



Spontaneous liver rupture associated with anticoagulant therapy

A case report



Ann Ital Chir, Digital Edition 2017, 6
pii: S2239253X17026408 - Epub, Jan. 20
free reading: www.annitalchir.com

Marco Clementi, Sara Colozzi, Stefano Guadagni, Beatrice Pessia, Federico Sista, Mario Schietroma, Andrea Della Penna, Gianfranco Amicucci

Department of Surgery, University of L'Aquila, L'Aquila, Italy

Spontaneous liver rupture associated with anticoagulant therapy. A case report

Spontaneous hepatic rupture without underlying liver diseases is uncommon entity. We report a rare case of spontaneous rupture of liver hematoma in patient treated with warfarin and enoxaparin sodium because of pulmonary embolism. Two days after admission the patient complained generalized abdominal pain and hemodynamic instability. The abdominal US and TC scan revealed free fluid and lesion at right liver lobe. The patient, despite intravenous fluid support and blood transfusion, was hemodynamically unstable and urgent laparotomy was needed. At laparotomy, it was found that a subcapsular haematoma, involving the diaphragmatic face of the right liver, had ruptured into peritoneum. Hepatic bleeding was stopped using a conservative approach by Pringle manoeuvre, parenchymal suture and fibrin sealant. There was no complication related to hepatic surgery but the patient died because of new massive pulmonary embolism 10 days after surgery. The absence of underlying liver pathology was confirmed by autopsy examination. This case report suggests that the possibility of spontaneous liver rupture should be considered in patients being treated with oral anticoagulants. Early diagnosis are critically important given the high morbidity and mortality. Aggressive resuscitation and immediate exploratory laparotomy is needed when hemodynamic instability occurs. In our case a quick, safe and effective control of bleeding was provided by partial vascular occlusion, parenchymal suture and topical haemostatic agent.

KEY WORD: Anticoagulant therapy, Atraumatic hemoperitoneum, Liver hematoma

Introduction

Atraumatic liver rupture is a uncommon event, associated with high morbidity and mortality. In most cases the spontaneous liver ruptures is consequent to an underlying hepatic disease like a primary benign or malignant neoplasms, metastatic liver disease, inflammatory disor-

ders and pregnancy related conditions ¹. During anticoagulant therapy cases of hematoma of the rectus abdominalis muscle, spleen, small intestine, adrenal gland, kidney and retroperitoneum have been reported ². Spontaneous liver hematomas induced by anticoagulation therapy are rare ³⁻⁵.

We describe a case of spontaneous rupture of liver hematoma in a patient treated by Warfarin for pulmonary embolism.

Case Report

86 years old male, treated in intensive care for pulmonary embolism subsequent to a thrombosis of left femoral vein. He had an history of hypertension and peripheral vascular disease, but no history of trauma or bleeding

Pervenuto in Redazione Settembre 2016. Accettato per la pubblicazione Dicembre 2016.

Correspondence to: Sara Colozzi, Università degli Studi di L'Aquila, Facoltà di Medicina e Chirurgia Dipartimento di Scienze Chirurgiche, clo Ospedale "S. Salvatore", Edificio Delta 6, 67100 Coppito (AQ), Italy (e-mail: sara.colozzi@libero.it)

diathesis. He was treated two months before with an aneurysm endovascular repair of an aorto-iliac aneurysm. On admission to the hospital a total-body CT-scan showed no hepatic lesions. He was initially treated with anticoagulant warfarin (8.75 mg per day) and enoxaparin sodium (8000 U.I.) once daily by subcutaneous injection. Other medications was omeprazole (20 mg) once daily. His blood pressure was 110/70 mmHg, pulse rate was 85 p/min and laboratory test showed 12.9 g/dl hemoglobin, %PT 53%, aPTT 33sec and INR, 1.49. Two day later, the patient complained abdominal pain in the right upper quadrant, abdominal distention and hemodynamic instability (blood pressure 90/65 mmHg, pulse 115/min). Abdominal ultrasonography (US) revealed a large liver haematoma involving the right lobe and extensive free abdominal collection. A contrast CT scan confirmed the presence of blood density of the abdominal free fluid and a large liver haematoma in segments VIII, VII, VI, and IVB with rupture of the Glisson's capsule at the surface of VII segment. There was no enhanced contrast leakage (Fig. 1). The patient, despite intravenous fluid support and blood transfusions, continued to present hemodynamic instability and a fall in hemoglobin to 8.0 g/L with PT 36%, aPTT 35 sec and INR 1.96.

