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Obstetric cholestasis: A case report on rapid bile acid elevation

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ABSTRACT

Obstetric cholestasis is a pregnancy-specific liver disorder which most commonly develops in the second or third trimester. It typically presents with generalised pruritus, often worst on the hands and feet, and no rash. Diagnosis is made on the basis of clinical presentation and elevated bile acid levels. Whilst obstetric cholestasis usually has no significant maternal adverse outcomes, aside from decreased quality of life from pruritus, it can lead to significant foetal complications, including stillbirth. There are no treatments for obstetric cholestasis, which resolves only following delivery. Thus, depending on the severity of obstetric cholestasis, early induction of labour may be recommended. As symptoms may precede bile acid elevation, repeat testing after a week is usually recommended when initial levels are normal. This report describes a case where a 35-year-old pregnant woman presented with pruritus but a normal bile acid level of 3 μmol/L. On repeat testing the following day the level had risen to 62, diagnosing obstetric cholestasis, and resulting in an urgent induction of labour at 38 weeks and 2 days of gestation. The patient gave birth to a healthy girl. This highlights the importance of close monitoring and consideration of early repeated blood tests where clinical suspicion is high, and/or a diagnosis of obstetric cholestasis would have significant management implications, to prevent adverse foetal outcomes.

1. Introduction

Obstetric cholestasis (OC), also known as intrahepatic cholestasis of pregnancy, is a liver disorder which develops only during pregnancy, most commonly during the late second or third trimester [1,2]. It affects 0.2–2% of pregnancies, with the incidence varying with ethnicity and geographic location; it is most common in Scandinavia, South America and South Asia [1,3–6]. It is characterised by generalised pruritus without rash, typically worse on the palms and soles, derangement in liver function tests, and elevated bile acid levels [1,7]. The aetiology of OC is still unclear, but is likely multifactorial [3,5,7]. There is no cure and the condition persists until delivery, with spontaneous resolution of symptoms usually within days of delivery, and normalisation of liver functions tests and bile acids over several weeks [2,3,6,8]. Whilst OC is a relatively benign condition for the mother with very rare adverse maternal outcomes, it can have significant fetal outcomes [6]. OC increases the risk of complications such as preterm delivery, fetal distress, meconium-stained liquor, and stillbirth. These risks are directly proportional to bile acid levels [1–3,9].

This report describes a case of OC diagnosed following a sudden and dramatic rise in bile acids, necessitating prompt induction of labour to prevent adverse fetal outcomes.

2. Case Presentation

A 35-year-old pregnant woman, gravida 2, parity 1, with a low-risk pregnancy presented at 38 + 1 weeks of gestation to the hospital's pregnancy assessment unit with a few days of worsening generalised pruritus, primarily on her back and abdomen. Her symptoms were worse at night, interrupting her sleep. She reported normal foetal movements and had no abdominal pain or vaginal bleeding.

On examination, there was no visible rash, and her abdomen was soft and non-tender. Her cardiotocography was reassuring. Initial blood tests showed mildly deranged liver function tests, with an AST of 69 and ALT of 43 and a bile acid level of 3 μmol/L. She was trialled on calamine lotion and oral anti-histamines.

She re-presented the next day later with significantly worsening symptoms, especially on her palms and soles. Although the bile acid result had been normal the day before, the assessing doctor repeated testing, given her persistent and worsening symptoms. The level was now 62 μmol/L, >20 times the result of the previous day. This result, in conjunction with her symptoms, was diagnostic of moderate-severity

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OC. The decision was made to offer an induction of labour given the dramatic change in her bile acid level and her stage of gestation. She presented to the delivery suite for an induction of labour and gave birth to a healthy girl with no complications via a normal vaginal delivery. Apgar scores at one minute and five minutes were 9 and 9. Birth weight was 3430 g (68th centile). The mother's symptoms resolved and her post-natal recovery was unremarkable.

3. Discussion

OC typically presents in the second or third trimester of pregnancy, though there have been reports of onset in the first trimester [1,2,10]. The main presenting symptom is pruritus, classically affecting the palms and soles of the feet, but can be generalised or occur anywhere. [1,7]. The pruritus worsens as the disease progresses, and may be worse at night, causing insomnia, as seen in this case [1,2]. There are no rashes or dermatological features at disease onset, though secondary skin changes ranging from excoriations to prurigo nodules can develop as a result of scratching [7,9]. Jaundice may also occur, usually manifesting 1–4 weeks after pruritus, but rarely can precede it [2]. Some women may also have pale stools, dark urine, and steatorrhea. The latter theoretically can lead to vitamin K deficiency and, subsequently, prolonged prothrombin time and an increased risk of post-partum haemorrhage, but reports are rare [2,3]. Pruritus was the only clinical symptom in the patient described here, and was initially on her back and abdomen, not her palms and soles, which is a reminder that presentations are not always classical.

