

# Pruritus during Pregnancy

**Chan Kok Seong, Vijayan Valayatham**

Sabah Women & Children Hospital, Obstetrics & Gynecology, PO Box 187, Kota Kinabalu, Sabah 88996, Malaysia

### CASE REPORT

A 26 year old primigravida with an established diagnosis of systemic lupus erythematosus (SLE) attended the combined obstetric-medical clinic at 9 weeks period of gestation (POG). Her platelet counts were normal. An antiphospholipid screen was negative. She did not have anti-Ro and anti-La antibodies. She was on the following medications when she conceived: azathioprine (AZA) 100mg OD, hydroxychloroquine 300mg OD, prednisolone 10mg OD and calcium lactate 600mg BD. She had conceived while in remission as had been advised to her during pre-pregnancy consultation.

An ultrasound scan confirmed a singleton pregnancy and the dates. She had normal full blood count (FBC), renal and liver functions tests (RFT and LFT). She was seen monthly in the joint obstetric-medical clinic. She showed no symptoms or signs of a relapse. A detailed ultrasound scan at 20 weeks POG confirmed a structurally normal male fetus.

Her progress in pregnancy was uneventful up until she was 30 weeks period of gestation (POG). She presented with intense generalized pruritus. She denied history of fever or rash and did not have gastrointestinal symptoms. Her pruritus involved her palms and soles of her feet. She also described how it also affected her ear lobes. Her sleep was significantly affected. She was not jaundiced. Her abdomen was soft and non tender. There was no hepatosplenomegaly. Her blood pressure was 110/58. A bedside urinalysis for protein and red cells was negative. She had excoriation marks on her abdomen and limbs. There was no skin rash otherwise.

Her LFT was abnormal: ALT 138 U/L AST 122 U/L Bilirubin 9 U/L. The FBC and RFT were normal. Infective (Hepatitis A, B and C) and autoimmune hepatitis screens were negative. An ultrasound scan of the hepatobiliary system was unremarkable.

A presumptive diagnosis of AZA induced hepatopathy was entertained. AZA was withdrawn. She was prescribed chlorpheniramine for her pruritus. Her symptoms however did not resolve despite an interval of 2 weeks off AZA. AZA was not recommenced due the persistently deranged LFT.

At 32 weeks gestation a working diagnosis of obstetric cholestasis was made. She was commenced on ursodeoxycholic acid (UDCA) at 250mg bd. A blood sample for bile acids was requested. Her pruritus significantly

resolved within one week of commencement of UDCA. She was able to sleep well for the first time since the onset of pruritus. The transaminase levels declined but did not normalize and remained between 50-75 IU/L. The fetus was followed up with weekly Doppler USS of the umbilical artery (UA) and cardiotocograms (CTG). Oral vitamin K was commenced at 10mg per day from 36 weeks POG. She was followed as such up until 37 weeks POG when labour was induced. The bile acid level was 32µmol/L and retrospectively confirmed the diagnosis of obstetric cholestasis (OC).

Labour was successfully induced. Abnormal cardiotocogram was recorded at 4 cm of cervical dilatation and an emergency caesarean section was performed. A healthy baby boy weighing 2.9kg was delivered. The liquor was clear. The estimated blood loss was 200mls.

Her postpartum recovery was uneventful. The UDCA was withdrawn as delivery is the definitive treatment. Her symptoms completely resolved by the 1st postpartum week. The liver transaminases normalized by the 2nd postnatal week. AZA was recommenced with no adverse effect. She breastfed her baby for 9 months. A copper intrauterine contraceptive device was inserted by her primary care team at her 2nd menstrual cycle.

### DISCUSSION

Obstetric cholestasis is a multifactorial pregnancy specific condition characterized by pruritus and increased fetal morbidity and mortality. It is associated with mildly increased serum liver enzymes. It is thought that oestrogen causes stasis of flow of bile and this causes a regurgitation of bile acids into the maternal circulation and ultimately into the fetoplacental unit. The symptoms and altered liver enzyme level resolve after delivery. OC is associated with increased risk of prematurity, fetal distress, meconium amniotic fluid staining, and intrauterine fetal demise. There are no proven theories how OC causes fetal morbidity and demise. Amniotic fluid bile acid is thought to cause vasospasm in umbilical vessels in animal models.

