

# Delayed bleeding after liver biopsy: a dreaded complication

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## ABSTRACT

**We present an unusual case of percutaneous liver biopsy complicated by delayed haemothorax in a 55-year-old Chinese man with hepatitis C cirrhosis and severe haemophilia A. The patient presented ten days after the initial liver biopsy, and was managed with prompt investigations for confirming the diagnosis, infusion of factor VIII and fresh frozen plasma, and early referral to the surgeon for consideration of surgical repair. The importance of early detection and aggressive therapy is emphasised.**

**Keywords:** biopsy complication, haemothorax, haemophilia, liver biopsy complication, post-biopsy bleeding

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## INTRODUCTION

Percutaneous lesional biopsy under image guidance is a well-accepted means of diagnosing suspicious lesions in patients with cirrhosis.<sup>(1)</sup> Risk of biopsy is usually minor, and consists of pain or small subcapsular liver haematoma. Risk of significant complications, such as haemoperitoneum or need for surgery, are generally unusual at < 1%.<sup>(2)</sup> Though rare, delayed bleeding complications could occur, and prompt recognition is the key to successful management. We hereby present a case of delayed haemothorax, occurring ten days after an image-guided liver biopsy.

## CASE REPORT

The patient was a 55-year-old Chinese man with a known history of severe haemophilia A (0% factor VIII), requiring regular factor VIII transfusion since birth. He was diagnosed with chronic hepatitis C in 1999 during a blood screening test. Subsequent evaluation showed that he was cirrhotic with a Child Pugh score of five (bilirubin 9  $\mu$ M, albumin 42 g/L, prothrombin time 16.5 seconds, activated partial prothrombin time (APTT) 70 seconds, platelets 68  $\times 10^9$ /L). He had no ascites or encephalopathy. Treatment with standard interferon-alpha was attempted in 1999, but was stopped prematurely after four weeks due to intolerable

side-effects. The patient was followed-up for surveillance of hepatocellular carcinoma (HCC) and hepatic decompensation, with liver panel, alpha-fetoprotein level (AFP) testing, and liver ultrasonography performed at six-monthly intervals.

In September 2004, his AFP was noted to be above the upper limit of normal for the first time at 16.8 (normal < 15) ng/dL. Serial computed tomography (CT) and magnetic resonance (MR) imaging of the abdomen performed from September 2004 till October 2005 did not show any enhancing liver lesion. His AFP level remained steady at about 16–20 ng/dL during the same period. CT done in March 2006 showed two 2-cm lesions in segments I and IVb, with features of arterial enhancement and portal venous washout (Figs. 1a and 1b). Diagnosis was consistent with HCC, and the treatment option with liver transplantation was considered.

An ultrasonographically-guided lesional biopsy was arranged in May 2006 to confirm the diagnosis of HCC. His baseline liver panel was: bilirubin 14  $\mu$ M, ALT 70 U/L, and AST 141 U/L. His baseline complete blood count was: haemoglobin 12.7 g/dL, platelets 70  $\times 10^9$ /L, PT 16.3 seconds, APTT 80.7 seconds. 3,000 IU of intravenous factor VIII was given prior to the procedure, with the aim of increasing his factor VIII levels to 100% (patient body weight was 60 kg). A percutaneous subdiaphragmatic approach was employed. Two passes were made at each lesion with an automated spring driven 18G Tru-Cut needle (Travenol Laboratories, Deerfield, IL, USA) during end-expiration, under real-time ultrasonographical guidance. Factor VIII was continued at 3,000 IU 12-hourly for 48 hours post-procedure. He was haemodynamically stable after the biopsy, with no evidence of abdominal tenderness or chest abnormality, and was discharged 48 hours after the procedure.

