ACUTE FATTY LIVER OF PREGNANCY

Description of a case of survival

A. PACHÌ (*), P. PASQUALETTI (**),
F. CAPPA (*), G. NATALI (**)

(*) Department of Obstetrics and Gynecology
(**) Chair of Medical Pathology
and Clinical Methodology
University of L'Aquila (Italy)

SUMMARY

The Authors describe a case of acute fatty metamorphosis of the liver in pregnancy in a patient who survived and delivered a living female child. Clinical and istopathologic features, possible etiologic factors and possible treatment for the mother and fetus are discussed. The Authors, finally, think that acute fatty liver of pregnancy is more frequent than expected and that it should be considered in all cases of jaundice in pregnancy.

An important, even if rare, cause of jaundice during pregnancy is fatty liver of pregnancy, also known as fatty metamorphosis of the liver or acute yellow atrophy of pregnancy ([2, 3, 10, 14, 27]).

This form represents only a very small percentage of the cases of jaundice, viral hepatitis and recurrent cholestasis in pregnancy being much more frequent ([10, 17, 19, 29]). This condition, which has a characteristic clinical and anatomopathological pattern, was first described by Stander and Cohen ([33]) in 1934 and up to 1980 some 100 cases had been reported in literature ([8, 15, 18, 35]). It affects prevalently primigravid women, particularly between the 32nd and 38th week pregnancy ([18, 27, 31]), and it is associated with a high death rate both in the fetus (in almost all cases) ([2]) and in the mother (in 75-85% of cases) ([2, 10, 35]). The main features of the clinical pattern are progressively severe jaundice, epigastric pain, vomiting, diarrhea, nausea, severe headache, tachycardia, lethargy, progressive liver and kidney insufficiency ([10, 18, 27, 31]). Liver biopsy and/or the histological pattern reveal a pattern characterized by mild necrosis, and fibrosis, preservation of the lobular structure, droplet changes located in perinuclear areas, without displacement of the nucleus, normal cells in portal areas indicating the acute process ([6, 10, 15, 18, 22, 27, 31]).

The present report deals with a patient with acute fatty liver of pregnancy who survived and gave birth to a living female child.

CASE REPORT

D'U. O., 32 years old, at the 32nd week of her second pregnancy (1 0 0 1) with continuous fever, cough with mild expectoration, pain in the pharinx, uncontrollable vomiting, nausea, headache, subjaundice of the sclera. These symptoms had been present for two weeks and showed no improvements following antibiotic treatment.

Table 1. — *Results of liver function tests during the 5 months hospitalization.*

	week 32 of pregnancy	delivery	10 days after delivery	1 month after delivery	2 months after delivery	3 months after delivery	5 months after delivery
SGOT (IU)	214	221	290	145	107	97	20
SGPT (IU)	95	129	130	99	107	63	32
GGT (IU)	36	36	150	190	285	25	21
Alk. Phosph. (IU)	240	980	800	820	870	162	170
Serum bilirubin D (g/l)	2.5	3.5	2.4	1.9	0.7	0.2	0.1
I (g/l)	5.9	9.0	5.6	4.7	1.7	1.1	0.8
QT	1.0	1.1	1.2	1.1	1.1	1.1	1.0
Blood ammonia (γ %)	114	162	185	132	122	114	88
Serum cholesterol (mg %)	250	200	300	600	300	275	180
Serum triglycerides (mg %)	600	720	1050	1100	580	580	150

Family history and previous history revealed nothing of importance; furthermore the patient reported never having taken oral contraceptives and/or tetracycline. In 1969, following an episode of acute articular rheumatism, the patient had undergone tonsillectomy, but no medical treatment.

Examination upon hospitalization (S. Salvatore Hospital of L'Aquila, clinical chart No. 116083 - 1071/82) revealed jaundice color of the skin and eyes; rhythmic cardiac action, but tachycardic (110/min), presence of systolic murmur of medium intensity on the centrum cordis; slight obtusity of the mid right lung and respiratory silence and, despite the large size of the uterus, marked hepatomegaly with a roundish lower border, of parenchymatous consistency, painful upon deep palpation and mild splenomegaly. Arterial blood pressure was 120/70 mmHg and remained virtually unchanged during hospitalization.

Data concerning liver function tests are shown in table 1. Kidney function tests showed no modification and coagulation parameters also remained unchanged. It is worthwhile to point out that fibrinogen and fibrin degradation products were always within normal limits despite the presence of slight platelet deficiency. The hormonal pattern upon admission was within normal limits for the time of pregnancy. Due to persistent fever both before and after delivery, blood and urine cultures were repeatedly carried out: results were negative. The patient was also submitted to various investigations including ultrasonographic study of the liver and biliary tract which only revealed marked hepatosplenomegaly; chest X-ray, which demonstrated the presence of a thin atelectasic shadow in the right median pulmunary field; obstetric ultrasounds, performed two days before delivery showed the placenta localized anteriorly to the uterine wall, of advanced grade I maturity, a decreased amount of amniotic fluid, the presence of a single fetus with rhythmic activity, but slightly reduced movements, which however, increased following external mechanical stimulation; the brain structure appeared normal, the femur measured 5 cm in length and the biparietal diameter 7.8 cm.

