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CASE REPORT

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HELLP syndrome as a cause of unexpected rapid maternal death– A case report and review of the literature

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Abstract Unexpected rapid death after delivery due to HELLP syndrome (HS) may become the subject of a forensic expertise. Since this syndrome is rarely encountered in forensic pathology, our objective was to point to some specific findings which might present forensic aspects of HS. These include unexpectedness, suddenness and fulminant course of this syndrome, which may confuse physicians, and on the other hand these characteristics cast doubt on violent injury, diagnostic oversights or iatrogenic injuries. Absence of classical signs of preeclampsia and non-specific clinical symptoms cause considerable differential diagnostic problems leading to a diagnostic delay or initial wrong non-obstetric diagnosis. A definitive postmortem diagnosis of HS in questionable cases of maternal death and consecutive forensic expertise of suspected medical malpractice should be based on accepted laboratory criteria and characteristic histopathological alterations.

Keywords Preeclampsia · HELLP syndrome · Liver hemorrhage · Forensic medicine · Malpractice

Introduction

As described by Weinstein in 1982 [1], HELLP syndrome (HS) is a variant of severe preeclampsia recognized as a serious, life-threatening disease characterized by hemolysis, elevated liver enzymes, and low platelets, whose pathogenesis is unclear. The incidence of the disease is reported as being 0.17–0.85% of all live births [2], i.e. between 4 and 18.9% of patients with preeclampsia/eclampsia develop HS [3].

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Diagnosis of HS is based on the classical signs of preeclampsia, clinical symptoms of disease and laboratory abnormalities proposed by Sibai et al. [3]. Martin et al. [4] proposed a classification of patients with HS, which is based only on the platelet count into class 1 (maternal platelet nadir $<50\times10^9$/l), class 2 (between 50–100×10^9/l), and class 3 (between 100–150×10^9/l).

The onset of HS occurs during pregnancy or after delivery. Numerous maternal multi-system complications may occur, as well as fatal outcome in a short time. Since Weinstein's publications maternal death from HS is rarely encountered in forensic pathology [5].

Case report

A 34-year-old secundipara was admitted for cesarean section. On admission, her blood pressure was 120/80 mmHg and without subjective difficulties. Cesarean section was performed on the same day at 10 a.m. and a healthy, male weighing 4,880 g, body length 53 cm, was born. The postoperative course was initially inconspicuous. Unexpectedly, at 16.20 p.m. the patient became anxious and irritable and shortly after that developed acute cardiopulmonary arrest. Due to suspected pulmonary embolism, she was transferred to the emergency pulmonary clinic. On admission to the intensive care unit the patient was unconscious, GCS 4. Laboratory findings were as follows: serum lactic dehydrogenase (LDH) 4800 U/l, aspartate aminotransferase (AST) 3600 U/l, alanine aminotransferase (ALT) 3270 U/l, total bilirubin 0.7 μmol/l, fibrinogen 0.7 g/l. Other analyses were performed on two, some on three occasions with the following tendency: oliguria with increasing creatinine values up to 180 μmol/l, decreasing hemoglobin to 0.101 g/l, hematocrit to 37L/l, RBC to 1.15×10^{12}/l, platelet count to 36×10^9/l and increasing INR to 8.04. Since a coagulation disorder and suspected intraabdominal bleeding were established, laparatomy was performed at 21.00 p.m. A subcapsular liver hematoma was discovered as well as capsular and liver tissue rupture. During surgery, the liver bleeding was

stopped, but despite resuscitation attempts and permanent transfusion, the outcome of surgery was lethal.

Both surgeries were performed under general anesthesia with nitric oxide and oxygen and standard premedication.

Since death occurred in less than 24 h after admission, according to the legal regulations, a medico-legal autopsy was ordered. At autopsy slight cerebral edema was present, but the lungs showed the characteristic signs of shock. Marked petecheal and suffusive hemorrhages were observed under the peritoneum. Greater collections of clotted blood were found in the space between the liver and diaphragm, as well as below the liver. The liver was slightly enlarged, with smooth capsulation and several small or large subcapsular hematomas in the right lobe (Fig. 1). The anterior liver segment presented with capsular lacerations, the underlying liver parenchyma was necrotic, with multiple lacerations, which had been surgically treated (Fig. 2). The liver had a rigid consistency and cross-sections of the liver parenchyma showed yellow-brown cut surfaces with multiple dark-reddish confluent hemorrhagic foci. Hyperemia and enlargement of the spleen and shock kidneys were present. In the adrenal glands a diffuse hemorrhage was established. The right arm presented with necrotic skin lesions (Fig. 3). Macroscopically and microscopically, the placenta and placental implantation did not show any abnormalities.

