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Raised first-trimester cholestasis unmasking the diagnosis of autoimmune hepatitis in a pregnant mother with recurrent pregnancy loss: A Rare Case Report with positive outcome

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Abstract

First-trimester cholestasis of pregnancy must be aggressively evaluated, as it may indicate an underlying liver disorder as rare as autoimmune hepatitis. Autoimmune hepatitis (AIH) is a rare chronic liver disorder that disproportionately affects women of childbearing age. Pregnancy in patients with AIH poses unique clinical challenges, especially when coexisting with intrahepatic Cholestasis of Pregnancy (ICP), another hepatobiliary disorder associated with significant fetal risk. AIH in pregnancy has historically been linked to increased rates of maternal hepatic flares, fetal growth restriction, and preterm labour, whereas ICP is associated with adverse perinatal outcomes, including stillbirth. We report a case of a 30-year-old multiparous woman with a history of chronic uveitis and adverse pregnancy outcomes who presented with jaundice at 13 weeks of gestation. Workup revealed positive autoimmune markers, and a liver biopsy confirmed chronic hepatitis. Despite immunosuppressive therapy and close surveillance, preterm labour ensued at 28+5 weeks, necessitating emergency Lower Segment Caesarean Section (LSCS). The postpartum course was favorable, with normalization of liver function. This report underscores the importance of early diagnosis, interdisciplinary management, and vigilant fetomaternal monitoring in optimizing outcomes.

Keywords: Pregnancy, adverse perinatal outcome, early-onset, intrahepatic cholestasis of pregnancy, lateonset.

Introduction

Intrahepatic Cholestasis of Pregnancy (ICP) typically presents in the second or third trimester, but rare cases of early onset have been documented, including as early as 13 weeks of gestation [1]. These cases often feature intense pruritus and markedly elevated bile acids, sometimes exceeding 100 µmol/L, which are associated with increased risks of meconium passage, preterm birth, and stillbirth. Early onset ICP may reflect underlying genetic or hepatic predispositions and requires vigilant monitoring and timely intervention to optimize maternal and fetal outcomes [2]. Autoimmune Hepatitis (AIH) is an immune-mediated inflammatory liver disease that predominantly affects women. The female-to-male ratio is 4:1, and it impacts all age groups, with bimodal peaks during adolescence and perimenopause [3-5]. Although the course of the disease can vary from incidental abnormalities in liver biochemistry to fulminant liver failure, it usually has phases of remission and relapse. AIH may be diagnosed de novo during pregnancy or may exacerbate during gestation or in the postpartum period. Disease flare-ups are particularly concerning due to the potential for hepatic decompensation and associated obstetric complications such as miscarriage, preterm birth, and fetal growth restriction [6]. AIH usually has an insidious course with elevated transaminases, but severe acute hepatitis is seen in 25% and acute liver failure in 6% of cases [6]. AIH is a diagnosis of exclusion; therefore, it is essential to exclude other causes of chronic liver diseases, such as Wilson's disease, hemochromatosis or alpha-1 antitrypsin deficiency, or other inflammatory hepatitis, such as alcoholic or nonalcoholic steatohepatitis, and viral infections [7-9].

Intrahepatic cholestasis of pregnancy (ICP) is a liver disorder in the late second and early third trimester of pregnancy. It is also known as Obstetric Cholestasis (OC) and is characterized by pruritus with increased serum bile acids and other liver function tests.

ICP incidence rate is between 0.2 to 2% of pregnancies. The pathophysiology of ICP is still not completely understood. The symptoms and biochemical abnormalities rapidly resolve after delivery. ICP is associated with an increased risk of adverse obstetrical outcomes, which include stillbirth, respiratory distress syndrome, meconium passage, and fetal asphyxiation [10]

This case report explores the rare and challenging scenario of overlapping AIH and ICP during pregnancy. The successful management of such cases requires a high index of suspicion, early diagnosis, and a multidisciplinary care plan involving obstetricians, hepatologists, and neonatologists.

Case summary

A 30-year-old woman, Gravida 5, Para 3, with a history of poor obstetric outcomes, presented at 13 weeks of gestation with clinical jaundice and was referred to AIIMS Hospital, Raipur, for further evaluation. Her obstetric history included two successive pregnancy loss; one preterm vaginal delivery resulting in neonatal death within one week, and one first-trimester spontaneous abortion. The patient also had a known history of chronic bilateral granulomatous anterior uveitis, with a history of intermittent blurring of vision over the past three years, likely because of an underlying autoimmune condition.

On admission, the patient was afebrile and hemodynamically stable, with mild pallor and icterus. Obstetric examination was unremarkable. Initial laboratory evaluation showed elevated total bilirubin (2.45 mg/dL), direct bilirubin (1.44 mg/dL), AST 122 U/L, ALT 96 U/L, alkaline phosphatase 570 U/L, serum bile acids 200 mmol/L, INR 1.61, and haemoglobin 9.1 g/dL. Considering the above blood reports and Bad obstetrics history, initial management included inj. Vitamin K 10 mg intramuscular for 3 days, tab. Aspirin 150 mg per oral once at night, progesterone soft gelatin capsules 200 mg per vaginal HS, and anemia corrective measures started.