There is no international consensus on the diagnostic criteria for OC. The local guidelines at this case's hospital allow a diagnosis to be made when unexplained pruritus occurs in pregnancy, with normal-appearing skin, and a peak random total bile acid concentration of >10 μmol/L, whereas the latest guidelines from the Royal College of Obstetricians and Gynaecologists (RCOG) uses a higher cut-off, of ≥19 μmol/L [11,12]. Regardless, according to both guidelines, the patient's status rapidly changed from not meeting diagnostic criteria to moderate-severity OC the next day. Whilst liver function levels above the normal pregnancy-specific range have historically also been accepted as an alternative biochemical diagnostic criterion, emerging evidence now suggests that only total bile acid levels are correlated with stillbirth risk [12]. As pruritus often precedes biochemical changes, in women with normal bile acids, repeat blood tests in 1–2 weeks is recommended [7,12]. This case, however, demonstrates a rapid change in bile acid levels in <36 h, suggesting that where clinical suspicion is high, or where diagnosis would have urgent delivery implications (in this case, the patient was induced promptly after), earlier repeat blood tests should be considered.

The risk factors for OC are both genetic and environmental [3]. OC has a recurrence risk of 45–90%, and risk is higher amongst women with a family history [1,2,13]. Certain ethnicities are also predisposed to OC, including women of Scandinavian, South American, and South Asian descent [1,3–6]. Risk is also increased with multiple gestations, IVF, positive hepatitis C serology, and advanced maternal age [1,3,6,7]. Environmental factors include low vitamin D or selenium levels, and OC may also be more common in winter [2,7]. In this case, the patient had no obvious risk factors for OC, nor did she have it in her first pregnancy. Should she have any future pregnancies, however, monitoring for the development of OC would be required.

No pharmacological treatments have been proven to improve foetal outcomes [12]. Symptomatic treatments include topical emollients and oral anti-histamines are often routinely offered to try to alleviate pruritus; however, effectiveness tends to be limited [12]. Ursodeoxycholic acid, which is routinely used as a treatment for gallstones and certain liver conditions such as primary biliary cirrhosis, is also sometimes prescribed for OC. It is in itself a secondary bile acid, and is thought to increase bile flow, change bile composition, and have hepatoprotective effects [14]. However, it is important to note that studies have found that ursodeoxycholic acid does not reduce the risk of adverse foetal outcomes, and is thus not routinely recommended [12,13]. As the only cure for OC is delivery of the infant, the focus of definitive management is the timing of birth. Induction of labour, should spontaneous labour not begin prior, is guided by bile acid levels [12]. The local guidelines at this hospital recommend induction of labour at 39 weeks if bile acid levels are <40 μmol/L, and 37 weeks if >40 μmol/L, possibly earlier, depending on severity. Accordingly, having moderate OC, the patient in this case was immediately contacted and presented to hospital that night for an induction of labour at 38 weeks and 2 days of gestation. Women with OC are instructed to follow up with their general practitioner for repeat liver function tests and bile acid levels at their routine 6-week post-natal check.

4. Conclusion

Obstetric cholestasis is still a poorly understood complication of pregnancy that requires careful monitoring given the risk of adverse fetal outcomes. As symptoms of pruritus often precede a rise in bile acid levels required for the diagnosis of OC, clinician vigilance is required to avoid missed or late diagnoses. This reported case, where the bile acids rose rapidly, from 3 to 62 μmol/L in under 36 h, suggests that closer monitoring and earlier repetition of blood tests should be considered in women with a high clinical suspicion, or where a diagnosis would have significant implications for delivery. A missed diagnosis could have led to significant complications, including stillbirth.

Contributors

Jennifer J. Yang contributed to patient care and obtaining consent for the case report, acquiring and interpreting the data, undertaking a literature review, drafting of the manuscript, and revising it critically for important intellectual content.

Mikhail Sarofim contributed to patient care, conception of the case report, interpreting the data, drafting of the manuscript, and revising it critically for important intellectual content.

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Patient consent

Prior consent has been obtained from the patient for their inclusion in this case report.

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Conflict of interest statement

The authors declare that they have no conflict of interest regarding the publication of this case report.

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