Ten days postbiopsy, he presented acutely to the emergency department, complaining of right hypochondrial pain aggravated by movement. He did not have any respiratory complaints of cough or shortness of breath, and he denied any trauma to the chest or abdomen. Physical examination revealed tenderness in the right hypochondrium with no rebound or guarding. He was afebrile and haemodynamically stable, with no hypotension or tachycardia. Initial blood tests showed liver panel bilirubin

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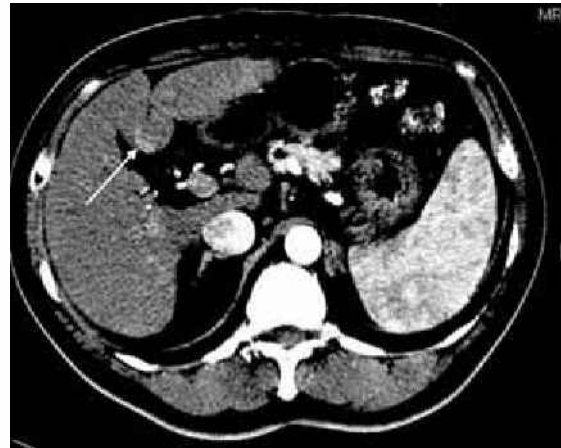
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at 13 uM, ALT 142 U/L, and AST 127 U/L. The initial haemoglobin level was 12.9 g/dL, which was stable compared to the prebiopsy haemoglobin level. The initial chest radiograph showed a small right-sided pleural effusion (Fig. 2). Urgent CT of the abdomen showed a small subcapsular hepatic haematoma, and small right-sided pleural effusion (Fig. 3).

Coagulopathy was urgently corrected with transfusion of factor VIII and fresh frozen plasma. However, he became hypotensive and acutely dyspnoeic on day three of admission. A repeat radiograph showed worsening right-sided pleural effusion (Fig. 4), and his haemoglobin level dropped acutely to 9.1 g/dL. A chest tube was inserted and stale clots were drained. Despite continuous infusion of factor VIII, there was persistent fresh blood draining from his chest drain. Due to the massive and rapid drop in haemoglobin level, and fresh blood noted in the chest tube despite continuous infusion of factor VIII, emergency right exploratory thoracotomy was performed. Intraoperatively, an oozing diaphragmatic vessel was identified and sutured. His recovery following the operation was uneventful. Factor VIII at 3,000 IU 12-hourly was continually administered till one week after thoracotomy. He was last reviewed nine days after thoracotomy, and he remained well and stable. Liver histology revealed well-differentiated HCC.

## DISCUSSION

Percutaneous liver biopsy is a well-established investigation for the accurate diagnosis of focal liver disease.<sup>(3)</sup> Though generally safe, liver biopsy can be accompanied by serious complications. One large prospective study of 9,212 patients by McGill et al reported a mortality rate of 0.11%, and a 0.24% risk of non fatal haemorrhage.<sup>(4)</sup> Haemoperitoneum, usually due to accidental puncture of hepatic vessels during the biopsy procedure with resultant bleeding into the peritoneum, is the most common bleeding complication, occurring in 0.032% of cases. Haemothorax is rarer, occurring in 0.018% of cases, and is thought to be due to accidental injury of diaphragmatic vessels during transdiaphragmatic approach to hepatic lesions.<sup>(5)</sup> There are at least two other case reports in the English literature on haemothorax complicating percutaneous liver biopsy.<sup>(6,7)</sup> Comparison with our case is shown in Table I. In the other two cases, bleeding occurred within hours of the biopsy. This is similar to experience in the literature, where 96% of bleeding complications occurred within 24 hours post-biopsy. Pneumothorax and haemothorax were always diagnosed early, usually within the five days after biopsy,<sup>(3-5)</sup> although the first signs of effusion usually appear 2–5 days after the biopsy.<sup>(5)</sup> It is therefore very unusual for a



**Fig. 1a** Axial CT image of the abdomen taken during the arterial phase shows an enhancing lesion at segment 4b (white arrow).



**Fig. 1b** Axial CT image of the abdomen taken during the portal venous phase shows washout at segment 4b (white arrow).



