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Abstract:

Letter to the Editors – brief communications:

**Antiphospholipid syndrome during pregnancy:
associated with early onset of HELLP syndrome and liver
infarctions**

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Dear editors,

The antiphospholipid syndrome (APS) is an acquired thrombophilic disorder, best known among obstetricians for arterial and venous thrombosis, repeated miscarriages and intra-uterine fetal death. APS is, however, associated with other less known life-threatening conditions, important for obstetricians. In this report APS led to a life-threatening HELLP syndrome with several pitfalls.

A 27-year-old nulliparous woman was referred to the University Hospital at a gestational age of 21 weeks with severe epigastric pain and vomiting. An abdominal ultrasound performed earlier at the peripheral hospital had been documented as normal. History taking revealed a deep venous thrombosis at the age of 26, treated by an oral anticoagulans. Since the begin of pregnancy, enoxaparin, a low molecular weight heparin, had been given (80 mg/day). At the time of arrival the abdominal pain was severe and suggestive of lithiasis. Ultrasound and x-ray of the abdomen was normal. Various analgesics were administered consecutively, but without effect. Blood results at 4-hourly intervals showed biochemical signs of a HELLP syndrome: decreasing platelets (106 000, 4 hours later 90 000, and 8 hours later 92 000/microliter), increasing transaminases (AST: 204, 4 hours later 233, and 8 hours later 249 U/l; normal range < 31 U/l and ALT: 375, 4 hours later 415, and 8 hours later 417 U/l; normal range < 31 U/l) and an elevated LDH of 792 U/l (normal range: 231-462 U/l). On the other hand, the blood pressure was within normal range. There was no significant proteinuria and the serum uric acid was not elevated. After 24 hours the pain decreased and the patient felt better. A repeat ultrasound of the abdomen was performed, revealing no deviations. During the 2nd day of admission the pain increased again, this time in the right lumbar region. The blood pressure rose concomitantly from 140-130/90-75 mmHg to 153/94 mmHg. Paracetamol and diclofenac had to be given in regular intervals, upon which the pain improved. A third pain episode occurred at 3rd day. Transaminases reached maximal levels: (AST = 370 and ALT = 1034 U/l) and the C-reactive protein increased to 16.8 mg/dl and 19.4 mg/dl at day 4.

Further imaging by nuclear magnetic resonance showed a liver infarction (Fig 1, left side). The patient was transferred to the intensive care unit and the antithrombotic therapy was expanded to 80 mg enoxaparin twice daily. Deep venous thrombosis was excluded by duplex ultrasound. Her

history of a deep venous thrombosis remained puzzling, but the patient was unable to provide the necessary information. Four days after admission, we had contact with her former general practitioner, who had been on a leave.

Two years ago, a deep venous thrombosis in the left calf had been the trigger for antiphospholipid testing. Lupus anticoagulans and anticardiolipin antibodies were found to be positive, the antinuclear factor was marginally positive, and the APTT was increased. Because of the APS, treatment with fenprocoumon was initiated for an indefinite period. A retesting in 6 months had been advised, in order to exclude the development of a systemic lupus erythematosus. Pregnancy was not considered contraindicated, if a strict follow-up could be provided. The patient became pregnant and fenprocoumon was switched to enoxaparin.

At day 4 of admission she was in a stable condition and could be transferred from the intensive care to the maternity ward. Thrombocytes were 88 000/microliter, and increased steadily. Progressively, the transaminases normalised. At day 7, she reported severe pain again in the right epigastric region, related to breathing. The liver enzymes AST and ALT had increased to 247 and 508 U/l, respectively. Abdominal ultrasound of the liver did not reveal any abnormalities, but computer tomography showed a new infarction (Fig 1 right side). Methylprednisolone 80 mg daily was added to the therapeutical schedule. The patient's condition was alarming and intensive care had to be provided. Because of the extent of necrotizing hepatic tissue and liver damage, there was no other choice but to terminate the pregnancy at 22 weeks of gestation. Because of the maternal condition and the unfavorable cervix a caesarean section was performed. A non-viable, male foetus of 350 g was born. AST and ALT declined thereafter and postoperative care was uneventful.

In this case, a patient with initially unknown APS presented as early as 21 weeks of gestation with the clinical picture of HELLP syndrome. This very early onset is in agreement with the literature, where a HELLP syndrome in association with APS has been described at 16 weeks of pregnancy [1]. Another pitfall was the acute pain in the right epigastric region, which is a classical sign of a HELLP syndrome. But its unbearable character led to further investigations: whereas ultrasound examinations were not conclusive, nuclear magnetic resonance was able to identify the

liver infarctions. Noone [2] et al recently described MRI as the most accurate investigation for the diagnosis of hepatic disease. Liver infarctions in pregnant patients with APS have been described [3], but are not specific for APS. They may also occur in combination with pre-eclampsia [4] or HELLP syndrome [5]. Despite high doses of low molecular weight heparin, the patient developed a second event. This time computer tomography showed new lesions at the periphery of the liver. It is noteworthy, that ultrasound of the liver could not demonstrate any changes, although the examiner was aware of the first liver infarction.

In summary, APS led to a life-threatening course of a HELLP syndrome at an early stage in gestation with repeated liver infarctions, diagnosed by nuclear magnetic resonance and computer tomography, but not by ultrasound.

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Fig 1

On the left side: MR T2-weighted image shows the lesion of the hepatic infarction as a wedged-shaped area of high signal intensity.

On the right side: CT scan of the liver demonstrating multiple peripheral wedged-shaped areas of low attenuation with hepatic infarction sharply distinct from the surrounding liver parenchyma.

Fig 1