

## Spontaneous liver rupture in hypereosinophilic syndrome: A rare but fatal complication

Yue-Sun Cheung, Shun Wong, Philip Koon-Ngai Lam, Kit-Fai Lee, John Wong, Paul Bo-San Lai

Yue-Sun Cheung, Kit-Fai Lee, John Wong, Paul Bo-San Lai,  
Department of Surgery, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, China

Shun Wong, Department of Pathology, Princess Margaret Hospital, Hong Kong, China

Philip Koon-Ngai Lam, Department of Anesthesia and Intensive Care, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, China

**Author contributions:** Cheung YS, Lam PKN, Lee KF and Lai PBS designed the work; Cheung YS, Wong S, Lam PKN, Lee KF and Wong J performed the work; Cheung YS, Wong S, Lee KF and Wong J wrote the paper.

**Correspondence to:** Paul Bo-San Lai, Professor, Department of Surgery, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong, China. [paullai@surgery.cuhk.edu.hk](mailto:paullai@surgery.cuhk.edu.hk)

Telephone: +852-26321411 Fax: +852-26377974

Received: August 16, 2009 Revised: October 1, 2009

Accepted: October 9, 2009

Published online: December 14, 2009

Cheung YS, Wong S, Lam PKN, Lee KF, Wong J, Lai PBS. Spontaneous liver rupture in hypereosinophilic syndrome: A rare but fatal complication. *World J Gastroenterol* 2009; 15(46): 5875-5878 Available from: URL: <http://www.wjgnet.com/1007-9327/15/5875.asp> DOI: <http://dx.doi.org/10.3748/wjg.15.5875>

### INTRODUCTION

Spontaneous intrahepatic hemorrhage and liver rupture usually occur in patients with underlying hepatocellular carcinoma or adenoma<sup>[1,2]</sup>. This has also been described in patients with HELLP syndrome, Ehlers Danlos disease and graft-vs-host disease<sup>[3-6]</sup>. In this report, we described a rare case of spontaneous liver rupture in a patient with hypereosinophilic syndrome (HES), of which the diagnosis was delayed, resulting in a fatal outcome.

### CASE REPORT

A 48-year-old man with good past health was admitted because of fever associated with flu-like symptoms and left loin pain for a few days. Initial physical examination showed mild suprapubic and left loin tenderness, and urine dipsticks revealed microscopic haematuria. The chest radiograph was normal and initial blood tests showed eosinophilia and mildly deranged liver function (Table 1). The patient had no clinical signs of allergic reaction. Ultrasound examination of the abdomen revealed no abnormality in the hepatobiliary and urinary system. Urine microscopy showed microscopic haematuria. Ova or parasites were not detected in stool samples. The cultures from blood, sputum and urine were all negative.

Five days after admission, while awaiting further investigations, the patient suddenly developed hypovolemic shock. He rapidly deteriorated to pulseless electrical activity. Cardiopulmonary resuscitation was initiated immediately. He was pale and his abdomen was distended. His pulse returned after resuscitation with 2 L gelofusine. His hemoglobin level dropped from 14.5 to 5 g/dL. In addition, ultrasound examination of the abdomen confirmed the presence of free intraperitoneal fluid. The patient was given six units of unmatched blood during resuscitation. Owing to the unstable hemodynamic state and the diagnosis of exsanguinating intra-abdominal pathology, emergency laparotomy was arranged.