Jaundice and liver impairment became progressively more severe (table 1), with marked deterioration of the general conditions, decrease in 24-h urine volume, and mental confusion. It was, therefore, decided, 10 days after admission, to induce delivery by means of oxitocyn (10 IU i.v.) infusion. A female child, 1380 g, Apgar index 8/10, was born by vaginal delivery, and immediately transferred to the neonatal intensive care unit.

During the next few days, the general conditions of the mother slowly but progressively improved, with liver function tests returning to normal limits two months later (table 1). Lipids and bile acids levels continued to increase. Two months after delivery, liver needle (Menghini) biopsy revealed: medium and large droplet steatosis, involving about 70% of the hepatocytes, the presence of focal necrosis, with fibrillar reticulum in part collapsed, presence, in several hepatocytes, of biliary pigment granules, portal areas with no significant modifications (table 1; figs. 1, 2, 3).

Five months after delivery the clinical picture and laboratory findings had returned to normal, with complete regression of hepatosplenomegaly and control liver biopsy showing medium droplet steatosis in 20% of the hepatocytes and disappearance of the focal necrosis areas (table 1; figs. 4, 5, 6).

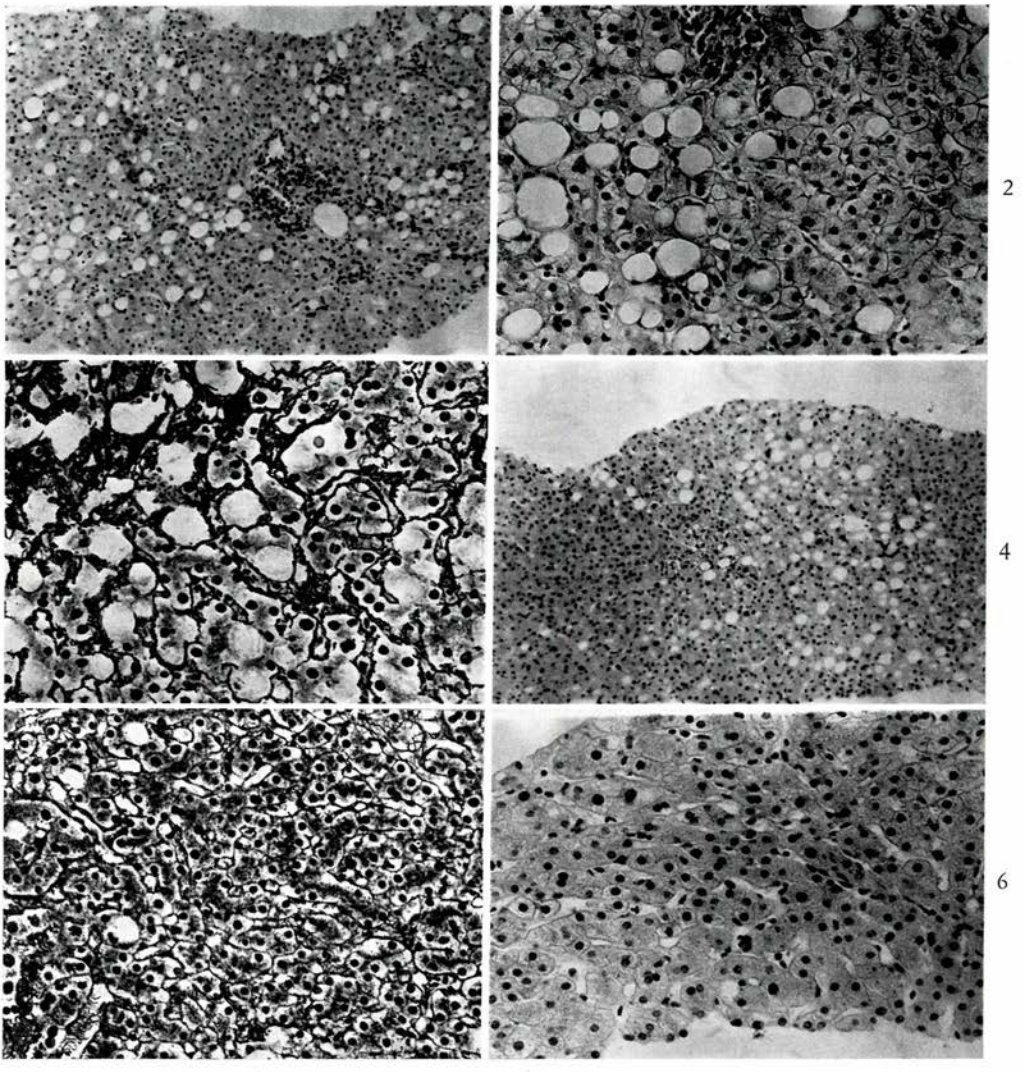

Fig. 1. — Liver biopsy: areas of focal necrosis associated with small and medium droplet steatosis (× 20). Fig. 2. — Liver biopsy: detail of fig. 1 (× 250). Fig. 3. — Liver biopsy: collapse of reticular fibres (× 250). Fig. 4. — Liver biopsy at follow-up examination: mild fatty liver, absence of focal necrosis (× 20). Fig. 5. — Liver biopsy at follow-up examination: detail of fig. 4 (× 80). Fig. 6. — Liver biopsy at follow-up examination: normal reticular (× 200).

DISCUSSION

The clinical picture and laboratory findings in acute fatty liver of pregnancy suggest liver failure in absence of hepatocyte necrosis. The typical features are rapresented by rise in hepatocyte enzymes, progressive rise in serum bilirubin of the mixed type, hypoprothrombinemia, hypoglycemia and high blood ammonia values.

Furthermore, most patients present an initial renal failure. Prerenal factors are usually considered responsible even if lipid deposits have been observed in renal tubular cells. Phenomena of lipid clotting, modifications in Central Nervous System (CNS), possibly of ischemic origin, and other clinical signs may also be observed.

On account of these different associated conditions it has been hypothesized that even if the liver is the most severely impaired organ in this disease, this could be the result of a systemic involvement. This hypothesis would not exclude, on the other hand, the generally accepted opinion [3,9,18] that the primary liver failure may be complicated by other pathological conditions, such as disseminated intravascular coagulation (DIC) which would in fact be the cause of the disease. DIC would explain the intestinal bleeding, the fibrin deposits in the renal glomerulus [3, 9] and the high levels of fibrin degradation products [13].

The clinical sign at onset may vary considerably, with, in some cases as the above mentioned, a simple infection of the upper airways preceding a more definite clinical picture [4] and would account for fever, which is not usually present in these patients [3, 9]; an isolated increase in blood uric acid has also been reported as the first clinical sign [24].

