The management of the surgical complications of HELLP syndrome

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ABSTRACT

INTRODUCTION Complications from HELLP (Haemolysis, Elevated Liver enzymes and Low Platelet) syndrome may present as an emergency to any surgeon. We review the ten-year experience of a tertiary hepatobiliary centre managing HELLP patients. Three selected cases are described to highlight our management strategy and a systematic review of the recent literature is presented.

METHODS All patients with HELLP syndrome were identified from a prospectively maintained database and their details collated. Subsequently, a detailed search of PubMed was carried out to identify all case series of HELLP syndrome in the literature in the English language since 1999.

RESULTS On review of 1,002 cases, 10 patients were identified with surgical complications of HELLP syndrome. Seven of these patients had a significant liver injury. Only three of these required surgical intervention for liver injury although four other patients required surgical intervention for other complications. There was no maternal mortality in this series. Review of the literature identified 49 cases in 31 publications. The management approaches of these patients were compared with ours.

CONCLUSIONS We have presented a large series of patients with surgical complications resulting from HELLP syndrome managed without maternal mortality. This review has confirmed that haemodynamically stable patients with HELLP syndrome associated hepatic rupture can be conservatively treated successfully. However, in unstable patients, perihepatic packing and transfer to a specialist liver unit is recommended.

KEYWORDS

Hepatopancreatobiliary – HELLP – Management – Surgery

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The HELLP (Haemolysis, Elevated Liver enzymes and Low Platelet) syndrome was first described in 1982.¹ It occurs in 0.17–0.85% of pregnancies and is more common among older, multiparous, Caucasian women.² As its name suggests, it is characterised by haemolysis (diagnosed from a blood film), elevated liver enzymes (greater than 3 standard deviations above normal for the hospital) and a low platelet count ($<100 \times 10^9/l$).³

The pathogenesis of HELLP syndrome is not completely understood and has been reviewed in detail elsewhere.⁴ Abnormal placental development can lead to increased oxidative stress as a result of ischaemia, similar to pre-eclampsia. This leads to the release of a variety of factors and cytokines, particularly products of abnormal metabolism of nitric oxide, prostaglandins and endothelin, which results in complement activation leading to endothelial dysfunction. This will then lead to platelet aggregation with consumption and, eventually, thrombocytopenia. The haemolysis that occurs is microangiopathic, probably due to shearing stresses fragmenting red blood cells as they pass through small blood vessels with damaged intima and fibrin mesh deposits.⁵ This leads to microthrombi and fibrin deposition

in the kidney, bringing about acute renal failure, and sinusoidal obstruction in the liver, disrupting hepatic blood flow and causing swelling, ischaemia and hepatic rupture.

Although rare, patients with HELLP syndrome may present as an emergency with complications of hepatic infarction, hepatic rupture with life threatening haemorrhage or other surgical complications associated with this condition. Despite being a condition managed primarily by obstetricians, if patients develop complications from HELLP, they invariably need to be managed by surgeons. In this paper, we review the ten-year experience of a single tertiary centre managing patients presenting with surgical complications as a result of HELLP. Three selected cases are reported as well as a systematic review of the recent literature on this subject to assess how our series compares with regard to presentation, management and outcomes.

Methods

A prospectively maintained database was reviewed of all patients managed in the liver unit of St James's University Hospital in Leeds. All patients with pregnancy associated

Table 1 Patient characteristics

	Age (yrs)	Gestation	Platelets ($\times 10^9/l$)	ALT (iu/l)	Operations	Complications	Blood transfused
1	38	29 wks (twins)	70	271	4 laparotomies for liver rupture	Brain stem lesion	30 units
2	34	34 wks	43	324	Clinical observation and monitoring	Subcapsular haematoma	10 units
3	32	31 wks	62	1,508	Perihepatic packing (x3)	Haemodialysis, laparostomy, intraventricular bleed, pleural effusions	45 units
4	39	28 wks	*	*	Thoracotomy, embolisation	Haemothorax, GI bleed, acute renal failure	*
5	35	35 wks (twins)	13	150	Clinical observation and monitoring	Haematemesis, ileus, encephalopathy, liver haematomas	4 units
6	20	36 wks	38	45	2 laparotomies for liver rupture	Encephalopathy	4 units
7	31	30 wks	92	4,128	Perforated duodenal ulcer repair	Acute renal failure, respiratory failure, liver haematoma	3 units
8	32	35 wks	97	200	Right hemicolectomy	Ischaemic bowel, liver haematomas	5 units
9	17	32 wks	38	235	Drainage of pelvic abscess	Haemodialysis, ascites, splenomegaly, multiple haemorrhagic liver lesions	Nil
10	30	34 wks (twins)	30	133	Clinical observation and monitoring	Haemodialysis, seizures, cellulitis	3 units

