holroyd-Leduc J. How do I perform a lumbar puncture and analyze the results to diagnose bacterial meningitis? *JAMA*. 2006 Oct 25;296(16):2012-22. doi: 10.1001/jama.296.16.2012. PMID: 17062865.
- Sternbach G. Lumbar puncture. *J Emerg Med*. 1985;2(3):199-203. doi: 10.1016/0736-4679(85)90397-x. PMID: 3833922.
- Negro A, Delaruelle Z, Ivanova TA, Khan S, Ornello R, Raffaelli B, Terrin A, Reuter U, Mitsikostas DD; European Headache Federation School of Advanced Studies (EHF-SAS). Headache and pregnancy: a systematic review. *J Headache Pain*. 2017 Oct 19;18(1):106. doi: 10.1186/s10194-017-0816-0. PMID: 29052046; PMCID: PMC5648730.
- van de Beek D, de Gans J, Spanjaard L, Weisfelt M, Reitsma JB, Vermeulen M. Clinical features and prognostic factors in adults with bacterial meningitis. *N Engl J Med*. 2004 Oct 28;351(18):1849-59. doi: 10.1056/NEJMoa040845. Erratum in: *N Engl J Med*. 2005 Mar 3;352(9):950. PMID: 15509818.
- Magro I, Nurimba M, Doherty JK. Headache in Pregnancy. *Otolaryngol Clin North Am*. 2022 Jun;55(3):681-696. doi: 10.1016/j.otc.2022.02.013. Epub 2022 Apr 27. PMID: 35490045.
- Schoen JC, Campbell RL, Sadosty AT. Headache in pregnancy: an approach to emergency department evaluation and management. *West J Emerg Med*. 2015 Mar;16(2):291-301. doi: 10.5811/westjem.2015.1.23688. Epub 2015 Feb 25. PMID: 25834672; PMCID: PMC4380381.
- Committee Opinion No. 723: Guidelines for Diagnostic Imaging During Pregnancy and Lactation. *Obstet Gynecol*. 2017 Oct;130(4):e210-e216. doi: 10.1097/AOG.0000000000002355. Erratum in: *Obstet Gynecol*. 2018 Sep;132(3):786. PMID: 28937575.
- Doherty CM, Forbes RB. Diagnostic Lumbar Puncture. *Ulster Med J*. 2014 May;83(2):93-102. PMID: 25075138; PMCID: PMC4113153.
- Pinto VL, Tadi P, Adeyinka A. Increased Intracranial Pressure. 2022 Aug 1. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. PMID: 29489250.



12. Logan SA, MacMahon E. Viral meningitis. *BMJ*. 2008 Jan 5;336(7634):36-40. doi: 10.1136/bmj.39409.673657.AE. PMID: 18174598; PMCID: PMC2174764.
13. Tamune H, Takeya H, Suzuki W, Tagashira Y, Kuki T, Honda H, Nakamura M. Cerebrospinal fluid/blood glucose ratio as an indicator for bacterial meningitis. *Am J Emerg Med*. 2014 Mar;32(3):263-6. doi: 10.1016/j.ajem.2013.11.030. Epub 2013 Nov 26. PMID: 24361137.
14. Mor G, Cardenas I. The immune system in pregnancy: a unique complexity. *Am J Reprod Immunol*. 2010 Jun;63(6):425-33. doi: 10.1111/j.1600-0897.2010.00836.x. Epub 2010 Mar 29. PMID: 20367629; PMCID: PMC3025805.
15. Gundamraj V, Hasbun R. Viral meningitis and encephalitis: an update. *Curr Opin Infect Dis*. 2023 Jun 1;36(3):177-185. doi: 10.1097/QCO.0000000000000922. Epub 2023 Apr 12. PMID: 37093042.
16. Ruth R, Savita L. Viral meningitis in pregnancy: A case report. *Clinical Journal of Obstetrics and Gynecology*. 2020; 3(2):121–2. doi:10.29328/journal.cjog.1001063
17. Ooi MH, Wong SC, Lewthwaite P, Cardoso MJ, Solomon T. Clinical features, diagnosis, and management of enterovirus 71. *Lancet Neurol*. 2010 Nov;9(11):1097-105. doi:10.1016/S1474-4422(10)70209-X. PMID: 20965438.
18. Adriani KS, Brouwer MC, van der Ende A, van de Beek D. Bacterial meningitis in pregnancy: report of six cases and review of the literature. *Clin Microbiol Infect*. 2012 Apr;18(4):345-51. doi: 10.1111/j.1469-0691.2011.03465.x. Epub 2011 Mar 7. PMID: 21375656.
19. Noska A, Kyrillos R, Hansen G, Hirigoyen D, Williams DN. The role of antiviral therapy in immunocompromised patients with herpes simplex virus meningitis. *Clin Infect Dis*. 2015 Jan 15;60(2):237-42. doi: 10.1093/cid/ciu772. Epub 2014 Oct 1. PMID: 25273082.
20. Centers for Disease Control and Prevention; 2020. <https://www.cdc.gov/non-polio-enterovirus/pregnancy.html>