The patient was transferred immediately to the operating room for an urgent laparotomy. At the opening of peritoneum 1500 ml of free hemoperitoneum was drained. Liver exploration showed an extensive haematoma involving almost the entire right lobe of the liver that was bleeding from a Glisson's tear on VII segment. The right liver was mobilized severing the falciform, coronary and triangular ligaments to optimize lesion exposure. We packed the liver waiting in vain for possible cessation of bleeding, but it was still active owing

a deep laceration of the liver parenchyma across the hematoma. Therefore after performing the Pringle maneuver to block the blood inflow and reduce the active bleeding has been reduced, we packed again the liver and at stop bleeding we completed hemostasis by suture ligation of the bleeding points and hepatorrhaphy. At the end of the procedure fibrin sealant patches was used on cut surface of liver to secure haemostasis.

During surgery 2 U of packed red cells and 6 U fresh frozen plasma units were administered to the patient. Two more transfusion of packed red cells was administered the day after surgery. The patient remained hemodynamically stable in the 48hours after surgery and hemoglobin rose to 11.0 g/dl, PT 52%, aPTT 33 sec and INR 1.51. Patient received anticoagulant therapy with enoxaparin sodium 8000UI. Unfortunately the patient developed a new pulmonary embolism and died from cardiac arrest (autopsy findings) during the post-operative day 10. The absence of underlying pathology was confirmed by autopsy examination.

Discussion

Atraumatic liver rupture is a rare condition most often associated with a malignant or benign liver disease or occurs in context of pregnancy related syndrome (HELLP syndrome)^{1,6-13}. Although in literature atraumatic and spontaneous liver rupture are considered synonymous, they should be classified like two different entities: the atraumatic one when the rupture occurs in a liver with underlying disease and spontaneous one when the rupture occurs in a normal liver.

Chen et al shown that in 85.7% of cases, the atraumatic pathologic rupture of the liver is associated with HCC,

