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From Unit "B," Kandang Kerbau Hospital for Women.
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Two Cases of Jaundice in Late Pregnancy

Case Reports

Presented by Doctor E. K. Koh.

CASE No. 1: Gravida VI, aet 42, Patient was admitted in coma IV. A live female infant weighing 6 lbs. 8 ounces had been delivered at home 24 hours before. The relatives discovered that she was unable to answer questions 13 hours after delivery. Further questioning the relatives revealed that the patient had diarrhoea and jaundice for one week. There was no history of convulsions.

On Examination: The patient was in Coma IV, Temp—99.4°F, BP.110/70. Urine — Albumin free. Lungs/Heart — N.A.D. Abdomen — Liver not palpable, liver dullness absent. Uterus palpable to the level of mid-way between symphysis and umbilicus.

Laboratory Investigations:

1. Bile in urine: + + +
2. Bilirubin in serum: 1 min 6.5 mgm%
   30 min 19.5 mgm%
3. Alkaline Phosphatase: 33.5 King-Armstrong Units.
4. Thymol Turbidity: 5 units.
5. Blood urea: 20 mgm%.

Progress Notes: Coma treatment was instituted. Intravenous Sodium Glutamate. Vitamin B and Calcium Gluconate were given. In spite of treatment, the patient died on the 4th day with pulmonary oedema and renal failure.

Post-mortem examination revealed a small liver weighing 1½ lbs. shrunken and pale with peritoneal adhesions The kidney cortex was swollen.

Cause of Death: Acute Liver Necrosis.

CASE No. 2 was also a 6th gravida, aged 39 years. She was admitted in labour.

On Examination: She was conscious but without jaundice. Temp=99.4°F. BP—200/120. Urine Albumin +. Oedema of legs +. She appeared drowsy and slightly irrational. The uterus was about 38 weeks pregnant on palpation.

Pelvic examination revealed a fully dilated cervix. A live foetus 6 lbs. 4 ounces was delivered by forceps.

Lab. Investigations:

1. Prothrombin time: 30 seconds.
2. Clotting time : 6 minutes.
3. Blood urea : 52 mgm.

Post-partum: After delivery the patient became more drowsy and went into Coma II three hours after delivery. Coma treatment was instituted but 12 hours after delivery, marked jaundice was noticed in the patient. The condition gradually deteriorated and the patient died 36 hours later.

Post-mortem examination revealed a large liver 5 lbs. in weight, showing massive haemorrhagic areas of yellow necrosis. The pituitary and the supra-renal glands showed definite haemorrhage.

Cause of Death: Acute liver necrosis with supra-renal and pituitary haemorrhage.

Discussion

Doctor Sinha opened the discussion with a brief summary of the aetiology, signs and symptomatology of toxaemia of pregnancy.

He classified the signs and symptoms into three groups:

Group I: Generalised. e.g. oedema, hypertension and albuminuria.

Group II: Localised:

(a) Cerebal—headache.

(b) Visual—from blurred vision to total blindness.

(c) Gastric—nausea and vomiting.

(d) Hepatic—jaundice.

(e) Renal—oliguria, haematuria. anuria.

Group III:

(a) Haemorrhagic tendencies.

(b) Coma and convulsions (eclampsia.)

Most of the symptoms in Group II, he said, were associated with severe pre-eclamptic toxaemia requiring immediate attention, and were usually preceded by a rise of blood pressure. It was the rise in blood-pressure that was the significant pointer rather than the actual degree of hypertension and this rise could occur suddenly and steeply.

Becker in 1925 showed that toxaemia was likely to develop when there was increased resistance in the blood-vessels of the pregnant uterus, and McClure Browne and Veall in 1953 showed by means of radio active isotopes that the maternal blood flow was appreciably reduced in the placenta in cases of toxaemia. This reduction varied from 30 to 50%. Morris in 1955 demonstrated a similar reduction in blood flow in the pregnant uterus.

These several observations formed the basis of the *"Utero-Placental Ischaemic Theory"* of toxaemia. A further significant observation was also made by Parviainen et alia in 1951 e.g. the increased tone in the uterus of toxaemic patients

Pari passu with these vaso-motor disturbances continued Doctor Sinha, there were also concomitant physio-chemical changes in the maternal blood, which today are known to be the cause of haemorrhages in severe toxaemia of pregnancy and eclampsia. These changes were generally the result of liver damage and resultant aberration in the blood coagulating mechanism. They were manifested in alterations in:

(1) Prothrombin time.

(2) Coagulation time.

(3) Bleeding time.

(4) Hypo-fibrinogenaemia.