ALT = alanine transaminase; GI = gastrointestinal

*Laboratory results were not available as this patient was early in the series. Liver biopsy histology showed acute obliterative microangiopathy and the discharge letter gave a diagnosis of HELLP syndrome owing to low platelets and elevated liver enzymes.

liver disease were identified by searching for the terms “pregnancy” or “pregnant”. The database records all patient care episodes managed by the hepatology and liver transplant service at the hospital, which delivers quaternary level care in these specialties. Data recorded include patient demographics, diagnosis, test results and details of interventions (eg radiological or surgical). Patients’ case notes were obtained and all patients with HELLP syndrome were evaluated retrospectively.

The definition of HELLP used was the presence of haemolysis (diagnosed from a blood film) associated with elevated liver enzymes (greater than 3 standard deviations above normal) and a low platelet count ($<100 \times 10^9/l$).³ The patient’s demographics, presentation, laboratory and imaging findings, and outcomes were assessed. This study was reviewed and approved by a departmental review board.

A detailed search of PubMed and MEDLINE® was carried out to identify all case series of HELLP syndrome in the literature in the English language since 1999. The last search was conducted on 31 January 2012. The following categories were combined using the Boolean term ‘AND’:

- > HELLP syndrome/therapy OR HELLP syndrome/complications OR HELLP syndrome/epidemiology OR HELLP syndrome/surgery
- > liver diseases/diagnosis OR liver diseases/etiology OR liver diseases/mortality
- > surgery OR laparotomy
- > injury OR injuries OR haemorrhage OR bleeding OR rupture OR complication OR complications

Results

A total of 1,002 patients were identified from the database. Of these, 962 were excluded as they were a duplicate entry, mentioned pregnancy as a risk while on post-transplant immunosuppression or were included owing to gallstone disease. Of the 40 cases remaining, 14 were due to cholestasis of pregnancy and 6 to acute fatty liver disease of pregnancy, 10 were confirmed cases due to HELLP syndrome and there were also 10 others.

The characteristics of the ten patients diagnosed with HELLP syndrome are shown in Table 1. The median age at presentation was 32 years (range: 17–39 years). Three of the patients were pregnant with twins. Only two patients developed HELLP prior to their delivery with the remaining eight diagnosed following delivery. Seven patients had a significant liver injury and four of these were managed conservatively. Seven patients required surgical intervention; three of these were for liver rupture and four were for other complications of microangiopathy. The median blood transfusion was 4 units (range: 0–45) although all patients received multiple platelet transfusions. There was no maternal mortality in this series.

Case 1

A 38 year-old woman (Patient 1 in Table 1) who was 29 weeks pregnant with twins presented to a district general hospital with hypertension, proteinuria, right upper quadrant pain and vomiting. (Obstetric aspects of this case have been described previously.)⁶ Liver function tests and platelet counts were normal but uric acid was raised. An

emergency Caesarean section was performed owing to abnormal cardiotocography. One infant was delivered alive with the other stillborn. Approximately 200ml of fresh blood was found in a haemoperitoneum with no apparent cause. Intraoperative blood results showed a haemoglobin (Hb) level of 7.1g/dl, a platelet count of $70 \times 10^9/l$, an international normalised ratio of 1.0, an alkaline phosphatase level of 853iu/l and an alanine transaminase (ALT) level of 271iu/l. She was transferred to the intensive care unit, and was transfused blood and platelets.

Increasing abdominal distension developed overnight and the patient became haemodynamically unstable. At relaparotomy, there was a tense haemoperitoneum secondary to bleeding from multiple hepatic tears and capsular disruption, and so the liver was packed. Postoperatively, she deteriorated and was transferred to the tertiary referral centre. Prior to transfer, she had received 20 units of blood as well as 16 units each of platelets, fresh frozen plasma and cryoprecipitate.

Following transfer to the tertiary centre, the patient underwent a further laparotomy by a consultant hepatobiliary/transplant surgeon. Access was difficult owing to obesity and a cruciate incision was employed. A tense haemoperitoneum was found with continued bleeding from multiple parenchymal tears. The liver was mobilised, bleeding was controlled by packing and a liver biopsy was taken.