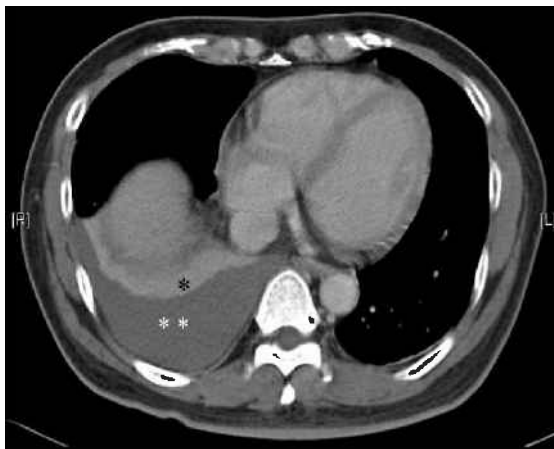
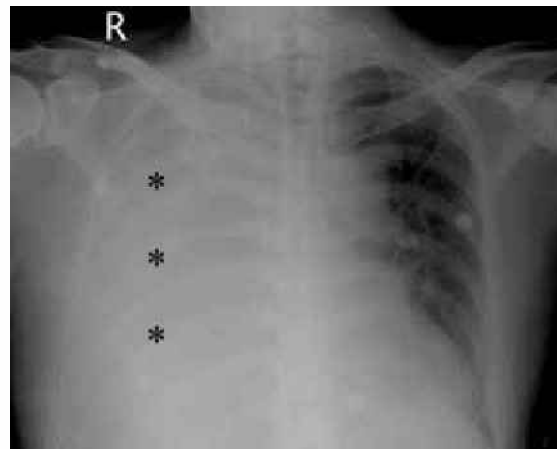
**Fig. 2** Frontal chest radiograph taken on admission for right hypochondrial pain, i.e. ten days after liver biopsy and eight days after initial discharge, shows mild blunting of the right costophrenic angle (black arrow).

haemothorax to present ten days after the biopsy, as in our patient.

**Table I. Comparison of three case reports of haemothorax post-liver biopsy.**

	Majid <sup>(6)</sup>	Chahal and Ready <sup>(7)</sup>	Yeo et al <sup>*</sup>
Age (years)	54	65	55
Gender	Male	Female	Male
Concomitant disease	Nil	Hepatitis C Hepatocellular carcinoma Post-liver transplant Tuberculosis with lung resection of the left upper lobe	Hepatitis C Haemophilia A Diabetes mellitus Previous laparotomy
Indication	Drug-induced liver disease	Transaminitis post-liver transplantation	Suspected HCC
Approach	Percutaneous	Percutaneous	Ultrasonographical-guided, percutaneous
Type of needle	Tru-Cut	15g microvasive ASAP	18G Tru-Cut
Presence of coagulopathy	INR 1.11 APTT 9s delayed Platelet $732 \times 10^9/L$	None	PT 16.3s APTT 80.7s Platelet $70 \times 10^9/L$
Blood loss	4.2 L	No mention	6 L
Time to presentation post-biopsy	Several hours	45 minutes	Ten days
Outcome	Died from hepatic failure two days after thoracotomy	Spontaneous resolution and recovery	Unremarkable recovery after thoracotomy

\* Current study

**Fig. 3** Axial CT image of the abdomen shows a right-sided pleural effusion (white double asterisks) and small subcapsular hepatic haematoma (black asterisks), which were not seen in previous CT images.**Fig. 4** Frontal chest radiograph taken three days after admission (i.e. 13 days after liver biopsy and three days after the chest radiograph shown in Fig 2), shows a massive right-sided pleural effusion (black asterisks), with mild shifting of the mediastinum to the left.

It is likely that adequate haemostasis was initially achieved with periprocedural factor VIII infusion, as evident from his stable haemodynamics and absence of chest signs upon discharge 48 hours after biopsy. The initial clot was probably dislodged in the ensuing days, leading to the massive haemothorax. Hence, our initial management was infusion of factor VIII to correct the underlying coagulopathy. In the setting of haemophiliac patients undergoing liver biopsy, various factor VIII infusion regimes have been employed: factor VII levels were generally increased to 100% level for 2–4 days post-biopsy.<sup>(8–10)</sup> As demonstrated by our case, correction of coagulopathy may