It has also been suggested that acute fatty liver of pregnancy is related to the use of tetracycline treatment during pregnancy [16, 22, 30]. Nevertheless, despite the demonstration of a correlation with this type of antibiotic, other factors shoud be considered since this syndrome had already been described prior to the introduction of antibiotics and also in patients who had never received this type of drugs. The similarity with fatty acid metamorphosis due to tetracycline and with Reye's syndrome [6, 23] suggested different clinical pictures classified under a single term, and of which pregnancy represented a risk factor [16]. In Reye's syndrome, a lack of ornithintranscarbamylases [32] leads to acute fatty metamorphosis of the liver due to the accumulation of triglycerides [12], which, as in the present case, are also increased in the circulation. If this similarity were true, patients with acute fatty liver of pregnancy should respond favourably to parenteral treatment with ornithin and citrullin [2].

As far as concerns pathogenesis of this disease, a drop in the hepatic secretion of lipoproteins and the toxic effect of free fatty acids have been hypothesized [7].

Nowadays acute fatty liver of pregnancy is considered as the response to various unfavourable conditions, whether nutritional, metabolic, toxic, viral or genetic, the effects of which are enhanced by pregnancy [18].

There is no specific treatment: survival of the fetus depends upon rapid induction of delivery or upon surgical delivery [11], even if there is no evidence to show that delivery modifies the prognosis of the mother [18]; heparin treatment is required in cases of DIC [25].

Death of the mother, which usually occurs within few days after delivery [10], or at the most, within two weeks [15], is due to non-hepatic causes [8], including massive gastrointestinal bleeding [15], acute respiratory distress [34], pancreatitis [36], renal failure [3, 8, 9, 15, 20], blood clot [34]. These are due to DIC, platelet deficiency, with ultrastructural and biochemical modifications of the thrombocytes [26], and possibly to the release into circulation of intestinal polypeptides with a systemic toxic effect [21, 37].

This syndrome would not appear to be recurrent ([1, 8]). However, this supposition is based on the observation that three patients who survived had a normal second pregnancy, with delivery at term ([1, 8]).

In conclusion, it appeared worthwhile to report the case that came to our observation because of the rarity of the association of acute fatty liver and pregnancy in absence of known pathogenetic factors, and for favourable course, which contrasts with data from literature. Moreover, we think it is worthwhile to point out, that a rapid diagnosis of the disease and a careful choice of the delivery time may represent favourable prognostic elements for both mother and child and that the absence of renal failure may lead to a more favourable prognosis.

Finally, this rare clinical picture should be considered in all cases of jaundice in pregnancy since it is probably more frequent than expected ([2, 10, 18]).

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