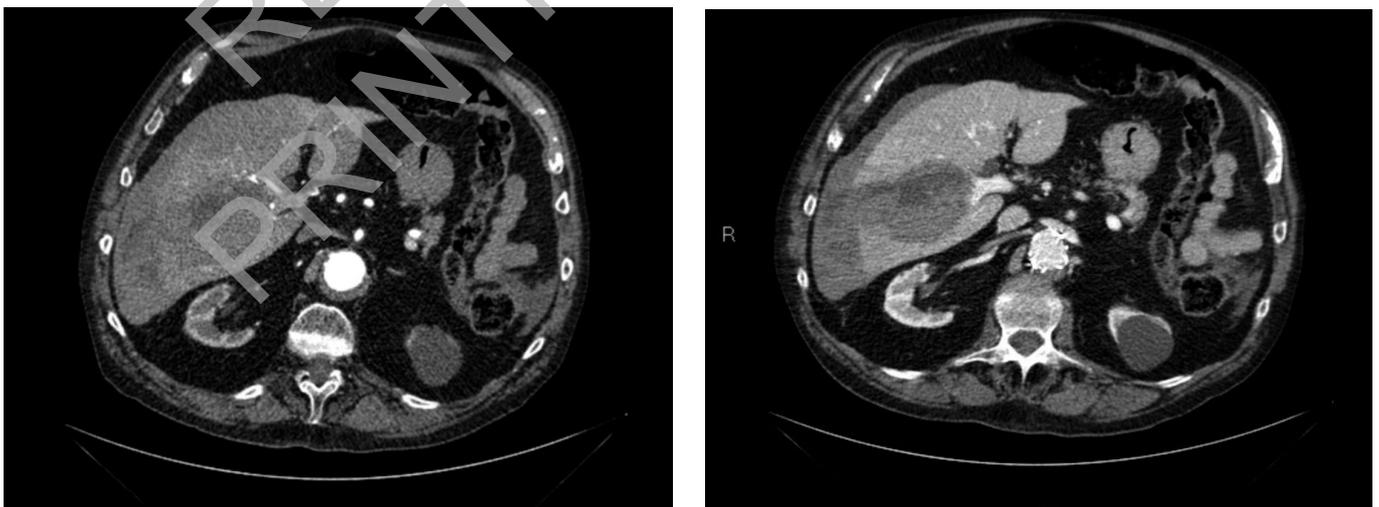


Fig. 1: Abdominal CT scan showing abdominal free fluid and a large liver haematoma involving almost the entire right lobe of the liver with a Glisson's tear on the surface of VII segment – (A: arterial phase, B: venous phase)

followed by adenoma, cirrhosis, hemangiomas and liver metastases⁶. Hepatic rupture in absence of underlying pathology is an extremely rare occurrence¹⁴. Warfarin is a widely used anticoagulant prescribed for patients with venous thrombosis, pulmonary embolism, chronic atrial fibrillation, and prosthetic heart valves. During treatment with oral anticoagulants the risk of severe bleeding has been estimated to be 0.6%-1.0% per year's treatment and the gastrointestinal tract was the most common site of bleeding^{15,16}. The most common site of anticoagulant-related bleeding resulting in acute abdomen is the wall of the small intestine and colon^{17,18}. Only few cases of spontaneous liver hematomas have been reported in literature following oral anticoagulant therapy³⁻⁵. Warfarin sodium can cause severe gastrointestinal bleeding even when administered in the therapeutic range¹⁹. Drugs interactions may influence the efficacy of Warfarin therapy and may make significant contribution to hemorrhagic complications interfering with its pharmacokinetic or pharmacodynamic¹⁵. Other risk factors have been associated with a significantly increased risk of bleeding during warfarin therapy: old age, diabetes mellitus, the presence of malignancy, hypertension, liver dysfunctions, severe chronic kidney disease, elevated creatinemia, anemia, bleeding disorder and instability of the INR (INR > 3.0, pre-treatment INR > 1.2)^{16,17}. Using warfarin together with omeprazole may increase the risk of bleeding in rare cases²⁰⁻²². However, the effect of the interaction between warfarin and omeprazole has been described as having minor or limited clinical significance²³ and, when it occurs, should occur with an increase in INR and prothrombin time. In our case the concomitant administration of omeprazole and warfarin did not affect the coagulation times that remained within the expected range during the whole period of treatment. Furthermore, to obtain a rapid anticoagulant effect because of pulmonary embolism, the patients received low-molecular-weight heparin during the first days of warfarin therapy as a "bridge" but, when liver rupture occurred, the PT and INR were still below the recommended therapeutic range²⁴. Detailed history and careful physical examination excluded any cutaneous or subcutaneous symptoms or signs like wounds, ecchymosis, hematoma, swelling or pain related to traumatic injury during treatment. The autopsy examination confirmed the absence of underlying hepatic disease so that the definite cause of the liver rupture in our case remain undetermined.

Spontaneous liver rupture is usually preceded by subcapsular hematoma⁹. Initial symptoms related to the capsular distension are the epigastric/right hypocondrial pain. The free hemoperitoneum resulting from capsule rupture causes abdominal distension, peritoneal signs and can lead to hypovolemic shock⁷. The diagnosis of hemoperitoneum is confirmed by imaging studies like abdominal US and abdominal CT scan. The management of atraumatic liver injury include conservative treatment,

trans-catheter embolization of hepatic artery and surgery. In stable patients with intact liver capsule and contained hematoma conservative treatment with serial haemoglobin and US monitoring, and CT scan is indicated¹⁴. Conservative treatment with Transarterial Hepatic embolization has been proposed to treat liver injuries with bleeding for hemodynamically stable patients in which extravasation of contrast on the initial abdominal CT scan was demonstrated²⁵⁻²⁷. However this procedure require expertise of interventional radiologist which is usually only available in specialized centers.