Postoperatively, the patient required cardioversion and drainage of a pleural effusion. Following correction of the coagulopathy, she returned to theatre two days later and the packs were removed. There was good haemostasis and the wound was closed. She recovered well and was discharged after 35 days. Six months after discharge, she remained well.

Case 2

A 34-year-old primigravida woman (Patient 2 in Table 1) presented at 34 weeks with hypertension, proteinuria, platelets of $130 \times 10^9/l$ and ALT of 36iu/l. Her blood pressure continued to rise despite intravenous labetalol, and she started vomiting and developed fundal tenderness. Cardiotocography was abnormal and so an emergency Caesarean section was performed. This was uneventful and a live infant was delivered. Platelets were $90 \times 10^9/l$, ALT was 324iu/l and Hb was 12.2g/dl.

The patient experienced shortness of breath four hours following surgery, and her platelet count and Hb level fell to $54 \times 10^9/l$ and 6.5g/dl respectively. She became hypotensive, and developed abdominal distension and right-sided abdominal pain. Abdominal ultrasonography showed perihepatic fluid and computed tomography (CT) demonstrated a large subcapsular haematoma of the right lobe with ongoing bleeding. Three units of blood and one unit of platelets were transfused prior to transfer to the tertiary centre. There, magnetic resonance imaging (MRI) (Fig 1) showed a large subcapsular haematoma of the right lobe with oedema and free fluid in the abdomen but conservative management was continued. The patient received a further seven units of blood but made an uneventful recovery.

Figure 1 Magnetic resonance imaging showing a large subcapsular haematoma of the right lobe with oedema and free fluid in the abdomen

Case 3

A 32-year-old primigravida woman (Patient 3 in Table 1) was admitted at 31 weeks with epigastric and right upper quadrant pain. She had proteinuria and was hypertensive (228/115mmHg), which persisted despite best treatment. She deteriorated suddenly; her Glasgow coma scale score fell to 9 and repeat ultrasonography failed to identify a fetal heartbeat. Blood results demonstrated a platelet count of $62 \times 10^9/l$ and an ALT of 1,508iu/l. HELLP was diagnosed and an emergency Caesarean section performed with delivery of a stillborn baby.

Two litres of blood were found in the peritoneal cavity secondary to liver rupture. The patient suffered a hypovolaemic cardiac arrest and the liver was packed. She received a total of 30 units of blood, 16 units of fresh frozen plasma, 8 units of platelets, 10 units of cryoprecipitate and 2 units of factor VIIa. She was transferred to a tertiary centre where she had several further pack changes in theatre and vacuum therapy to assist in wound closure. She required inotropic support, haemofiltration and ventilation for four weeks, and a further 15 units of blood. She was discharged after 64 days, having recovered completely.

Discussion

Abercrombie described the first case of spontaneous hepatic rupture in pregnancy in 1844.⁷ In 1954, Pritchard *et al* first described the association of haemolysis, elevated liver enzymes and thrombocytopenia.⁸ The acronym HELLP was assigned by Weinstein in 1982.¹

Cases of hepatic rupture in pregnancy are rare, with a reported incidence ranging from 1 in 45,000 to 1 in 225,000 deliveries, but it carries maternal mortality rates of 60–86%.⁹ The present case series is likely to have been subject to a degree of referral bias since patients who died rapidly or were unable to be transferred were excluded. However, zero maternal mortality in this series and the success of patients managed conservatively are important findings.

All published case reports or series subsequent to those reviewed in a previous paper by Reck *et al*¹⁰ were analysed. We identified 34 cases in 16 publications describing hepatic rupture associated with HELLP syndrome (Appendix 1 – available online only).^{11–26} Four patients (12%) were treated

conservatively, one of whom underwent radiologically guided percutaneous drainage of bloody ascitic fluid. Two case reports described incidences of hepatic rupture in association with HELLP that resulted in maternal death at admission.

Two patients underwent subsequent elective liver resection surgery, for intrahepatic haematoma and an atrophic left lobe due to recurrent cholangitis. Twenty-six patients underwent emergency surgery with eight requiring multiple laparotomies to manage the hepatic complications. A range of surgical techniques were employed including tamponade (perihepatic packing), suture ligation, fibrin gluing or a combination of the three. One patient received factor VIIa. Four patients required liver transplantation (one of whom required retransplantation).

