A CASE OF ACUTE FATTY LIVER OF PREGNANCY

UKRIST PLENGVANIT, NIVAT CHANTARAKUL and VARINTR LEKPRASRET

Departments of Medicine, Pathology, Obstetric and Gynecology, Faculty of Medicine and Siriraj Hospital, Mahidol University, Bangkok, Thailand.

Jaundice in pregnancy is a diagnostic problem and may represent a serious prognostic sign, the incidence being 1 : 1500 gestations, or 0.067% (Haemerli, 1966). One of the rare forms, associated with pregnancy, is acute fatty liver of pregnancy. It is also known as acute yellow atrophy (Svanborg, 1959) or obstetric acute yellow atrophy (Sheehan 1940). It occurs in the last trimester of pregnancy, the onset is sudden, the course very acute with profound jaundice, bile in the urine, delirium, coma and death. Up to the present (from 1934 to 1965) at least 44 cases with this syndrome have been described (Kühn *et al*, 1967). Eight others are known to have been studied but not reported (Kühn *et al*, 1967). The purpose of this paper is to report a case of acute fatty liver of pregnancy, with an enlarged liver weighing 3,850 gm.

A 41-year-old Thai woman, secundipara, with full term pregnancy was admitted to the obstetrical ward of the Siriraj Hospital, Mahidol University on June 20, 1967. The clinical picture presented was that of a full term pregnant woman with anasarca. She gave a history of edema of the ankles 4 months prior to admission but proteinuria was not detected and blood pressure was in the normal range. Otherwise her antenatal course was uneventful. A week before hospitalization, edema increased rapidly.

On physical examination the blood pressure was 130/80 mm. Hg. and a trace of albumin was found in the urine. Serum potassium was 2.9 m Eq/L and BUN of 38 mg. per cent. She was treated with hydrochlorothaiazide and supplementary potassium. On the fifth day of admission, jaundice and dark coloured urine were noticed. Blood chemistry on the following day revealed BUN 58.3 mg. per cent, total bilirubin 12.5 mg. per cent, normality in seroflocculation tests, SGOT and SGPT were 112 and 68 units respectively. On the seventh day during labour, uterine inertia developed, an attempt to use vacuum extraction was unsuccessful, therefore, Cesarean section was performed. Anaesthetics used were nitrous oxide and ether. During the operation the blood pressure dropped to 70/40 and persisted. The foetus was still born and weighed 4,100 gm. After the operation the patient developed anuria and jaundice deepened. She lapsed into coma on the second post-operative day. The laboratory findings were BUN 76.6 mg. per cent, direct bilirubin of 9.0 and total bilirubin of 15.5 mg. per cent. Blood ammonia was 1.276 microgram, almost three times the normal value. There was also hyperkalemia (K 6.9 m Eq/L). Despite giving dexamethasone 40 mg. per day and infusion mixture of glutamate and arginine, the patient expired on the 3rd post-operative day; that was, the tenth day of hospitalisation.

Necropsy findings:

Necropsy was performed 20 hours after death. The postmortem findings showed a deeply jaundiced body with anasarca. There was no fluid in the pleural and peritoneal cavities. The heart was normal in shape, size and position. Both lungs were congested with small areas of atelectasis of both lower lobes. The liver was markedly enlarged,

about one-hand's breadth below the right costal margin, weighing 3,850 gm, with a distended smooth surface rubbery in consistency and greenish yellow in colour. Gross sections of the liver showed bile-stained cut surfaces. The spleen was normal in shape and size. The gastric mucosa showed multiple small erosions with no evidence of haemorrhage. The pancreas, gall-bladder, small and large intestines showed no abnormality. Both kidneys weighed 160 gm. The capsule was easily removed and the capsular surface was smooth and pale yellow in colour. The kidneys showed cloudy swelling and mild fatty degeneration of the distal convoluted tubules. The ureters and urinary bladder were normal. The uterus was enlarged, the fundus was about the level of the umbilicus, the cesarian section wound was intact. There was slight cervical erosion.

