Cirrhosis and pregnancy

A case report and review of the literature

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Summary: A clinical case of a pregnant suffering from hepatic cirrhosis with ascites, splenomegaly and portal hypertension is described. The pregnancy carried on till the 31st week, even though with the repeated use of tocholytic agents. Cesarean section was performed because of the onset of serious jaundice and the decline of general maternal conditions. The infant, who had an Apgar score of 8 at the 1st and 5th minute, died on the 10th day because of acuse haemorrhagic interstitial pneumonitis in premature lungs and hepatopathy associated with widespread jaundice. The mother was discharged on the 25th day of the postpartum period, in light of the nett improvement of her general metabolic condition, the sudden regression of the jaundice and the decrease of the cholestasis indices.

A review of the literature discussing maternal complications, fetal risks, management of pregnancy and delivery and outcome of the newborn are presented.

Key words: Liver cirrhosis; Pregnancy; Neonatal outcome.

INTRODUCTION

Pregnancy in a patient suffering from hepatic cirrhosis is a rare event, since an hepatic illness of that kind is more frequent at an older age than in the reproductive age ([1-5]). The incidence rate of pregnancies in patients affected by cirrhosis, especially not compensated, or in case of post-hepatic cirrhosis in the active phase, is an even less frequent event ([1]). The incidence rate of viral hepatitis in women is increasing, thus resulting in a decrease in the mean age of incidence of cirrhosis. Moreover, the wide and varied range of hepatotoxic agents which are more and more numerous and of widespread use, justifies the increased incidence rate of liver cirrhosis. Otherwise, the long-term results of the immuno-modulating treatment with interferons, in case of chronic active hepatitis, have so much increased the life expectancy of hepatopathic patients that this illness is no longer considered a counterindication of pregnancy ([1, 3]). Nor can we ignore the nett increase, in the female sex, of alcohol dependency, which is a well-known predisposing factor for cirrhosis ([1, 6, 7]).

Hepatic cirrhosis produces such metabolic and hormonal alterations that in

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most cases is itself the cause of amenorrhea and infertility ([1, 3, 4]). Because of the hepatic damage, sexual steroids are not metabolized and this determines ovulation impairment and reduction of the fertility rate ([1, 5]). However, the coexistence of pregnancy and cirrhosis is possible, the interference and the relations between them are variedly described in literature. We must particularly consider on the one hand, the alterations pregnancy may produce on hepatic disease and on the other hand, how hepatic disease influences the outcome of pregnancy and fetus condition.

CASE REPORT

A patient aged 42, para 0, gravida 1, suffering from posthepatic cirrhosis with ascitis, splenomegaly and cholestasis, was being followed for pregnancy at the Department of Obstetrics and Gynaecology, of the Hospital "Ospedali Riuniti" of Foggia, University of Bari. The diagnosis of hepatic illness was made in 1988 following the onset of dyspeptic symptoms such as pyrosis, bloated abdomen especially post-prandially, occasional vomiting and right hypochondriac pain. A needle biopsy of the liver showed micronodular cirrhosis. The liver disease was well-compensated from a clinical and hematological point of view, so there was no need for any kind of therapeutic aid apart from a hypercaloric diet and total abstension from alcohol. In December 1990 the patient became pregnant. During the 12th week of amenorrhea the patient was admitted to the Obstetrics Department with diagnosis of threatened abortion. On this occasion the blood tests were normal. During the 16th week of amenorrhea the hepatic function tests started to alter: the necrosis indices were abnormal, while the excretion parameters were normal.

In the meantime the patient grew increasingly asthenic. The fetus was regularly checked by ultrasound serial scans and the biometry was normal for the gestational age. The placenta and the amniotic fluid were also normal. The serological search for viral B hepatitis antigens and antibodies proved negative, apart from the positivity of humoral antibodies (IgG) anti-HBc. The pregnancy progressed uneventfully, and the liver function tests remained unvaried until the 31st week of amenorrhea when the patient was admitted to hospital with an admission diagnosis of "jaundice in the third thrimester of pregnancy in a hepatopathic patient". The patient had progressively worsening jaundice, marked alteration of the hepatic necrosis factors, intrahepatic cholestasis and alterations of the excretional hepatic function (Table 1). The biometry was normal and the estimated weight of the fetus (according to the Shepard formula) was approximately 1,500 gr.