In view of the elevated liver enzymes and bile acids in early pregnancy with a history of jaundice in previous pregnancies, a gastro-medicine consultation was obtained. A comprehensive workup was initiated to rule out viral hepatitis, intrahepatic cholestasis of pregnancy, and autoimmune liver disease. Viral serologies (HAV, HBV, HCV, and HEV) were negative. Autoimmune screening revealed strong positivity for antinuclear antibodies (ANA) and antimitochondrial antibodies (AMA), weak positivity for anti-smooth muscle antibody (ASMA), and elevated total serum IgG. Repeat serum bile acid level was 167 mmol/L. These findings raised a strong suspicion of autoimmune hepatitis (AIH).

Ultrasonography showed hepatosplenomegaly (liver span: 21.2 cm; spleen: 12.3 cm). An ultrasound-guided percutaneous liver biopsy demonstrated chronic interface hepatitis with dense lymphocytic infiltrate, confirming the diagnosis of AIH.

A multidisciplinary management plan was implemented. The patient was initiated on oral prednisolone 40 mg daily (tapered gradually), azathioprine 25 mg daily, and ursodeoxycholic acid (UDCA) 300 mg three times a day. Low molecular weight heparin (enoxaparin 40 mg subcutaneous once daily) was started for thromboprophylaxis. Ophthalmology consultation revealed active anterior uveitis with complicated cataracts in both eyes. Management included topical atropine thrice daily and prednisolone acetate 1% eye drops with a tapering schedule. Elective cataract surgery was deferred to the postpartum period. In the first 2 weeks of Prednisolone and azathioprine treatment, her liver parameters initially decreased slightly, but after that plateaued and then started increasing (graph 1st, 2nd), hence a

dose of tab. Azathioprine increased to 50 mg od (initially 25 mg od) and also serum bile acid level persistently high (more than 100 mmol/lt), graph 3rd, hence the dose of Udilive increases to 1050 mg/day (initially 900 mg/day). After 1 week of dose modification of liver parameters, mainly SGOT, SGPT, decreased significantly, but the bilirubin level slightly decreased. The patient underwent strict fetomaternal surveillance throughout the antenatal period. Liver function tests, coagulation profiles, and serum bile acids were monitored twice weekly. Initially, liver enzymes showed a partial decline but then plateaued; dose escalation of azathioprine and UDCA led to further biochemical improvement. Fetal echocardiography at 22 weeks showed an echogenic intracardiac focus in the left ventricle. Quadruple marker screening was low risk. At 25 weeks, she was diagnosed with gestational diabetes mellitus, which was managed with diet alone. A growth scan at 28+1 weeks revealed a live fetus in cephalic presentation with an estimated fetal weight of 1041 grams, an amniotic fluid index of 7.8 cm, and normal Doppler indices. The anterior placenta showed increased vascularity and myometrial thinning, raising suspicion for placenta accreta spectrum (PAS). MRI was scheduled for further evaluation.

At 28+5 weeks, at midnight, the patient went into spontaneous preterm labour. Tocolytics, including oral nifedipine and intravenous magnesium sulphate, were administered, but labour progressed. In view of her obstetric history and suspected Placenta Accreta Spectrum (PAS), an emergency lower segment caesarean section was performed. A live female neonate weighing 1005 grams was delivered and admitted to the neonatal intensive care unit for prematurity care. The intraoperative and immediate postoperative periods were uneventful.

In the early postpartum period, serum bile acid levels declined significantly from 156 to 39 mmol/L, while AST, ALT, and bilirubin levels showed a transient rise. A repeat gastromedicine consultation advised continuation of prednisolone (20 mg/day), azathioprine (50 mg/day), and UDCA (300 mg TID). Over the next three weeks, liver parameters progressively normalized. At discharge, the patient was stable on maintenance doses of prednisolone (10 mg daily), azathioprine (50 mg daily), and UDCA (300 mg twice daily). Ophthalmic therapy was continued as per the tapering protocol. She was advised to attend regular follow-up in gastroenterology, obstetrics, and ophthalmology clinics. Elective cataract surgery was planned in the postpartum period. The neonate remained in the NICU for prematurityrelated care. This case underscores the importance of timely diagnosis and coordinated multidisciplinary care in managing autoimmune hepatitis with cholestasis (overlap syndrome) during pregnancy, contributing to a favourable maternal and neonatal outcome despite complex comorbidities and obstetric risks.

