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CASE REPORT

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Maternal death in pregnancy from HELLP syndrome. A report of three medico-legal autopsy cases with special reference to distinctive histopathological alterations

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Abstract Maternal death from HELLP syndrome, a complication of (pre-) eclampsia during pregnancy or postpartum, is rarely encountered in forensic pathology. We report three cases of HELLP syndrome with fatal outcome putting the main focus on the histopathological features of the disease. We found an almost identical histopathological pattern in the liver (periportal coagulation necrosis, hepatic haemorrhages sharply demarcated by an extended fibrin network from the surrounding unaffected liver parenchyma, focal leukostasis in liver sinusoids and swelling of Kupffer's cells, absence of inflammatory cellular infiltrates in liver plates, lack of fatty transformation of hepatocytes) and kidneys (bloodless glomeruli with swollen and vacuolated intracapillary cells, cigar-shaped capillary loops, enlarged glomerular tufts with herniation of capillary loops into the proximal convoluted tubules, swelling of mesangial cells) in all three cases. The histopathological alterations in the liver and kidneys can be considered characteristic for the disease and their presence may enable the forensic pathologist to establish the definite post-mortem diagnosis of HELLP syndrome in questionable cases.

Keywords HELLP syndrome · Pre-eclampsia · Eclampsia · Pregnancy · Maternal death · Intrahepatic haemorrhage · Liver pathology · Forensic histopathology

Introduction

HELLP (i.e. haemolysis, elevated liver enzymes, low platelet count) syndrome is a severe and life-threatening complication of (pre-) eclampsia during pregnancy or postpartum [1, 2, 3, 4, 5] associated with a maternal mortality rate of 1.1–3.4% [3, 6]. Whereas pregnancy-related fatalities of various kinds, for the most part presenting as sudden unexpected death, have been published repeatedly in the medico-legal literature [7, 8, 9, 10, 11], to our knowledge this is the first report dealing with maternal death from HELLP syndrome from the *ex post* viewpoint of forensic pathology. The observations from three cases of HELLP syndrome are presented putting the main focus on the pathomorphological features of the disease.

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Case reports

Case 1

A 28-year-old black female was admitted to hospital in an unconscious state and the previous medical history was unknown. Pregnancy (gestational age between the 24th and 28th weeks) was diagnosed and due to the constellation of laboratory parameters (AST 1,277 U/l, ALT 921 U/l, hematocrit 28%, platelet count 49,000/mm^3, PTT 40.3 s) HELLP syndrome was suspected. A caesarean section was performed immediately and a liveborn female infant was delivered. Postoperatively, the patient developed fever and tenderness in the abdomen and died 80 h after admission without gaining consciousness. Due to the fact that death occurred in hospital a short time after a surgical intervention, a medico-legal autopsy was ordered. At autopsy marked oedema of the lower extremities was present and petechial and suffusional haemorrhages were observed under the pleura, under the endocardium of the left ventricle, in the mucosae of the renal pelvis and peritoneum of the small and large bowel and in the grey and white matter of the brain (purpura cerebri). The liver had a rigid consistency and cross-sections of the liver parenchyma showed yellow-brown cut surfaces with multiple dark-reddish confluent haemorrhagic foci. Besides oedema of the brain and lungs, a dilatation of the right ventricle, hyperaemia of the spleen and shock kidneys were present. The field of operation of the caesarean section was unremarkable. Histology revealed periportal hepatocellular necrosis and haemorrhages sharply demarcated by an extended fibrin network from the surrounding unaffected liver parenchyma (Fig. 1), bile stasis and swelling of Kupffer's cells but no inflammatory cellular infiltrate or fatty transformation of hepatocytes. In the kidneys bloodless glomeruli with swollen and vacuolated intracapillary cells and herniation of capillary loops into the proximal convoluted tubules were detected and the mesangial cells appeared swollen; thrombus for-