Microscopic examination of the liver, stained with Hematoxylin and Eosin, showed apparently normal lobular pattern. The sinusoids were indistinct due to the distension of the liver cells. The individual liver cell contained clear vacuoles of varying sizes in the cytoplasm. These vacuoles were more prominent at the central and midzonal areas than at the periphery of the liver lobules. The nuclei of the liver cells were centrally situated. No necrosis of the liver cells were present (Fig. 1). Section stained with Scarlet red proved that the clear vacuoles were lipids in nature (Fig. 2).

The portal area showed small amount of lymphocytic infiltration. There were no bile pigments within the bile duct and the ductules. There were several fine granular brownish yellow pigments and in some parts stained bright green for bile pigments (Stein's bile pigment stain), but showed no reaction for hemosiderin pigment (Prussian blue reaction). The rest of pigmented granules failed to demonstrate ceroid by Ziehl-Nielsen acid fast stain, so they probably were lipochrome pigments.

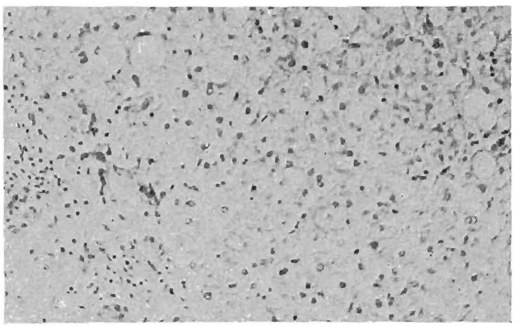

Fig. 1—Liver cells with clear vacuoles in the cytoplasm.

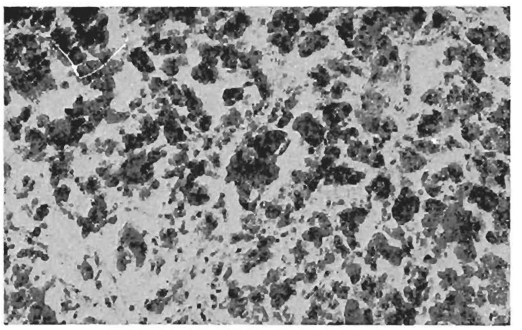

Fig. 2—Section of liver cells stained with scarlet red.

DISCUSSION

Sheehan (1940) was the first scientist who reported this syndrome and termed it "Obstetric acute yellow atrophy of the liver" but the term "acute fatty liver of pregnancy" is now widely used. It occurs in the last trimester of pregnancy (Lewis *et al*, 1961). The onset of the illness is abrupt with non-specific symptoms, headache, nausea and vomiting, abdominal and back pain, hematemesis and later jaundice and coma. Laboratory findings are also not diagnostic. Death is the usual outcome, but survivals have been reported (Duma *et al*, 1965., Woolf *et al*, 1964).

In our case there were no symptoms as mentioned above except for the edema and proteinuria which led one of us to make the provisional diagnosis as toxemia of pregnancy. The jaundice developed so rapidly that one day after detection of icteric sclera and dark urine, total serum bilirubin was 12.5 mg. per cent. Acute viral hepatitis could be differentiated only because of the slight hypertransaminasemia in the early course. The only evidence when she developed hepatic coma was blood ammonia of 1,276 microgram.