Considering the poor general condition of the patient, caesarean section was performed under epidural anesthesia. This approach was preferred to general anesthesia so as not to charge the metabolic functions of the liver. During the laparotomy the liver appeared on inspection tendentially gray, with a speckled surface and the gallbladder seemed alithiasic. A female infant was born with a birth weight of 1,470 gr, 42 cm of length and with an Apgar index of 8 at the 1st and 5th minute. The baby was transferred to the Neonatal Intensive Care Unit. The instrumental exams after birth were not particularly informative: a chest X-ray on the 10th day revealed a uniform radiolucent appearance except for the ilar and the parailar regions where vascular and ilar structures produced an increased density, at cerebral ultrasound scan the choroid plexus appeared enlarged and more echogenic than normal on both sides. The blood sampling of the same day revealed marked cholestasis (serum total bilirubin level 22.4 mg% serum direct bilirubin level 7.1 mg/dl, alkaline phosphatase (AP) 242 IU/l, γGT 96 IU/l). Cultural searches in the blood and feces were negative despite a persitent fever. Haemogasanalysis showed marked acidosis and the infant died on the 16th day of life because of a bilateral acute pneumonitis and acute hepatitis. Necroscopic examination revealed diffused jaundice, cerebral edema and kidney tubular necrosis. Microscopically the autopsy showed the presence of a haemorrhagic interstitial pneumonitis, with intranuclear inclusions, probably of viral etiology and hepatitis with bridging necrosis. Research during histological examination for core of B virus hepatitis was negative. The mother remained in the obstetric department till the 4th day post-partum when she was transferred to the gastroenterologic division of the same hospital, on the advice of the gastroenterologist. Hematologic functional tests and ultrasound examination of the liver confirmed the cholostatic nature of the clinical picture. Serum antinuclear antimitochondrial auto-antibodies proved positive, while HbsAg remained negative. Due to a worsening of the pruritis, becoming more and more frequent and intense, the patients was treated with cholestyramine, which after a short time was substituted by corticosteroids because of poor tolerability. The general clinical conditions markedly improved after twenty days – the jaundice almost completely disappeared and the liver serological parameters normalized. Table 1

Table 1. — *Serological parameters before delivery, the day of delivery (*) and during puerperium.*

Parameters (normal values)	Sample date					
	5/7	10/7*	11/7	15/7	19/7	25/7
AST (10-42 U/l)	50	105	63	57	57	—
ALT (10-60 U/l)	32	65	73	48	48	—
Alkaline phosphatase (26-88 U/l)	374	251	711	233	233	—
Total Bilirubin (<0.35 mg%)	9.8	7.5	10.3	6.9	6.9	6.1
Direct Bilirubin (0.2-1.0 mg/dl)	7.2	6.5	4.2	2.9	2.9	2.9
Serum Total Proteins (6.0-8.0 g/dl)	8.1	7.6	6.3	—	—	—
PT (10-12-sec.)	12	12	10	11	11	—
PTT (27-39 sec.)	37	40	36	—	—	—
Cholinesterase (2150-4950 U/l)	1330	861	—	878	870	1344

comprehensively shows the serological parameters before delivery, the day of delivery and during the puerperium. Even the asthenia improved with the aid of fat-soluble vitamins, branched aminoacids and a hypercaloric diet. When, on the 25th day, the patient learned of her child's death, she left the hospital of her own accord and continued the therapy at home. The last hepatic ultrasound scan before the discharge revealed an ultrasonic dishomogeneous pattern with disseminated hyperechoic areas of fibrosis without dilatation of the intrahepatic biliary ducts. Two months after the delivery both the obstetrical and clinical conditions were fairly good. At a four-year control the patient is well compensated.