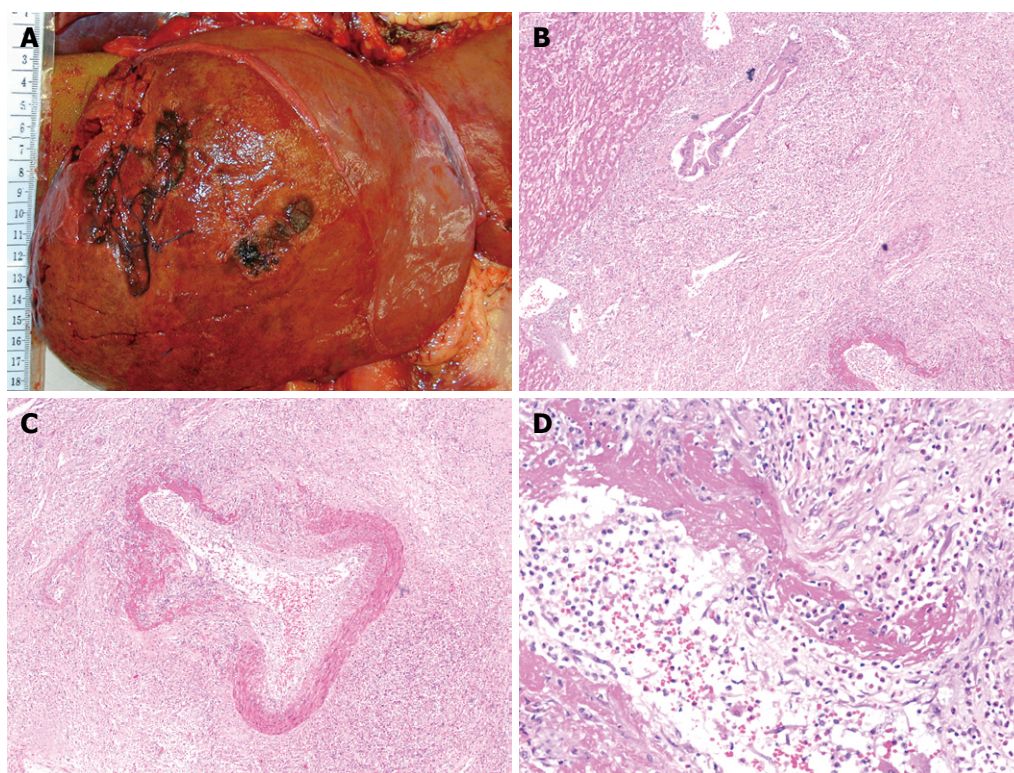
### Abstract

We report a rare case of spontaneous liver rupture in a patient with hypereosinophilic syndrome (HES), of which the diagnosis was delayed, resulting in a fatal outcome. The diagnostic criteria and treatment of HES with hepatic involvement were reviewed. The possible cause of spontaneous liver rupture in HES and its management were also discussed. To our knowledge, this is the first case report of spontaneous liver rupture in HES. We emphasized the need of a high index of suspicion in diagnosing HES, so that early treatment could be initiated.

© 2009 The WJG Press and Baishideng. All rights reserved.

**Key words:** Hypereosinophilic syndrome; Eosinophilia; Hemoperitoneum; Complication; Spontaneous liver rupture

**Peer reviewers:** Dr. Bijan Egtesad, Associate Professor, Department of General Surgery, Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195, United States; Salvatore Gruttadauria, MD, Assistant Professor, Abdominal Transplant Surgery, ISMETT, Via E. Tricomi, 190127 Palermo, Italy; Tadatoshi Takayama, Professor, Department of Digestive Surgery, Nihon University School of Medicine, 30-1 Oiyaguchikamachi, Itabashi-ku, Tokyo 173-8610, Japan



**Figure 1** Post-mortem examination of liver. A: The ruptured site over the right lobe of liver; B: Expanded portal tracts with fibrosis and inflammation (microscopy, HE stain, 100 × magnification); C: Hepatic artery with fibrinoid necrosis (microscopy, HE stain, 200 × magnification); D: Eosinophilic infiltration of the hepatic artery (microscopy, HE stain, 400 × magnification).

