No abstract provided,
The patient denied alcohol, acetaminophen or any other toxin use. Extensive laboratory evaluation including viral hepatitis testing (A, B, C, E, Epstein-Barr virus, cytomegalovirus, herpes simplex virus) and autoimmune serologies (ANA, anti-smooth muscle antibody, F-actin antibody IgG, serum immunoglobulin levels, anticyclics, beta-2 glycoprotein, SS-A antibody, SS-B antibody, Jo-1 antibody) were negative. Serum ceruloplasmin and alpha-1-antitrypsin were normal. Total bile acids later returned at 462 μmol/L supporting a diagnosis of severe ICP. Liver biopsy was pursued given the patient’s atypical presentation. Histopathology showed mild to moderately severe non-specific lobular hepatitis without evidence of chronic liver disease (Figures 1, 2).

**FIGURE 1:** Liver biopsy with canalicular cholestasis (at arrow), H&E, 1000x

**FIGURE 2:** Liver biopsy with mononuclear inflammation and intact bile duct, H&E, 400x
The patient was treated for ICP with ursodeoxycholic acid (UDCA) at 600 mg twice daily with gradual improvement in her pruritus and normalization of liver function tests late in her second trimester. Total bile acid level was monitored periodically and also progressively improved until the time of delivery.

After close obstetrical and biochemical surveillance of the maternal and fetal conditions, the patient was induced at 34 weeks 6 days gestation. Dexamethasone was administered to accelerate fetal lung maturation. The patient delivered a healthy female infant weighing 5 pounds 15 ounces via uncomplicated vaginal delivery. Both patient and baby followed a routine post-partum course with full resolution of symptoms and liver biochemical abnormalities.

**Discussion**

ICP is the most common pregnancy-associated liver disease, with a variable incidence worldwide between 0.2% and 25% [15]. The pathophysiology of ICP is incompletely understood. Family clustering and varying incidence in different geographic regions suggest an underlying genetic predisposition. Moreover, genetic defects in at least six canalicular transporters have been identified as associated with ICP [6]. Our patient did not have any obvious risk factors for ICP, and genetic testing was not pursued given that this was her first presentation with ICP.

A diagnosis of ICP should be considered in pregnant patients with intense pruritus of the extremities, concentrated primarily on the hands and soles, in the absence of rash. As the disease progresses, secondary skin changes can range from excoration to prurigo nodules [16]. Serum bile acid level exceeding 10 μmol/L is the gold standard for diagnosis. Higher bile acid levels (>40 μmol/L) are associated with increased rates of spontaneous preterm delivery and asphyxia events [1,4,5]. Biochemical abnormalities are variable and mostly resolve completely after delivery. Serum aminotransferases are usually less than two times the upper limit of normal but may reach values greater than 1000 IU/L. Bilirubin is increased only in exceptional cases [6].

ICP rarely occurs during the first trimester. Our patient first developed pruritus at five weeks gestation and is the earliest reported case of ICP from a spontaneous pregnancy [8]. The onset of ICP in the second and third trimesters is hypothesized to be related to the peak estrogen levels that occur during the later stages of pregnancy [7,8]. Patients who present in the first trimester potentially could have other factors causing elevated estrogen. Our patient did not have any of the defined risk factors for hyperestrogenemia. Of the previous reported cases of first trimester severe ICP, four out of 10 patients underwent ovarian stimulation for in vitro fertilization (IVF) and one patient had a twin pregnancy [8,15]. In women undergoing IVF, additional follicle-stimulating hormone induces an estrogen surge to stimulate ovarian stimulation and one patient underwent genetic testing which showed homozygous MDR3, and homozygous BSEP mutation, both of which were previously identified in the ICP cohort [10].

On review of 10 cases with first trimester severe ICP, gestational age ranged from five to 11 weeks and maternal age ranged from 21 to 32 years [8-14]. Regarding outcomes, there were no cases of maternal death. There were five patients who had term deliveries, two patients who had preterm delivery, one patient underwent pregnancy termination at 11 weeks due to persistent elevated liver enzymes despite UDCA treatment, one patient who had a blighted ovum, and one patient who developed a spontaneous miscarriage.

Management of ICP is focused on close obstetrical, clinical and biochemical surveillance. Treatment with UDCA improves both transport and secretion of bile acids, minimizing fetal exposure. UDCA is effective in reducing pruritus and improving liver biochemical abnormalities in patients with ICP. It also lowers the rate of prematurity and decreases the need for neonatal intensive care unit admission [18]. Moreover, UDCA is safe and well-tolerated [19]. Earlier delivery is indicated in patients with intractable pruritus, persistence of hepatic dysfunction and past history of bad neonatal outcome due to ICP. The ideal gestational age for elective induction of labor to minimize the risk of perinatal mortality is unknown, but a large cohort study has suggested that delivery at 36 weeks gestation may be optimal [20].

**Conclusions**

In conclusion, we present an unusual case of severe, early onset ICP at five weeks gestation prior to obstetric confirmation of pregnancy. ICP remains an enigmatic disease with variable clinical presentations and potentially serious fetal outcomes. Other types of liver disease should always be excluded and treatment with UDCA results in resolution of the symptoms and elevated liver enzymes in the majority of cases. In any female patient of childbearing age presenting with generalized pruritus, a diagnosis of ICP should always be considered regardless of known pregnancy status or the trimester of pregnancy.

**Additional Information**

**Disclosures**
Human subjects: Consent was obtained by all participants in this study. N/A issued approval N/A. Informed consent was obtained verbally from the patient for case publication. The consent was obtained during the patient encounter. However, with multiple attempts, we could not contact the patient to later obtain the signed informed consent. There is no patient’s identifying information included in the article. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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