DISCUSSION

Liver cirrhosis may influence pregnancy being dangerous both for the mother and the fetus ([3, 8]). Although numerous case reports on this association are available in the literature (Table 2), there are only a few original series dealing with pregnancy in cirrhotic patients ([3, 4, 5, 8]). The aim of this study was to describe, on the one hand, the risk of pregnancy and the eventual decompensation of hepatic illness for the mother and, on the other hand, to evaluate fetal outcome. Moreover, pertinent data have been collected about the outcome of pregnancy in patients with liver cirrhosis considering the mode of termination, the length of gestation, the birth weight and the eventual intrauterine growth retardation ([1, 4, 5, 8]).

Many Authors ([7-11]) consider that a patient with a compensated cirrhosis can have a normal pregnancy and delivery without any visible harm to the mother or the child; some other Authors do consider that pregnancy is an added hazard and that termination of pregnancy at an early stage is warranted ([8, 11-14]). Whelton ([5]) indicates that pregnancy will adversely influence the maternal prognosis of cirrhosis, while Borhanmanesh ([4]) states that pregnancy does not appear to have a deleterious effect on the disease by comparative evaluation of liver disease in pregnant and nonpregnant cirrhotic patients, although it should be considered that cirrhotic patients who become pregnant probably are a selected group of mild cases with relative good liver function ([5]).

Maternal complications occur in 42% of cirrhotic women ([3]). According to some

Table 2. — *Pregnancy in cirrhotic patients. Review of the literature.*

Author	Year	No. of patients	No. of pregnancies	Cirrhosis	Shunt
Scaglione	1923	1	1	Laennec	no
Kraul	1927	1	1	Postnecrotic	no
Hesseltine	1930	1	1	Banti	no
Tenney *et al.*	1933	1	1	Postnecrotic	no
Ashton	1934	1	1	Banti	no
Lascano *et al.*	1936	1	1		no
Golden	1949	1	1		no
Ahrens *et al.*	1950	3	3	Biliary	
Javert *et al.*	1951	3	3		no
Burslem *et al.*	1952	2	3		no
Puyo	1953	2	2		no
Mack *et al.*	1953	2	2	Biliary	no
Saave	1954	2	2		no
Slater	1954	1	1		no
Enrile *et al.*	1957	1	1		no
Nebrinki *et al.*	1958	2	5	Postnecrotic	no
Ohio State Med. J.	1958	1	1		
Bihl	1959	3	3	Wilson	no
Sherwing *et al.*	1960	1	4	Wilson	no
Moore *et al.*	1960	3	4	Laennec, Postnecrotic	no
Klecker	1960	2	2	Postnecrotic	no
Page *et al.*	1960	1	1	Chronic active hepatitis	no
Bennet *et al.*	1963	1	1	Postnecrotic	no
Joske *et al.*	1963	1	3	Chronic active hepatitis	no
Gordon *et al.*	1963	2	2	Biliary, Postnecrotic	no
Slaughter *et al.*	1963	1	2	Colangitic	no
Shattuck *et al.*	1965	1	3	Biliary	no
Mac Lachlan *et al.*	1965	2	2	Chronic active hepatitis	no
Seedat *et al.*	1965	1	1	Chronic active hepatitis	no
Dehalleux *et al.*	1965	1	1		no
Dreifuss *et al.*	1966	1	2	Wilson	no
Jochimsen *et al.*	1967	1	1	Postnecrotic	no
Mc Arthur *et al.*	1968	1	3	Chronic active hepatitis	no
Whelton *et al.*	1968	3	6	Biliary, Chronic	no
		5	8	active hepatitis	
Borhanmanesh *et al.*	1970	8	8	Postnecrotic,	no
		1	1	Chronic active hepatitis	
Bearn *et al.*	1956	1	1		yes
Abrams	1957	1	2		yes
Adno	1957	1	2	Banti	yes
Labby	1960	1	1	Postnecrotic	yes
Nelson *et al.*	1963	1	1	Pick's	yes
		1	2	pseudocirrhosis, fibrosis and hemosiderosis	
Slaughter *et al.*	1963	1	1	—	yes

Table 2.