When conservative treatment fails or hemodynamic instability occurs emergency laparotomy is needed. Local liver haemostasis can be achieved by hepatic suture, cauterization, argon laser use, perihepatic packing, hepatic artery ligation or hepatectomy^{10,13,28}. Surgical equipe experience on liver surgery, underlying hepatic disease, general condition of the patient and availability of advanced haemostatic surgical devices can affect the surgeon choice. Pads packing is the simplest procedure and has been indicated as an effective method to control haemorrhage from liver parenchyma injury^{29,30}.

Surgical procedures such as hepatotomy, hepatorrhaphy, direct vessel ligation and non-anatomic hepatic resection have replaced the prolonged and extensive procedures such as anatomic liver resection related to high morbidity and mortality³¹⁻³⁴. In our patients, immediate surgical exploration was mandatory because of hemodynamic instability. To reduce the operative blood loss, that seems the main determinants of perioperative morbidity and mortality especially in emergency conditions, we adopted the Pringle manoeuvre as blood inflow blocking method. More aggressive hepatic vascular occlusion was a time consuming procedure and may causes severe hypotension so that should be reserved when more simple vascular occlusion fails. When active bleeding was reduced, we completed hemostasis by packing, suture ligation of the bleeding points and hepatorrhaphy avoiding a liver resection. Finally, fibrin sealant patches was used on treated surface of liver to secure haemostasis. Topical hemostatic agents like fibrin sealant and cellulose are widely used for the control of bleeding during hepatic surgery when standard surgical techniques prove insufficient. We used fibrin sealant patches because they seems provide better secondary control of local bleeding than cellulose patches in patients undergoing liver resection.

Conclusion

Although rare, spontaneous liver rupture is to be considered in case of atraumatic hemoperitoneum during anticoagulant therapy even when INR remains inside the recommended therapeutic range. A high index of suspicion and early diagnosis are critically important to reduce the high mortality rate related to this adverse event.

Quick, safe and effective control of bleeding may be provided by Pringle maneuver, parenchymal suture and topical haemostatic agent.

Riassunto

La rottura spontanea di fegato in assenza di malattie epatiche concomitanti è un evento abbastanza raro. Nel nostro lavoro illustriamo un raro caso di rottura spontanea di fegato in un paziente in trattamento con warfarin ed enoxaparina sodica a causa di una embolia polmonare. Due giorni dopo la dimissione il paziente lamentava dolori addominali generalizzati e presentava instabilità emodinamica. L'ecografia addominale e la TC addome mostravano versamento libero in addome ed una lesione a carico del fegato destro. Nonostante la terapia infusione di supporto e le trasfusioni, il paziente continuava ad essere instabile da un punto di vista emodinamico; si decideva pertanto di eseguire una laparotomia d'urgenza. Alla apertura della cavità addominale vi è stato il riscontro di un ematoma sotto-glissoniano che coinvolgeva la faccia diaframmatica del fegato di destra e che si era aperto in addome. Il sanguinamento è stato controllato con approccio conservativo utilizzando la manovra di Pringle, sutura del parenchima ed uso di emostatici. Non si sono osservate complicanze correlate all'intervento ma il paziente è deceduto a causa di un nuovo episodio di embolia polmonare massiva, in decima giornata postoperatoria. L'esame autoptico ha confermato l'assenza di patologie epatiche concomitanti. La possibilità di una rottura spontanea di fegato andrebbe sempre considerata in pazienti in trattamento con anticoagulanti. La diagnosi precoce è fondamentale data l'alta morbilità e mortalità. Una terapia rianimatoria aggressiva ed una laparotomia esplorativa d'urgenza sono indicate in caso di instabilità emodinamica. Nel nostro caso, un rapido e sicuro controllo dell'emostasi sono stati possibili grazie ad una emostasi compressiva, sutura diretta del parenchima ed uso di emostatici.