Discussion

Intrahepatic Cholestasis of Pregnancy (ICP) during pregnancy is a rare but high-risk condition that requires meticulous multidisciplinary management. Likewise, AIH in pregnancy has been associated with high rates of maternal morbidity and adverse fetal outcomes. In a large cohort study by Stokkeland *et al.*, women with AIH demonstrated increased risks of preterm birth and low birth weight ^[5]. However, improved maternal and fetal outcomes have been reported in recent literature, largely due to advances in early diagnosis and individualized immunosuppression regimens ^[6, 8]. In the present case, the patient was presented with early trimester ICP, which was later diagnosed as AIH was supported by strong seropositivity for

ANA and AMA, weak ASMA, hypergammaglobulinemia, and confirmed histologically by interface hepatitis, aligning with the simplified diagnostic criteria outlined by the International Autoimmune Hepatitis Group (IAIHG) and validated by Hennes *et al.* ^[11].

Although liver biopsy is often deferred in pregnancy due to potential risks, it was safely performed in this case under image guidance and provided definitive histopathological confirmation, as previously documented in select antenatal AIH cases [14]. The co-presentation of markedly elevated serum bile acids, pruritus, and cholestatic biochemistry was indicative of IHCP, further supported by the patient's history of similar symptoms in previous pregnancies. Similar overlapping presentations have been rarely reported, like Efe, *et al.* describing cases where AIH was complicated by cholestatic features resembling IHCP, particularly during flare-ups [15].

Williamson *et al.* [10] have highlighted the obstetric risks associated with ICP, including fetal arrhythmias, preterm labor, and stillbirth, especially at serum bile acid levels > 100 µmol/L. In this case, persistent elevation of bile acids (> 100 mmol/L) despite initial UDCA therapy necessitated an increase in dosage to 1050 mg/day, resulting in gradual improvement a finding aligned with the dose-response benefit observed in studies by Glantz *et al.* and Geenes *et al.* [12-13]. Azathioprine and

corticosteroids remain the mainstay of immunosuppressive therapy in AIH and have been deemed safe in pregnancy by multiple reviews ^[7-9]. In our patient, prednisolone and azathioprine were administered with careful dose titration based on biochemical response. The need to escalate azathioprine from 25 mg to 50 mg due to plateauing liver enzymes and persistent cholestasis was consistent with previous literature, Gleeson D *et al.*, emphasizing the need for dynamic dose adjustment to control disease activity ^[16].

Comparatively, Heneghan *et al.* ^[3] have reported that outcomes in AIH pregnancies can mirror those of healthy pregnancies when disease remission is maintained and multidisciplinary care is implemented. Similarly, Chung and Heneghan ^[6] emphasized the significance of early immunosuppressive therapy and proactive fetal monitoring. Also, Martin *et al.* stressed the need for intensive surveillance and preparedness for preterm intervention in AIH pregnancies ^[17]. This case aligns with these findings, demonstrating successful maternal and neonatal outcomes despite overlapping hepatological disorders.

The present case adds to the growing body of evidence that AIH, even when complicated by ICP, can be effectively managed with tailored therapy and vigilant monitoring, thus improving maternal and fetal prognosis.

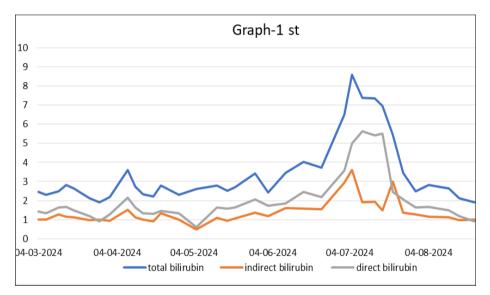


Fig 1: This graph shows the relationship between different types of bilirubin levels (mg/dl) and the treatment course

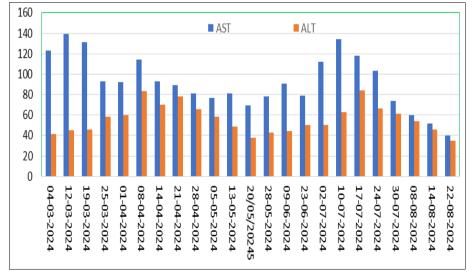


Fig 2: This bar diagram shows the relationship between serum transaminase levels (U/L) and the treatment course

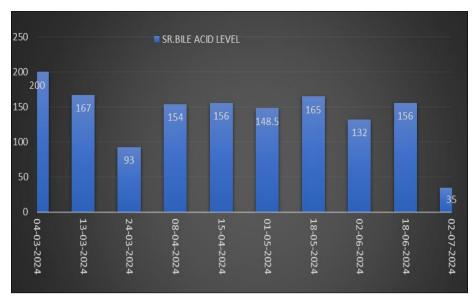


Fig 3: This graph shows the relationship between serum bile acid levels (mg/dl) and the treatment course

Conclusion

This case highlights the importance of considering autoimmune hepatitis in pregnant patients presenting with unexplained jaundice and transaminitis, especially in the presence of autoimmune comorbidities or a history of pregnancy losses. Autoimmune hepatitis pregnancy can achieve good outcomes with multidisciplinary input and the proactive management by obstetricians and hepatologists, assessment of liver disease for individualized risk stratification, and maintaining Biochemical Response with appropriate immunosuppression are all key requirements to ensure better outcomes.

Conflict of Interest

Not available

Financial Support

Not available

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