**Table 1** Blood tests on admission

Blood test	Value	Unit
WBC	22.6 <sup>1</sup>	10 <sup>9</sup> /L
Eosinophil	6.6 <sup>1</sup>	10 <sup>9</sup> /L
Haemoglobin	13.9	g/dL
Platelet	179	10 <sup>9</sup> /L
PT	12.9	s
INR	1.33	
APTT	38.7	s
Na	133	mmol/L
K	3.7	mmol/L
Urea	3.6	mmol/L
Creatinine	68	umol/L
Protein	74	g/L
Albumin	34	g/L
Bilirubin	25 <sup>1</sup>	umol/L
ALP	207 <sup>1</sup>	IU/L
ALT	55	IU/L
GGT	504 <sup>1</sup>	U/L
CRP	190.1 <sup>1</sup>	mg/L

<sup>1</sup>Elevated values.

On laparotomy, 4 L of blood in the peritoneal cavity and a 10 cm ruptured subcapsular haematoma at anterior sector of right lobe with capsular tear were found. Active bleeding was found at a 9 cm laceration of 5 cm deep at segment VI/VII of the liver (Figure 1A). The liver was not cirrhotic with no palpable space occupying lesion. No abnormality and retroperitoneal haematoma were detected in other intra-abdominal organs. Hemostasis was attempted by suturing the liver laceration and packing. Bleeding from

the raw surface was coagulated with a TissueLink device (TissueLink Medical Inc, Dover, U.S.). However, the patient developed coagulopathy with diffuse oozing after massive transfusion with blood products (10 units of platelet concentrates, 16 units of fresh frozen plasma, and 16 units of pack cells). He required high dose trabecular support during operation. Perihepatic packing was performed and the abdomen was closed. He finally succumbed 1 h after the operation at the intensive care unit.

Post-mortem examination of the patient confirmed the diagnosis of HES with diffuse eosinophilic infiltration to the heart, liver, pancreas, mesentery, kidneys and urinary bladder. Microscopic examination of the liver showed marked eosinophilic expansion in the portal tracts and dilated sinusoids. The portal tract hepatic arteries showed fibrinoid necrosis with eosinophilic infiltration (Figure 1A-D). The lacerated areas showed extensive tissue necrosis and eosinophilic infiltration.

## DISCUSSION

Eosinophilia, defined as an increased eosinophil count in peripheral blood and accumulation in various tissues<sup>[7]</sup>, can be caused by atopic disease, hypersensitivity reaction, parasitic infection, vasculitis and hematological disorders. It is also found in uncommon conditions, such as eosinophilic gastrointestinal disease, Churg-Strauss syndrome and HES<sup>[8]</sup>. The diagnostic criteria for HES, first described by Chusid *et al*<sup>[9]</sup> in 1975, include persistent peripheral blood eosinophilia for more than 6 mo with an absolute



eosinophil count greater than 1500 cells/ $\mu$ L, the presence of organ involvement by eosinophilic infiltration, and exclusion of secondary causes of eosinophilia<sup>[8]</sup>.

The common organ systems involved in HES are hematologic (100%), cardiovascular (58%), cutaneous (56%), neurologic (54%) and pulmonary (49%) systems<sup>[8]</sup>. Liver and gastrointestinal tract are involved in only 20%-30% of patients. Patients with hepatic involvement may develop chronic active hepatitis-like picture and some may suffer from Budd-Chiari syndrome secondary to strictures in inferior vena cava or hepatic veins as a result of eosinophilic infiltration<sup>[10]</sup>. Spontaneous rupture of bladder and esophagus due to eosinophilic infiltration has been reported in the literature<sup>[11,12]</sup>. To our knowledge, this is the first case report of spontaneous liver rupture in HES.

Patients with HES usually present with vague symptoms<sup>[8]</sup>, making its diagnosis difficult and delayed. In our case, the patient presented with fever and flu-like symptoms, which were not specific of any disease. Although his liver function was mildly deranged, the normal initial sonographic appearance of the hepatobiliary system gave further misleading reassurance to the clinicians in identifying the hepatic involvement. Without a high index of suspicion, it was difficult to diagnose HES early and to start treatment before the catastrophic event in our case, namely liver rupture and subsequent mortality.