Author	Year	No. of patients	No. of pregnancies	Cirrhosis	Shunt
Riddel *et al.*	1964	1	1	—	yes
Henrion *et al.*	1964	1	1	?	yes
Hassim	1965	1	1	—	yes
Hanzlik	1965	1	2	—	yes
Wilbanks *et al.*	1967	1	1	Postnecrotic	yes
Evans *et al.*	1972	1	1	Post-alcoholic	yes
Varma	1976	2	2	Chronic active hepatitis	no
Cheng	1977	1	1	Micronodular	yes
Homburg	1988	2	2	Macronodular	yes
Wong	1992	1	1	Primary biliary	no
Pajor	1994	11	11	9 Micronodular 1 Chronic active hepatitis 1 Chronic persistent hepatitis	no

Authors, hepatic cirrhosis influences the outcome of pregnancy negatively from the metabolical point of view ([3, 8]). The markedly decreased protein production of the mother cannot satisfy the high fetal metabolic needs; the coagulation defect is equally important, considering thrombocytopenia secondary to hypersplenism and the defective production of vitamin K dependent coagulations factors ([4, 9, 14, 15]).

The mortality index of the cirrhotic pregnant patient varies, according to different Authors, from 10.3% to 18% ([1-3, 8, 16]). The causes of death in these patients, according to decreasing degree of severity are: massive bleeding from esophageal varices, hepatic coma, post-partum hemorrhage, peritonitis, rupture of a splenic aneurysm and splenorenal shunt ([3, 8, 17]). These causes of a metabolic, immunological and mechanical nature, are of mutual influence on cirrhosis and pregnancy. While some Authors sustain that pregnancy does not determine reduction of life expectancy of the mother, or a worsening of the general clinical condition, except in case of hepatic decompensated patients, some others sustain that the major risk for the cirrhotic pregnant patient is acute hepatic failure ([4, 18]). Thus, they suggest therapeutic abortion in cases of ascites either before or during pregnancy, ascites being a sign of decompensation and thus a counterindication for pregnancy ([5, 8, 12-14]).

The primary risk for the mother is massive gastrointestinal hemorrhage, which has an incidence rate between 19.6% and 24% ([1, 3, 8, 18]). Many Authors share the opinion that there is an increased risk of bleeding from the esophageal varices in pregnancy ([12-14]), with a grave prognostic significance; this could be caused by the increased pressure in the azigos system on one side and the erosive esophagitis on the other ([7]), though the occurrence of hematemesis from esophageal varices, is unpredictable in terms of time and severity, even the size of the varices doesn't correlate with the severity of hematemesis ([11]). The higher risk of portal hypertension in the pregnant cirrhotic patient is well-known: it depends on the physiological changes determined by pregnancy. These are variations in hemodynamics and circulation caused by hypervolemia, altered venous return, vascular inhibition and edema, and mechanical changes because of the enlarged uterus. For this reason, some Authors perform porto-caval shunt

either before a planned pregnancy or in early pregnancy ([6, 7, 19]). Two cases of endoscopic sclerotherapy with good results have been recently described in the literature ([6]). The sites and the dimension of varices and the occurrence of bleeding before pregnancy are of poor predictive value ([8, 11]). Hematemesis is considered the major cause of intrauterine growth retardation in cirrhotic patients, as some recent studies show ([3, 6]). Bleeding from esophageal varices is quite a rare event although it is associated with a high mortality rate and is one of the major risks for a pregnant cirrhotic woman. Pregnancy does not appear detrimental to the maternal prognosis despite the theoretical probability of raised portal pressure, about 70% of those with demonstrable varices bleed during pregnancy and the overall mortality rate is of 20%. Endoscopy and sclerotherapy before and in early pregnancy may help to reduce the mortality rate. An awareness of the possibility of unpredictable bleeding and of the available treatments for a pregnant woman with esophageal varices is essential ([6]).