Serialsections of the liver blocks showed that development of subcapsular hematoma was the consequence of massive periportal parenchymal hemorrhagic necrosis (Figs. 4 and 5). Histologically, signs of disseminated intravascular coagulation (DIC) were present in the smaller lung vessels, intestines and kidneys. Vasculitis was excluded by the lack of inflammation in the arteriolar walls.

Discussion

The described case of maternal death from HELLP syndrome became the object of forensic expertise from the aspect of suspected medical malpractice. The aim of this study was to establish if timely diagnosis and therapy would have affected the outcome. The following specificities of HS also have forensic aspects:

Fig. 1 Subcapsular hematoma, bleeding into the liver, hemorrhagic liver cell necrosis

Fig. 2 Subcapsular bleeding, necrotic liver parenchyma with multiple lacerations

Fig. 3 Hand ischemia

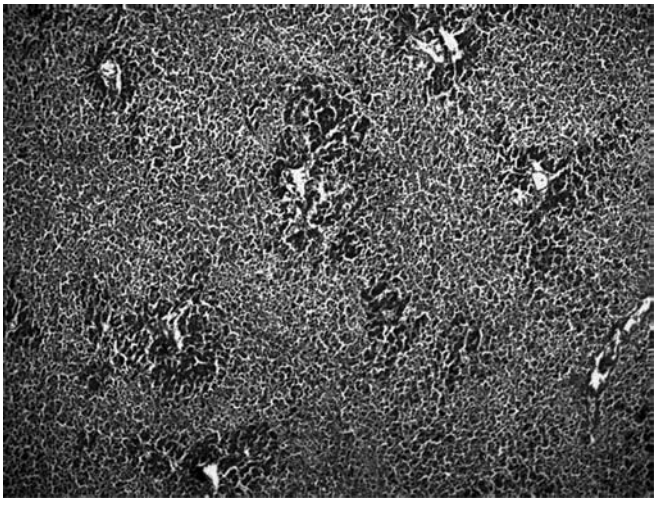

Fig. 4 Confluent periportal hepatocellular necrosis (HE 5×10)

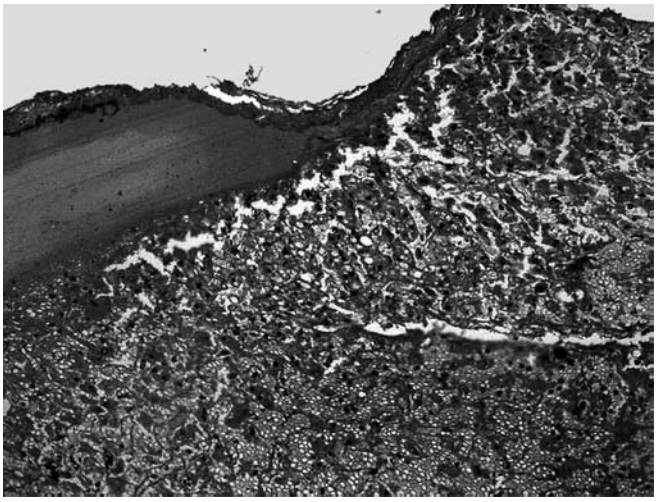

Fig. 5 Hepatocellular necrosis, hemorrhage and subcapsular hematoma (HE 10×10)