The geographical variation of the prevalence of OC is marked. It ranges from 0.2% in France to 4% in Chile<sup>1</sup>. The prevalence in Malaysia is unknown. In a study in London in 2002 it was observed that the prevalence of OC was higher among Asian (of Indian sub-continent origin) women<sup>2</sup>.

The index of suspicion needs to be raised for OC to be

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*Corresponding Author: Vijayan Valayatham, Sabah Women & Children Hospital, Obstetrics & Gynecology, PO Box 187, Kota Kinabalu, Sabah 88996, Malaysia Email: vj1vela@gmail.com*

considered. This is because pruritus is not an uncommon feature of a normal pregnancy. Prurigo of pregnancy affects up to 80% of pregnancy and occurs without a rash. Prurigo usually begins in the 3rd trimester and affects the trunks more than the limbs. Obstetric cholestasis, also without a rash, usually begins in the 3rd trimester, as is with most pregnancy specific conditions. It usually involves limbs and trunks and especially the palms and soles distinguishing it from its benign counterpart. Insomnia is not unusual. Occasionally there can be dark coloured urine with steatorrhoea. In this case, drug induced hepatitis was considered as there were likely candidates, the most likely being AZA.

The discriminatory features of OC lie in its intensity and distribution of pruritus with a propensity towards palm and sole. The LFT is deranged in all women with OC by the 4th week of onset of pruritus<sup>3</sup>. The transaminases are usually raised 2-3 times baseline. At the onset of pruritus the bile acids are more likely to be raised than the transaminases<sup>4</sup>. In a small number of women only the bile acids are raised. Pruritus precedes deranged LFT by 3 weeks<sup>3</sup>. It may be prudent to have a LFT repeated 2-4 weeks after onset of pruritus if the first was normal. Bile acid analysis is not available in Malaysia at the time of writing. Elevated bile acids (BA) are not pathognomonic of OC. It should be performed on a fasted sample interpreted within pregnancy specific ranges. A normal bile acid does not exclude OC. The BA was ordered in this case to entertain the diagnosis of OC against the background of drug-induced hepatitis.

OC is a diagnosis of exclusion. Other more common causes of deranged LFT must be excluded. This includes pre-eclampsia, acute fatty liver, infective and auto-immune hepatitis and choledocholithiasis. Some authorities recommend screening for primary biliary cirrhosis and Wilson's disease. These should be considered in prevalent populations.

As opposed to the benign prurigo of pregnancy OC carries high fetal morbidity and mortality risks. It is associated with prematurity (17%<sup>3</sup>), meconium staining of liquor and fetal distress. The perinatal mortality rate for OC is 10-15%<sup>4</sup>. The impact to the fetus is significant. Delivery is the definitive treatment. Routine fetal monitoring with fetal biometry,

umbilical artery Doppler surveillance and cardiotocographs have not reduced the impact of OC on the fetus. Early delivery reduces the perinatal mortality from OC to 2-3%<sup>5</sup>. Fetal outcomes do not correlate with symptoms and liver enzyme levels<sup>5</sup>. Robust evidence for early delivery is absent. The evidence that current modalities of fetal monitoring in OC do not prevent stillbirths is established. Most OC stillbirths occur beyond 37 weeks gestation. It would be seem prudent to plan delivery at 37 weeks gestation. There are no known long term maternal morbidity with OC. The combined oral contraceptives are contraindicated given the aetiology of OC.

There is an increase risk of postpartum hemorrhage (PPH) in OC. The depletion of BA dependant fat soluble vitamin K reduces synthesis of vitamin K dependant coagulation factors. This risk has not been observed in randomized controlled trials. The physiologic argument thus demands that vitamin K supplementation in the last month of pregnancy remains standard management.

More research is required to assess the prevalence of OC in Malaysia given its significant impact on fetal morbidity and mortality. Observations are needed if our pregnancies with preterm births, meconium stained liquor and perinatal deaths have a touch pruritus beneath. For a start all pregnant women who have had intrauterine deaths should be enquired for pruritus in any of their past pregnancies. Primary care antenatal workers should also begin to develop an urge to ask for the itch.

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