The necropsy findings of acute fatty liver of pregnancy both gross and microscopic was distinctive. According to Sheehan's personal observation in 14 cases, the livers weighed between 900 to 1350 gms, that is, the liver usually weighs less than normal (1400 gms). However, there were also reports stating that the weight of the liver increased. The maximum weight ever recorded was reported by Kahil *et al*, (1964), the liver weighing 2950 gms. whereas in this case, it was 3850 gms, which could be due to the marked distension of the parenchymal cells. The histological picture in our case was typical, the cytoplasm was distended by numerous small fat vacuoles in the centrolobular and midzonal areas. Sections of the liver failed to demonstrate ceroid pigment by special stains but it was found by the others (Kühn *et al*, 1967)

The etiology of acute fatty liver of pregnancy is unknown. It has been related to protein malnutrition, when there may be an element of dietary deficiency due to diversion of protein to the foetus. (Duma, *et al*, 1965) and to the depression of protein synthesis caused by certain substances such as tetracyclines (Kunelis *et al*, 1965). The liver in pregnancy increases demand for protein anabolism and may be more sensitive to such agents than the nonpregnant women. Kahil *et al*, (1964) have observed a similar histologic picture in the liver of a young boy who died of an acute febrile illness of unknown etiology. Rye, Morgan and Bural described a fatal disease of young children, known as "Encephalopathy and fatty degeneration of the viscera", in which the liver lesion was closely similar to that found in acute fatty liver of pregnancy. This syndrome is endemic in the north eastern part of Thailand and widely known as "Udorn Encephalopathy". Bourgeois (1969) and associates who reported Udorn Encephalopathy postulates the etiology in favour of a fungal toxin. Acute fatty liver of pregnancy may have the same cause owing to the rapid, unrelenting clinical course which is consistent with a lethal dose of some toxin.

REFERENCES

BOURGEOIS, C.H., KESCHAMRAS, N., COMER, S.D., HARIKUL, S., EVANS, H., OLSON, L., SMITH, T. and BECK, M.R., (1969). Udorn Encephalopathy, fatal cerebral edema and fatty degeneration of viscera in Thai Children, *J. Med. Ass. Thailand*, 52:553.

DUMA, R.J., DARLING, E.A., ALEXANDER, H.C., SIBRANS, D. and DEMPSEY, H., (1965). Acute fatty liver of pregnancy, report of surviving patient studied with serial liver biopsy. *Ann. Intern. Med.*, 63:851.

HAEMERLI U.P., (1966). Jaundice during pregnancy with special emphasis on recurrent jaundice during pregnancy and its differential diagnosis. *Acta med. Scand.*, 175 (suppl.):444.

KAHIL, M.E., FRED H.L., BROWN, H. and DAVIS, J.S., (1964). Acute Fatty Liver of Pregnancy, report of a case. *Arch. Int. Med.*, 113:63.

KÜHN, F.A., WEGENER, F., HAHN, J., (1967). Acute Fettleber in der Schwangerschaft mit Tödlichem Ausgang. *Acta-Hapatosplenologica*, 14:65.

KUNELIS, C.T., PETER, J.L., EDMONDSON, H.A., (1965). Fatty liver of pregnancy and its relationship to tetracycline therapy. *Amer. J. Med.*, 38:359.

LEWIS, P.L., TAKEDA, M. and WARREN W., (1961). Obstetric acute yellow atrophy, report of a case. *Obstet. Gynec.*, 81:427.

MOORE, H.C., (1965). Acute fatty liver of pregnancy. *J. Obstet. Gynaec. Brit. Comm.*, 63:189.

SHEEHAN, H.L., (1940). The pathology of acute yellow atrophy and delayed chloroform poisoning. *Obstet. Gynaec. Brit. Empire*, 47:49.

STANDE, H.J. and CADDEN, J.F., (1934). Acute yellow atrophy in pregnancy. *Am. J. Obstet. Gynec.*, 28:61.

SVANBORG, A. and OHLSSON, S., (1959). Recurrent jaundice of pregnancy, a clinical study of twenty-two cases. *Amer. J. Med.*, 27:40.

WOOLF, A.J., JOHNSTONS, A.W. and ROBERTSON, N.R.C., (1964). Acute liver failure in pregnancy: case report with survival of mother and child. *J. Obstet. Gynaec. Brit. Comm.*, 71:914.