Presentation

The most common findings in HELLP syndrome associated hepatic rupture are epigastric/right upper quadrant pain, hypotension, shock, nausea and vomiting, shoulder pain and headache.^{27,28} There is considerable variation in the presentation of hepatic rupture; signs and symptoms may be mild or completely absent until sudden circulatory collapse occurs.^{10,28} Hepatic rupture may occur prior to delivery, postpartum or during parturition.^{10,26} Consequently, a high index of clinical suspicion to the possibility of hepatic rupture is required when a patient with pre-eclampsia presents with upper abdominal pain.²⁸

Diagnosis

While diagnostic, the triad signs of haemolysis, elevated liver enzymes (ALT and aspartate transaminase) and thrombocytopenia are not invariably present from the outset, may be initially normal and could therefore be falsely reassuring.¹⁰ Elevated liver enzymes may reflect ongoing haemolysis as well as liver injury and the reduced platelet count is due to their increased consumption.²⁹ Radiological imaging may aid with diagnosis.

Ultrasonography may be useful in identifying increased echogenicity of the liver. However, it is operator dependent and of limited value in detecting subtle intra-abdominal changes.^{28,29} CT and MRI have both been described in the diagnosis of HELLP syndrome although imaging can only be used in stable patients. CT and MRI are also used for surveillance of postoperative patients as well as those managed conservatively.

In some cases, the diagnosis of liver rupture is made on finding a haemoperitoneum at the time of emergency Caesarean section.

Management

Early recognition of the gravity of the situation is likely to improve the outcome (Fig 2). In the first instance, the baby/babies and placenta must be delivered as this removes the stimulus of the pathologies. The systemic microangiopathy of HELLP syndrome also affects systems other than the liver. In our series, surgical intervention was necessary for both infarcted bowel and infarcted lung. In addition, there are the potential complications of prolonged intensive care

Figure 2 Management flowchart for patients with HELLP syndrome

admissions, as demonstrated in this series with one patient who required repair of a perforated peptic ulcer.

There are eight reports in the literature of patients with hepatic rupture associated with HELLP syndrome who were successfully managed conservatively in addition to the six patients in our series.^{10,13,14,16} In all cases, the liver haematoma was small and/or contained, and patients underwent serial imaging (CT or ultrasonography) to monitor the haematoma. This should continue until the injury is considered stable or is resolving as hepatic rupture has been reported up to six weeks after initial presentation.^{15,28,30} In unstable patients, urgent laparotomy is recommended, which will likely necessitate packing followed by subsequent transfer to a specialist liver unit.^{10,15} Transfer should only be considered in unstable patients once control of the haemorrhage has been established, usually by packing, followed by temporary closure of the abdomen.^{10,15}

Our approach has evolved following our widening experience of blunt liver trauma.⁵¹ Various techniques are described in the literature including perihepatic packing, fibrin gluing, hepatic artery ligation or embolisation, suture

ligation of the damaged liver tissue, hepatic lobectomy and orthotic liver transplantation.^{10,28,32–37}

For patients transferred after packing, following resuscitation with fluids and blood as well as correction of coagulopathy, a planned relaparotomy should be performed to remove or change packs and further management should be undertaken as appropriate. Liver biopsies may be required at this stage to assess parenchymal damage.¹⁰ In the event of refractory hepatic haemorrhage or progressive fulminant liver failure, a liver transplant should be considered. The decision to proceed to transplantation must be made early for the best chances of success.^{10,15,28} In extreme cases and where a suitable donor is not immediately available, a total hepatectomy with preservation of the inferior vena cava and a portocaval shunt may be considered until a donor organ becomes available. Such an anhepatic state can be survived for approximately 48 hours.^{10,28,36}

Conclusions

HELLP syndrome is fortunately a rare condition but can present acutely in any hospital as a surgical emergency. We have presented a large series of patients with surgical complications resulting from HELLP managed without maternal mortality. The literature review has confirmed that haemodynamically stable patients with HELLP associated hepatic rupture can be conservatively treated successfully. However, in unstable patients, perihepatic packing and transfer to a specialist liver unit is recommended.