be required in up to ten days after the biopsy. The overall complication rate of liver biopsy in haemophiliacs was 0.33%, which is similar to that quoted in the non-haemophiliac population.<sup>(3,8–10)</sup> While a longer duration of factor VIII infusion could potentially reduce risk of delayed haemorrhage, factor VIII is costly, and hence, further cost-analysis studies are needed to define the optimal duration of factor VIII infusion. Patient education on the risk of delayed haemorrhage, and a high index of suspicion is probably more important and cost effective in this respect. This was shown in our case when the patient attended to the emergency department once he was unwell, and prompt

investigations and transfusion of factor VIII were initiated once diagnosis of delayed bleeding was made. There is no general consensus on the management of postliver haemothorax, as it is a rare complication. While Majid managed their patient with thoracotomy, Chahal and Ready managed their patient conservatively.<sup>(6,7)</sup> Although percutaneous hepatic angiogram and embolisation are the first line of management for patients with postliver biopsy haemoperitoneum, the role of angiogram with embolisation of diaphragmatic vessel has not been well described, as blood supply to the parietal diaphragm arises from vessels from the chest wall and abdominal wall.<sup>(11)</sup>

In view of the higher risk of haemorrhagic complications in patients with bleeding tendency, several techniques have been described to reduce post-biopsy bleeding. Papini et al randomised 200 patients with chronic liver disease into percutaneous liver biopsy with or without ultrasonographical guidance, and found better biopsy sample size and lesser haemorrhagic complications in the ultrasonographical guidance group.<sup>(12)</sup> In a randomised, controlled trial by Sawyerr et al, 100 patients with coagulopathy were biopsied by either plugged percutaneous liver biopsy, or transjugular transvenous liver biopsy, and haemorrhagic complications were respectively present in 3.5% and 0% (p-value is not significant in the cases).<sup>(13)</sup> Inabnet and Deziel reported a case series of 22 patients with coagulopathy and ascites, all of whom underwent liver biopsy laparoscopically, and haemorrhagic complication was only reported in one of 22 patients.<sup>(14)</sup> More recently, Jeffers et al reported no haemorrhagic complications in 77 Child's B and C cirrhotic patients who were given recombinant factor VIIa prior to percutaneous liver biopsy.<sup>(15)</sup> Finally, use of a coaxial biopsy system where multiple biopsy could be obtained through a single puncture, could have been safer, when compared to multiple punctures of the liver lesion, as in our case.

These techniques are related to various mechanisms. Image-guidance helps avoid risk of puncturing hepatic vessels as compared to "blind" percutaneous biopsy. Although a randomised, controlled trial is lacking, CT or MR imaging-guided liver lesional biopsy may be better than lesional biopsy under ultrasonographical guidance, as lesions and other structures are better visualised on CT and MR imaging, compared to ultrasonography.<sup>(16)</sup> In plugged percutaneous biopsy, the biopsy tract is embolised after liver tissues are obtained. In transjugular transvenous liver biopsy, any hepatic blood loss would only be directed through the hepatic veins back to the intravenous space. Any immediate haemorrhagic complications in laparoscopic liver biopsy could be arrested by either

direct compression or thermal coagulation. In addition, recombinant factor VIIa is one of the most effective coagulative factors in patients with coagulopathy from liver cirrhosis. Last but not least, risk of complications increases when more passes are made during the biopsy procedure, and hence, better diagnostic yield of multiple biopsy passes must be balanced with potential higher risk of complications. On hindsight, haemothorax could possibly be avoided if only one pass of biopsy was made to one of the two liver lesions. Ultimately, the most cost-effective technique of performing liver biopsy in high risk patients could well be a combination of two or more of the techniques mentioned.

In conclusion, physicians must be aware of the potential risk of delayed a bleeding in patients undergoing liver biopsy, especially in those with a bleeding tendency. While the optimal duration of factor VIII infusion postliver biopsy is unknown, physicians must be vigilant in considering delayed bleeding complications in managing such patients. Patient education on the signs and symptoms of potential complications post-biopsy must be stressed upon discharge. Early detection of such complications and prompt correction of coagulopathy are the key to good patient outcome.

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