Much work had been done on the subject of hypo-fibrinogenaemia recently and broadly speaking two views were held:

(a) Presence of fibrinolysin, postulated by Weiner in 1950.

(b) Presence of a toxic principle resembling or identical with Thromboplastin (Schneider, 1950) allegedly originating from placental or decidual tissues. This thromboplastin like substance enters the maternal circulation converting prothrombin into thrombin, which in turn converts fibrinogen into fibrin which comes to be deposited in the large vascular spaces. This phenomenon may occur in cases of severe abruptio placentae.

The role of fibrinolysin was however a debatable point. Schneider maintained that the dissolution of the clot which he believed to result from the presence of fibrinolysin was explainable by the existence of low fibrinogen levels. When the fibrinogen level dropped to lower than 50 mgm% initial clotting could not occur as these low levels were conducive to fragmentation.

He summarised by saying it could be accepted that haemorrhages in toxaemia of pregnancy were the result of defects in the clotting mechanism, the fundamental disturbance being a reduction in the circulating fibrinogen to levels favouring spontaneous haemorrhages. The fibrinogen depletion resulted from extensive intravascular coagulation initiated by presence in the systemic circulation of a thromboplastin like substance derived from the placenta. That such material does enter the maternal circulation in cases of abruptio placentae and eclampsia was demonstrated by Page et alia (1953) by experiments with radio-active Iodine. These substances were found to be concentrated mainly in the liver and spleen.

Referring back to the two cases under discussion, he reiterated that both had exhibited jaundice and evidences of liver damage. Jaundice, he said, was always to be considered as a sign of grave prognostic import. David Miller (J.O.G. Brit. Emp. 61:405, 1951) described 17 cases of jaundice occurring in 9,782 deliveries, i.e., an incidence of 1 in 576 deliveries, with three maternal deaths. Before a diagnosis of jaundice due to liver damage in pregnancy

could be made, it was mandatory to exclude other possible causes of jaundice (e.g.)

1. Infective Hepatitis.
2. Leptospirosis.
3. Incompatible Blood-Transfusion.

He enumerated the possible sites of *haemorrhages in eclampsia as follows:*

1 Liver.
2. Kidney.
3. Brain.
4. Myocardium.
5. Mucous surfaces.
6. Skin.
7. Retina.

Doctor Sinha then called upon Professor Sheares to speak on the etiology and pathology of liver nercrosis in pregnancy.

Professor Sheares said that jaundice due to liver damage almost never occurred in pregnancy, except in the last trimester. Haemolytic and obstructive jaundice had to be ruled out in the differential diagnosis. The jaundice in pregnancy due to liver damage was one of the varieties of parenchymatous (hepato-cellular) jaundice. The symptoms, signs and laboratory studies indicated acute liver failure and clinically the condition was not distinguishable from fulminating epidemic hepatitis. Some cases of this type of jaundice used to be loosely diagnosed as "Acute Yellow Atrophy," but often they were not confirmed by necropsy, and the less fulminant types recovered, with or without residual fibrosis of the liver. Diagnosis could only be confirmed antemortem by liver biopsy.

He summarised the histological liver findings by saying that the predominant picture was diffuse fatty metamorphosis with preservation of lobular architecture. The peripheral portion of the liver lobule was spared or showed only minimal necrosis. There was absence of infiltration by inflammatory cells or this invasion may be very sparse. These lesions could not be classified as infectious hepatitis on purely histopathologic criteria. They resembled more the effects of an exotoxin or endotoxin and were similar to those described by Sheehan as "Obstetric Acute Yellow Atrophy" (J. Obst. & Gynaec. Brit. Emp. 47:49. 1940). Fatty changes in the liver could be produced experimentally by exotoxins or by dietary deficiencies in certain essentials, but in none of the cases occurring in pregnancy was there evidence produced in the history of dietary deficiency or the ingestion of an exotoxin. Hence the nature of the syndrome was still obscure.

Passing on to the essentials in treatment of the case once diagnosis had been confirmed by liver biopsy, he said they were: Fat-free diet, high protein diet, parenteral fluids, vitamins as indicated, administration of choline and methionine (though the therapeutic value of these aminoacids was still subjudice. The administration of parenteral protein hydrolysates was optional. Termination of pregnancy was indicated if the patient did not respond promptly to treatment, as this was in the best interests of mother and child. In any case the foetal mortality rate was high.

In conclusion he said that there were still some blind spots in our understanding of this disease. It was a moot point as to whether the condition was simply an acute infectious hepatitis in a very severe form. It had been shown that the usual mortality rate of epidemic infectious hepatitis was 5%, but the rate was 20-30% in the last trimester because of the decreased margin of hepatic reserve. He reminded that in eclampsia, hepatic lesions were common.