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Appendix 1 Summary of 34 case reports in 16 publications describing hepatic rupture associated with HELLP syndrome											
Authors	Age (yrs)	Gestation	Parity	CS?	Platelets ($\times 10^9/l$)	ALT (iu/l)	LDH (iu/l)	Treatment / operative technique	Maternal death?	Cause of death	
Yagmurdur, 2000 ¹¹	38	24 wks	++	N		598		Laparotomy, hysterotomy	N		
Mascarenhas, 2002 ¹²	26	38 wks	0	Y	325	69		Elective right hepatectomy	N		
	28	38 wks	0	Y	64	109		Perihepatic packing ($\times 2$), splenectomy	N		
	30	30 wks	0	Y (stillborn)	40	516		Perihepatic packing	N		
Carlson, 2003 ¹³	27	34 wks	0	Y	80	258		Clinical observation and monitoring	N		
Wicke, 2004 ¹⁴	33	37 wks	2	Y	33	116	383	Clinical observation and monitoring	N		
	26	36 wks	0	Y	143	573	632	Clinical observation and monitoring	N		
	26	22 wks	0	N (induced, stillborn)	35			Percutaneous drainage, ascites	N		
	30	40 wks	0	Y	25	990		Repeated perihepatic packing	N		
	29	34 wks	0	Y	44	730		Laparotomy, hysterectomy, progressive liver damage / complete parenchymal destruction, LTx	N		
Shames, 2005 ¹⁵	37	35 wks	4	N (NVD)	55	+++		Perihepatic packing. Developed coagulopathy, abdominal compartment syndrome, cardiac arrest, OLTx.	N		
Araujo, 2006 ¹⁶	36	36 wks	2		92.0	1,861	1,514	Hepatic artery ligation, cholecystectomy	N		
	44	Postpartum 14							Y	Dead at admission	
	43	24 wks	10					Omental patching	N		
	48	Postpartum 3						Suture ligation	N		
	43	37 wks	15					Hepatic artery ligation, omental patching	N		
	42	34 wks	5					Hepatic artery ligation, omental patching	N		
	45	40 wks	15					Suture ligation, omental patching	N		

(Continued)

Appendix 1 Summary of 34 case reports in 16 publications describing hepatic rupture associated with HELLP syndrome (Continued)

Authors	Age (yrs)	Gestation	Parity	CS?	Platelets ($\times 10^9/l$)	ALT (iu/l)	LDH (iu/l)	Treatment / operative technique	Maternal death?	Cause of death
	42	35 wks	3					Hepatic artery ligation, omental patching	N	
	38	38 wks	4	Y	91.4	768	2,207	Clinical observation and monitoring	N	
	27	33 wks	3					Hepatic artery ligation, cholecystectomy	N	
Mindikoglu, 2006 ¹⁷	25	Day 4 postpartum		N	48	166	475	Conservative management. Recurrent cholangitis 13 yrs later, atrophic left lobe, dilated CBD, left lobectomy.	N	
Dessole, 2007 ¹⁸	35	38 wks	0	Y	95	163		Perihepatic packing ($\times 3$)	N	
Sutton, 2008 ¹⁹	25	30 wks	3	Y					Y	Dead at admission owing to hepatic rupture / haemorrhagic shock
Pavlis, 2009 ²⁰	38	38 wks (twins)		Y	20	2,500		Perihepatic packing ($\times 2$), suture ligation	N	
	38	37 wks		Y	50	2,000		Perihepatic packing ($\times 2$), suture ligation, argon laser	N	
	32	40 wks		N	53	1,752		Perihepatic packing, factor VIIa	N	
Kelly, 2009 ²¹	35	18 wks (IVF)	0		105	2,823	14,361	Perihepatic packing, hysterotomy	N	
Connor, 2009 ²²	28	37 wks	1	Y	39	1,319	2,215	Initial OLTx (ABO incompatible), graft failure, re-LTx	N	
Miguelote, 2009 ²³	28	36 wks	0	Y				Perihepatic packing ($\times 3$)	N	
Varotti, 2010 ²⁴	43	38 wks	2	Y	55	822	2,220	Total hepatectomy, temporary portocaval shunt, OLTx	N	
Chou, 2010 ²⁵	33	26 wks	2	Y	153	315	652	Perihepatic packing	N	
Gutiérrez-Cafranga, 2010 ²⁶	25	39 wks		Y	17	1,060	1,941	Perihepatic packing	N	

CS = Caesarean section; ALT = alanine transaminase; LDH = lactate dehydrogenase; LTx = liver transplant; NVD = normal vaginal delivery; OLTx = orthotopic liver transplant; CBD = common bile duct; IVF = in vitro fertilisation