References

- Ching-Jung Liu, Rong-Nan Chien, Cho-Li Yen, Jia-Jang Chang: *Spontaneous rupture of the liver in a patient with chronic hepatitis B and D*. World J Surg, 2007; 28(13): 4405-407.
- Babb RR, J Spittel IA Jr, Bartholomew LG: *Gastroenterologic complications of anticoagulant therapy*. JAMA, 1968; 43:738-51.
- Erichesen C, Sndena K, SreiDe AJ, Andersen A, Tysvaer: *Spontaneous liver hematomas induced by anticoagulation therapy. A case report and review of the literature*. Hepato-gastroenterol, 1993; 40: 3402-406.
- Dizadji H, Hammer R, Strzyz B, Weisenberger J: *Spontaneous rupture of the liver. A complication of oral anticoagulant therapy*. Arch Surg, 1979; 114:734-35.
- Behranwala KA, Tisdall M, Habib NH, Canelo R: *Spontaneous bilobar subcapsular hematoma of the liver while undergoing anticoagulation therapy: our experience and review of the literature*. Int Surg, 2004; 89:212-16.
- Chen ZY, Qi QH, Dong ZL: *Etiology and management of hemorrhage in spontaneous liver rupture: A report of 70 cases*. World J Gastroenterol, 2002; 8: 1063-66.
- Miyamoto M, Sudo T, Kuyama T: *Spontaneous rupture of hepatocellular carcinoma: A review of 172 Japanese cases*. Am J Gastroenterol, 1991; 86:67-71.
- Chearana O, Plengvanit U, Asavanich C, Damrongsak D, Sindhvananda K, Boonyapisit S: *Spontaneous rupture of primary hepatoma: report of 63 cases with particular reference to the pathogenesis and rationale treatment by hepatic artery ligation*. Cancer, 1983; 51:1532-536.
- Ralston SJ, Schwaizberg SD: *Liver hematoma and rupture in pregnancy*. Semin Perinatol, 1998; 22:141-48.
- Aldemir M, Baç B, Taçyildiz I, Yagmur Y, Keles C: *Spontaneous Liver Hematoma and a Hepatic Rupture in HELLP Syndrome: Report of Two Cases*. Surg Today, 2002; 32:450-53.
- Xavier P, Melo R, Amândio V, Beires J, Pereira-Leite L: *Subcapsular hepatic hematoma in an otherwise uncomplicated pregnancy*. Arch Gynecol Obstet, 2002; 266:44-45.
- Calderon EG, Khawar S, Cunningham JA, Russell LD, Alpert MA: *Pulmonary artery thrombus and subcapsular liver hematoma in a patient with HELLP syndrome: A therapeutic conundrum*. Am J Med Sci 2002; 323:151-54.
- Smith LG Jr, Moise KJ Jr, Dildy GA 3rd, Carpenter RJ Jr: *Spontaneous rupture of liver during pregnancy: Current therapy*. Obstet Gynecol, 1991; 77(2): 1717-5.
- Ndzengue A, Hammoudeh F, Brutus P, Ajah Ofem, Purcell R, Leadon J, et al.: *An obscure case of hepatic subcapsular hematoma*. Case Rep Gastroenterol, 2011; 5:223-26.
- Coon WW: *Use of anticoagulant drugs*. Rational Drug Therapy, 1979; 13:1-6.
- Limdi NA, Beasley TM, Baird MF, Goldstein JA, McGwin G, Arnett DK, et al.: *Kidney function influences warfarin responsiveness and hemorrhagic complications*. J Am Soc Nephrol, 2009; 20: 912-21.
- Fitzmaurice DA, Blann AD, Lip GY: *Bleeding risks of antithrombotic therapy*. BMJ, 2002; 325: 828-31.
- G De Santis, F Sista, A Giuliuani, S Leardi: *Idiopathic intramural hematoma of the sigmoid colon. A case report*. Ann Ital Chir, 2011; 82 (5):395-97.
- Kostka R, Havluj L, Jirava D, Novák L, Vach B, Weiss J: *Hemorrhagic complications of warfarin therapy*. Rozhl Chir, 2010; 89:124-29.
- Klasco RK (Ed): *DRUGDEX® Drug Evaluation – warfarin*. Last modified 12/07/13 MICROMEDEX(R) Healthcare Series. Accessed via <http://www.thomsonhc.com/home/dispatch> on 23/07/13.
- Blume H, Donmath F, et al.: *Pharmacokinetic drug interaction profiles of proton pump inhibitors*. Drug Safety, 2006; 29(9):769-84.
- Uno T, Sugimoto K, et al.: *The role of cytochrome P2C19 in R-warfarin pharmacokinetics and its interaction with omeprazole*. Therapeutic Drug Monitoring, 2008; 30:276-81.