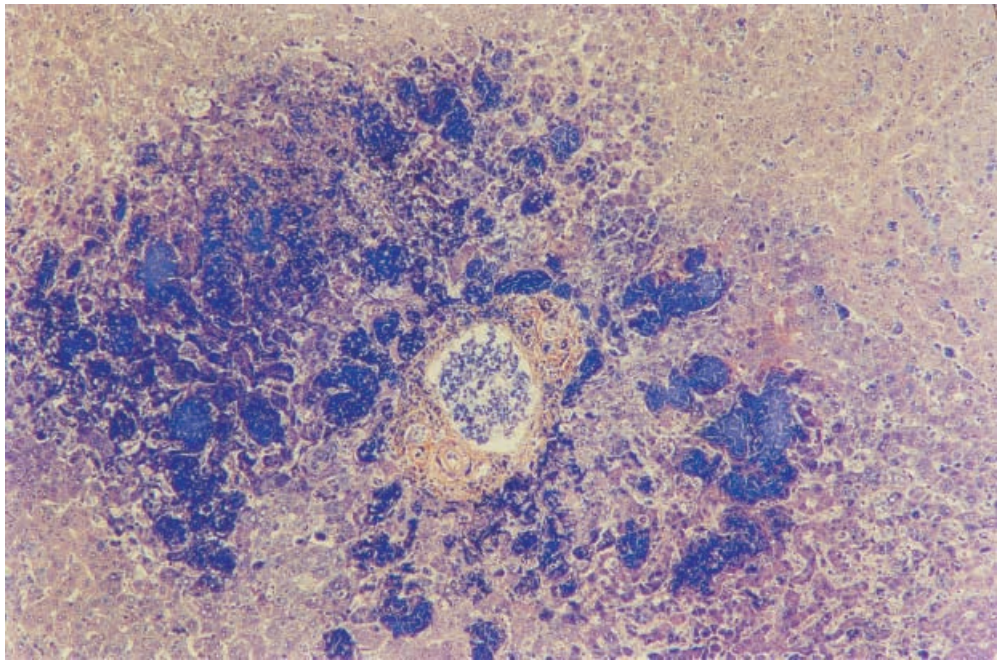

Fig. 1 Periportal hepatocellular necrosis and haemorrhages sharply demarcated by an extended fibrin network from the surrounding unaffected liver parenchyma in case 1 (PTAH, original magnification ×25)

mation was seen infrequently in the glomerular capillaries and vasa recta of the medulla. In the myocardium focal contraction band necrosis was found and serological tests for HIV and hepatitis were negative. Death was attributed to multiple organ failure due to DIC in the course of HELLP syndrome.

Case 2

The 20-year-old white primipara was admitted to hospital in the 37th week of gestation with pathological liver function tests and a suspected diagnosis of acute hepatitis. Initial physical examination showed cutaneous and mucosal petechiae and upper right quadrant abdominal pain. According to the patient's clinical symptoms and laboratory parameters (AST 1,030 U/l, ALT 710 U/l, platelet count 14,000/mm^3, low fibrinogen, positive fibrin split products) the diagnosis of DIC as a sequel to HELLP syndrome was made. A healthy female infant was delivered through caesarean section. The maternal postoperative course was complicated by DIC and progressive hepatic failure. The patient died 8 days after delivery under the clinical signs of multiple organ failure. A medico-legal autopsy was ordered which revealed oedema of the brain (weight 1,560 g), shock kidneys and hyperaemia of the spleen. The liver was pale and had a rigid consistency showing haemorrhagic and yellow patches. Petechial haemorrhages were present in the conjunctivae and in the thoracic skin and under the pericardium and endocardium. Histologically, signs of DIC such as microthrombi composed of fibrin and platelets were present in the smaller vessels of lungs, intestinum and kidneys. The liver showed confluent haemorrhages and periportal hepatocellular necrosis surrounded by an extended fibrin network and leukostasis in the liver sinusoids without inflammatory cell infiltration into the liver cell plates or fatty transformation of hepatocytes. In the kidneys the glomeruli appeared bloodless with distended cigar-shaped loops showing intracapillary vacuolisation. According to the previous medical history and autopsy findings the cause of death was ARDS and DIC-induced multiple organ failure due to HELLP syndrome.

Case 3

A 19-year-old white female was found dead in her appartment. Police investigations revealed a previous medical history of eclampsia. Due to unknown cause and manner of death a medico-legal autopsy was carried out. At external examination the deceased showed petechial haemorrhages in the conjunctivae and thoracic skin and a marked oedema of the lower extremities. Autopsy revealed late pregnancy with a dead male fetus in utero showing considerable cyanosis. Petechiae and suffusions were present in mucous surfaces and serous coats of internal organs. The liver was firm with yellow and red coloured patches under Glisson's capsule and in cross-sections. At the micromorphological level the liver showed substantial haemorrhages, periportal hepatocellular necrosis with a fibrin network sharply demarcating the surrounding unaffected liver parenchyma, focal leukocyte sticking strictly limited to liver sinusoids, swelling of Kupffer's cells and bile stasis but no inflammatory changes or fat accumulation in the hepatocytes. In the kidneys elongated bloodless capillary loops with vacuolisation of intracapillary cells in co-existence with enlarged glomerular tufts