1. Unexpectedness, suddenness and fulminant course of this syndrome are of essential forensic significance and may confuse physicians who lose precious time in reaching the correct diagnosis. The onset of manifestations is described as ranging from a few hours to 6 days, the majority developing within 48 h of delivery, and occurring in 20–30% of all cases [6], but the clinical course might be extremely rapid, while the medical history is uneventful in most cases [7]. The first, often the sole but always the most important symptom of HS, seen in 80–90% of cases, is right upper abdominal pain which is assumed to be the consequence of stretching of Glisson's capsule due to sinusoidal obstruction of blood flow. However, such non-specific abdominal symptoms may lead to a diagnostic delay, and initial wrong non-obstetrical diagnosis is not uncommon [4]. On admission the parturient described here did not complain about anything. The first symptoms occurred suddenly, about 6 h of delivery and started with the central nervous system, which very soon led to cardiopulmonary arrest and coma to GCS 4. Further follow-up of the parturient's subjective difficulties was not possible.
2. With regard to the forensic aspects of a timely diagnosis, an absence of obvious signs of preeclampsia significantly affected the clinicians who could not predict the development of HS. The literature data revealed that in 20% of women with HS, classical signs of preeclampsia might be absent or only slight before delivery [1, 2, 3, 4, 8, 9, 10]. The pregnancy was regularly controlled and no significant abnormalities from mother and baby were recorded. The day before delivery the mother underwent clinical investigations and standard laboratory analyses were performed. Since the only deviation was established in the bilirubin finding, it was not possible to predict the development of HS based only on this finding, since only 25% of patients have raised bilirubin levels at the time of diagnosis [11] Only laboratory findings on admission to the intensive care unit clearly pointed to development of HS, with worsening from class 2 to class 1. The platelet count, apart from clinical aspects, also has a documented forensic value as an indicator of development and severity of the disease.
3. Patients whose pregnancies are complicated by HS are at a higher risk for organ failure such as acute cardiopulmonary arrest, cerebral hemorrhage, renal insufficiency, subcapsular liver hemorrhage and liver rupture [4, 12, 13, 14]. The fact that development of complications cannot usually be predicted is of special forensic significance in considering timely medical interventions.

A subcapsular liver hematoma is a life-threatening, but fortunately rare complication of HS, which occurs in 2–3% of cases, but with maternal mortality in 56–61% and perinatal mortality in 62–77% [15]. Spontaneous hepatic rupture is also a rare event [16, 17] with only about 100 cases reported in the English literature. A single author or centre [13, 18] has only reported a maximum of six cases. Despite surgical efforts, about one-third of patients with liver rupture died in hemorrhage shock [3, 13]. When there is a strong clinical suspicion of liver rupture, a surgical emergency with control of bleeding based on trauma principles must be done without delay, before secondary shock-related organic complications develop. Such patients must be transferred to a multidisciplinary centre providing necessary experience in liver surgery [13]. The histopathological alterations in the liver and kidneys revealed a finding described by Tsokos et al. as characteristic for HS [5]. HS patients are at a higher risk for renal failure [8, 19, 20]. The hemorrhage of the adrenal glands and necrotic skin lesions of the right arm were probably the consequence of thrombotic microangiopathy [21, 22].

It is quite possible that the development of life-threatening complications or even sudden death after delivery due to HS may occur without adequate clinical and laboratory findings, especially if the diagnosis of HS was not timely. This may cast doubt on diagnostic oversights, such as natural causes, some violent forms of injury or iatrogenic injuries, causing doubt in forensic morphologists, whereas their conclusions may have serious consequences. Forensic analysis of this case considered various possibilities. However, due to rapid aggravation of difficulties in this parturient, some analyses had not been performed, such as immunological studies, hemoculture etc., whereas a blood culture taken postmortem was negative. However, none of these potential aggravating mechanisms present with such a rapid course and morphological complexity alone.

A definitive postmortem diagnosis of HELLP syndrome in questionable cases of maternal death after delivery and consecutive forensic expertise of suspected medical malpractice, must be based on accepted laboratory criteria proposed by Sibai et al. [3], and Martin et al. [4] and charateristic histopathological alterations proposed by Tsokos et al. [5]. When making decisions one must consider the fact that complications increase in frequency

as the severity of HS worsens in subgroups of patients with "classic or true HELLP" (class 1) syndrome [3, 4, 5, 12] and that surgical procedures, such as cesarean operations, anesthesia and related interventions resulting from those, could independently worsen the maternal condition and directly increase various types of morbidity.

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