23. Baxter K (Ed): *Stockley's Drug Interactions. Coumarins + Proton Pump Inhibitors* (Updated 2 November 2012). London: Pharmaceutical Press. Electronic version. Accessed via www.medicinescomplete.com on 23/07/13.
24. M Kuruvilla, C Gurk-Turner: *A review of warfarin dosing and monitoring*. Proc (Bayl Univ Med Cent), 2001; 14(3):305-06.
25. Petroianu A: *Arterial embolization for hemorrhage caused by hepatic arterial injury*. Digest Dis Sci, 2007; 52(10):2478-481.
26. Tzeng WS, Wu RH, Chang JM, Lin CY, Koay LB, Uen YH et al: *Transcatheter arterial embolization for hemorrhage caused by injury of the hepatic artery*. J Gastroenterol Hepatol, 2005; 20(7):1062-068.
27. Petroianu A: *Transcatheter arterial embolization for hemorrhage caused by injury of the hepatic artery*. J Gastroenterol Hepatol, 2005; 20(7):973-74.
28. Landon MB: *Diseases of the liver, biliary system and pancreas*. In Creasy RK, Resnik R, Iams JD(eds): *Maternal-Fetal Medicine: Principles and Practice*. Philadelphia: Saunders, 2004; 1132.
29. Krige JE: *Liver fracture and bleeding*. Br J Surg, 2000; 87:1615-616.
30. Being-Chuan Lin, Jen-Feng Fang, Ray-Jade Chen, Yon-Cheong Wongc, Yu-Pao Hsu: *Surgical management and outcome of blunt major liver injuries: Experience of damage control laparotomy with perihepatic packing in one trauma centre*. Injury, 2014; 45 122-27.
31. Beal SL: *Fatal hepatic hemorrhage: an unresolved problem in the management of complex liver injuries*. J Trauma, 1990; 30:163-69.
32. Duane TM, Como JJ, Bochicchio GV, Scalea TM: *Reevaluating the management and outcomes of severe blunt liver injury*. J Trauma, 2004; 57:494-500.
33. Fang JF, Chen RJ, Lin BC, Hsu YB, Kao JL, Chen MF: *Blunt hepatic injury: Minimal intervention in the policy of treatment*. J Trauma, 2000; 49:722-28.
34. Feliciano DV, Mattox KL, Jordan Jr GL, Burch JM, Bitondo CG, Cruse PA: *Management of 1000 consecutive cases of hepatic trauma (1979-1984)*. Ann Surg, 1986; 204(4):433-45.
35. Y Genyk, T Kato, JJ Pomposelli, JK Wright Jr., LS Sher, V Tetens, WC Chapman: *Fibrin Sealant Patch (TachoSil) vs Oxidized Regenerated Cellulose Patch (Surgicel Original) for the Secondary Treatment of Local Bleeding in Patients Undergoing Hepatic Resection: A Randomized Controlled Trial*. J Am Coll Surg; (in press).

READ-ONLY COPY
PRINTING PROHIBITED