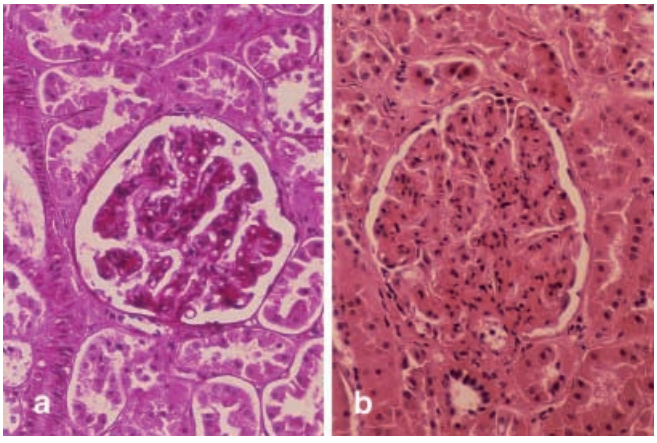

Fig. 2 Histopathological appearance of the kidneys in case 3 showing **a** cigar-shaped bloodless capillary loops with vacuolisation of intracapillary cells and **b** enlarged glomerular tufts filling Bowman's space with herniation of capillary loops into the proximal convoluted tubules and swelling of mesangial cells (→) (**a** PTAH, **b** HE, original magnification ×25)

filling Bowman's space and herniation of capillary loops into the proximal convoluted tubules and swelling of mesangial cells were present (Fig. 2a, b). In the myocardium, focal contraction band necrosis but no accompanying inflammatory changes were detected. The outcome of toxicological analyses was negative. According to the autopsy and histological findings, death was attributed to hepatic failure in the course of HELLP syndrome.

Discussion

The predominant morphological post-mortem findings in the three cases of maternal death from HELLP syndrome were (1) petechial haemorrhages and suffusions in conjunctivae, skin, mucous surfaces and serous coats of internal organs and purpura cerebri that can be attributed to DIC and (2) an almost identical feature of histopathological alterations in the liver and kidneys (Table 1).

Although severe maternal complications as a sequel to HELLP syndrome in the postpartum period are reported to be rare events [2, 12, 13], in both clinical cases included in this study the maternal course was complicated by deterioration of DIC with subsequent multiple organ failure and death (cases 1 and 2). DIC is reported to occur in 4–38% of cases of HELLP syndrome [6]. The development of a decompensation of coagulation correlates with the appearance of severe maternal complications such as renal failure and liver haematoma and rupture [3, 12] and is more frequent in patients with the HELLP syndrome than in those patients with (pre-) eclampsia without the HELLP constellation [14].

In the myocardium of cases 1 and 3, focal contraction band necrosis but no inflammatory changes were found histologically. Although an earlier study revealed the presence of contraction band necrosis in 35% of cases of fatal eclampsia in contrast to only 3% in controls and the authors attributed the frequent occurrence of myocardial contraction band necrosis in eclampsia-associated deaths to preceding coronary artery spasms [15], these myocardial alterations are a well known phenomenon to the forensic pathologist. Myocardial contraction band necrosis can be frequently observed not only in autopsy cases with myocardial ischemia of coronary origin but also in a variety of underlying pathological conditions prior to death such as protracted agony, prolonged resuscitation attempts, repeated defibrillation with automatic implantable cardioverter-defibrillators and as a sequel to administration of catecholamines during intensive care or before an operation [16, 17, 18, 19]. Therefore we suggest that myocardial contraction band necrosis is unspecific for the post-mortem diagnosis of (pre-) eclampsia or HELLP syndrome. To elucidate the origin of such unspecific myocardial alterations, a more comprehensive approach than provided by the use of conventional histological staining procedures can be achieved by the application of modern techniques [20, 21, 22, 23] thus allowing a clearer differentiation between potential causes of death [24].

In conclusion, when examining fatalities that have occurred during pregnancy or postpartum, the forensic pathologist should take HELLP syndrome with fatal outcome as a potential differential diagnosis into consideration. The histopathological alterations in liver and kidneys (Table 1) can be considered characteristic for the disease and their presence may enable the forensic pathologist to establish the definite post-mortem diagnosis of HELLP syndrome.

Table 1 Histomorphological alterations of liver and kidneys found in the HELLP syndrome

Histomorphological alterations
Liver
Periportal hepatocellular necrosis (coagulation necrosis) and haemorrhages sharply demarcated by an extended fibrin network from the surrounding unaffected liver parenchyma
Focal leukocyte sticking (leukostasis) in liver sinusoids and swelling of Kupffer's cells, bile stasis
Absence of inflammatory cellular infiltrates in liver plates and no fatty transformation of hepatocytes
Kidneys
Bloodless glomeruli with swollen and vacuolated intracapillary cells
Elongated and obstructed (cigar-shaped) capillary loops or enlarged glomerular tufts filling Bowman's space with hernia tion of capillary loops into the proximal convoluted tubules
Swelling of mesangial cells
Thrombus formation in glomerular capillaries and the vasa recta in cases with severe DIC

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