The incidence rate of postpartum hemorrhage is between 16% and 26%. This complication is strongly correlated to the coagulation defects of the cirrhotic patient and to the porto-caval anasthomosis in pregnancy, as stated by some Authors ([16, 20, 21]).

These patients are more susceptible to infections during pregnancy and puerperium, which may be due to an immunological defect secondary to reduction of plasma proteins and impaired hepatic and splenic metabolic functions ([1]).

Among the influences of pregnancy on the clinical condition of a cirrhotic patient, as in the case of jaundice, a partial submission can be observed in early pregnancy due to the immunosuppression action of progesterone, cortisol and hPL. Hepatic cytolysis in post-hepatic cirrhosis is secondary to immunodependent cell-mediated necrosis and not to the viral infection. The cytolysis index, particularly expressed by transaminase values, decreases in early pregnancy while it increases in the postpartum period. Jaundice is more frequent in cases of hemorrhage or hypotension, frequent conditions in pregnancy. Causes of jaundice in a cirrhotic pregnant patient are due to increase of steroids in pregnancy secondary to an overload of catabolism and the mechanical effect of the enlarged uterus. On the other side, high plasmatic cortisol has an anti-oedematous effect which delays the onset of jaundice in pregnancy.

Data regarding the effects of cirrhosis on the fetus are not homogeneous. Recent studies highlight that the incidence rates of prematurity/immaturity and of perinatal mortality are 25% and 8.3%, respectively ([3]). As before-mentioned, the main cause of intrauterine growth retardation is esophageal varices bleeding. The fetal prognosis varies according to different Authors: born alive ranges between 30% and 80%, stillbirth between 43% and 64%, spontaneous abortion (8th to 24th week of amenorrhea) between 39% and 78%. Other Authors have reported on the considerable increase of fetal wastage (17.9%), prenatal morbility (17.3%), prematurity (20.5%), and stillbirth rates (20%). Newborns are more sensitive to infections and have a slow and incomplete response to vaccines (not only because of immaturity), like the mother, who has a slight immunodeficiency as above-mentioned ([3, 5, 8, 22]). In our case, the maternal and neonatal serological and histological findings excluded the vertical transmission of viral hepatitis.

Controversial opinions in the literature are on the kind and timing of delivery. In the past the general tendency was towards elective cesarean section at term, if the fetal conditions were good and unvaried. Most Authors nowadays assert

that cesarean section should be preserved for obstetric indications or where urgent termination of pregnancy is required ([5, 8, 10, 23, 24]), considering the poor tolerance of laparotomy of cirrhotic patients. Otherwise, many Authors suggest vaginal delivery, possibly anticipated with sedation of the patient in the first phase, not allowing her to strain, and a shortened second stage by means of forceps delivery ([5, 10, 23, 24]).

CONCLUSION

The case presented is of particular interest because provides the opportunity to evaluate the effects of hepatic cirrhosis on pregnancy. It shows that pregnancy, adequately monitored may not have a negative effect on the preexisting hepatic decompensated phase, pregravidic care is illness. In case of hepatic disease in a recommended. The mortality index of pregnant cirrhotic patients in a decompensated phase is still high, as known in the recent literature. The clinical symptoms of the hepatopathy must be suspected and detected, and accurately treated particularly during the first trimester of pregnancy.

Many complications are secondary to the pregnancy, which must be actively monitored and prevented by therapeutic means, especially during the first trimester of pregnancy – for example, sclerotherapy of esophageal varices, considering the high hemorrhage risk.

The high incidence of intra-uterine growth retardation and the high frequency of immuno-immaturity of these babies, very often preterm, is of relevant importance. These babies are even more sensible to infectious disease and have a slow and incomplete response to vaccines.

The delivery has to be timed by taking into consideration the general condition of the mother and the condition of the fetus.

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