In order to avoid end organ damage by HES, it is important to establish the diagnosis and start treatment accordingly. Secondary causes of eosinophilia, such as atopic disease, hypersensitivity reaction or parasitic infestation, should be excluded. For patients with deranged liver function, non-invasive investigations including ultrasound of the liver and biliary system and hepatitis serology should be performed to exclude common disorders of the hepatobiliary system. In patients suspicious of HES with hepatic involvement, liver biopsy can be performed to demonstrate eosinophilic infiltration of the liver<sup>[13,14]</sup>. After the diagnosis of HES is confirmed, specific tests on Fip1-like-1 and platelet-derived growth factor receptor  $\alpha$  (FIP1L1-PDGFR $\alpha$ ) fusion gene mutation can guide further treatment using targeted therapy<sup>[8]</sup>.

Successful treatment using corticosteroids has been reported in patients with hepatic HES<sup>[13,14]</sup>. Studies also showed that patients with HES have a good response to targeted therapy according to the result of FIP1L1-PDGFR $\alpha$ <sup>[15,16]</sup>. HES patients showing positive FIP1L1-PDGFR $\alpha$  have a good response to imatinib mesylate, resulting in a normal eosinophil count<sup>[15]</sup>. For patients with negative FIP1L1-PDGFR $\alpha$ , mepolizumab (an anti-interleukin 5 antibody) can effectively stabilize the eosinophil count and reduce the daily steroid dose to less than approximately 7.5 mg prednisolone<sup>[16]</sup>.

The present case of liver rupture was likely caused by eosinophilic infiltration and fibrinoid necrosis of the vascular wall, leading to rupture of hepatic arteries as demonstrated in Figure 1B-D. Although reports are available on cardiopulmonary resuscitation (CPR)-related major liver injury<sup>[16]</sup>, this was unlikely in our case because

the event of deterioration occurred abruptly before the initiation of CPR. The right posterolateral located liver laceration in the absence of ribs fractures further made traumatic cause of the liver rupture unlikely. CPR-related liver trauma usually occurs in the left lobe where it is anatomically close to the point of chest compression<sup>[17]</sup>.

Management and prognosis of spontaneous liver rupture heavily depend on its severity and the hemodynamic stability of patients. For stable patients, non-operative management with transfusion or transarterial selective embolization of the feeding artery has been described with promising results<sup>[1,4]</sup>. For patients with hemodynamic instability or failure in non-operative treatments, surgery for haemostasis is recommended as in our case. Hemostasis can be achieved by temporary tamponade of the liver using packs and portal triad occlusion (Pringle manoeuvre)<sup>[18]</sup>. After initial operative resuscitation and identification of the site of bleeding, different surgical techniques, including direct suture ligation, hepatic resection, selective hepatic artery ligation and perihepatic packing, can be employed for hemostasis depending on the case scenario<sup>[17]</sup>. Despite all these methods, if patients develop coagulopathy, acidosis and multi-organ failure, the chance of survival is low.

Although the clinical course of HES is highly variable and dependent on the degree of organ involvement, early diagnosis and initiation of treatment are of paramount importance. Delay in diagnosis may lead to catastrophic complications. A high index of suspicion is crucial in the management of patients with eosinophilia.

## REFERENCES

- 1 **Leung KL**, Lau WY, Lai PB, Yiu RY, Meng WC, Leow CK. Spontaneous rupture of hepatocellular carcinoma: conservative management and selective intervention. *Arch Surg* 1999; **134**: 1103-1107
- 2 **Erdogan D**, Busch OR, van Delden OM, Ten Kate FJ, Gouma DJ, van Gulik TM. Management of spontaneous haemorrhage and rupture of hepatocellular adenomas. A single centre experience. *Liver Int* 2006; **26**: 433-438
- 3 **Sheikh RA**, Yasmeen S, Pauly MP, Riegler JL. Spontaneous intrahepatic hemorrhage and hepatic rupture in the HELLP syndrome: four cases and a review. *J Clin Gastroenterol* 1999; **28**: 323-328
- 4 **Wicke C**, Pereira PL, Neeser E, Flesch I, Rodegerdts EA, Becker HD. Subcapsular liver hematoma in HELLP syndrome: Evaluation of diagnostic and therapeutic options—a unicenter study. *Am J Obstet Gynecol* 2004; **190**: 106-112
- 5 **Gelbmann CM**, Köllinger M, Gmeinwieser J, Leser HG, Holstege A, Schölmerich J. Spontaneous rupture of liver in a patient with Ehlers Danlos disease type IV. *Dig Dis Sci* 1997; **42**: 1724-1730
- 6 **Barnett SJ**, Weisdorf-Schindle S, Baker KS, Saltzman DA. Spontaneous liver rupture in a child with graft-versus-host disease. *J Pediatr Surg* 2004; **39**: e1-e3
- 7 **Sade K**, Mysels A, Levo Y, Kivity S. Eosinophilia: A study of 100 hospitalized patients. *Eur J Intern Med* 2007; **18**: 196-201
- 8 **Sheikh J**, Weller PF. Clinical overview of hypereosinophilic syndromes. *Immunol Allergy Clin North Am* 2007; **27**: 333-355
- 9 **Chusid MJ**, Dale DC, West BC, Wolff SM. The hypereosinophilic syndrome: analysis of fourteen cases with review of the literature. *Medicine (Baltimore)* 1975; **54**: 1-27
- 10 **Inoue A**, Michitaka K, Shigematsu S, Konishi I, Hirooka M, Hiasa Y, Matsui H, Matsuura B, Horiike N, Hato T,

- Miyaoka H, Onji M. Budd-Chiari syndrome associated with hypereosinophilic syndrome; a case report. *Intern Med* 2007; **46**: 1095-1100
- 11 **Hwang EC**, Kwon DD, Kim CJ, Kang TW, Park K, Ryu SB, Ma JS. Eosinophilic cystitis causing spontaneous rupture of the urinary bladder in a child. *Int J Urol* 2006; **13**: 449-450
- 12 **Cohen MS**, Kaufman A, DiMarino AJ Jr, Cohen S. Eosinophilic esophagitis presenting as spontaneous esophageal rupture (Boerhaave's syndrome). *Clin Gastroenterol Hepatol* 2007; **5**: A24
- 13 **Dillon JE**, Finlayson ND. Idiopathic hypereosinophilic syndrome presenting as intrahepatic cholestatic jaundice. *Am J Gastroenterol* 1994; **89**: 1254-1255
- 14 **Ung KA**, Remotti H, Olsson R. Eosinophilic hepatic necrosis in hypereosinophilic syndrome. *J Clin Gastroenterol* 2000; **31**: 323-327
- 15 **Baccarani M**, Cilloni D, Rondoni M, Ottaviani E, Messa F, Merante S, Tiribelli M, Buccisano F, Testoni N, Gottardi E, de Vivo A, Giugliano E, Iacobucci I, Paolini S, Soverini S, Rosti G, Rancati F, Astolfi C, Pane F, Saglio G, Martinelli G. The efficacy of imatinib mesylate in patients with FIP1L1-PDGFRalpha-positive hypereosinophilic syndrome. Results of a multicenter prospective study. *Haematologica* 2007; **92**: 1173-1179
- 16 **Rothenberg ME**, Klion AD, Roufosse FE, Kahn JE, Weller PF, Simon HU, Schwartz LB, Rosenwasser LJ, Ring J, Griffin EF, Haig AE, Frewer PI, Parkin JM, Gleich GJ. Treatment of patients with the hypereosinophilic syndrome with mepolizumab. *N Engl J Med* 2008; **358**: 1215-1228
- 17 **Meron G**, Kurkciyan I, Sterz F, Susani M, Domanovits H, Tobler K, Bohdjalian A, Laggner AN. Cardiopulmonary resuscitation-associated major liver injury. *Resuscitation* 2007; **75**: 445-453
- 18 **Parks RW**, Chrysos E, Diamond T. Management of liver trauma. *Br J Surg* 1999; **86**: 1121-1135

S- Editor Tian L L- Editor Wang XL E- Editor Zheng XM