CT and MRI imaging at the acute phase of inaugural non-traumatic hepatic haemorrhages

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Abstract
Purpose: Although rare, non-traumatic hepatic haemorrhage is a known complication of liver tumors. In cases where the haemorrhage is the first clinical event, diagnostic work-up is critical.
Material and methods: This retrospective study was conducted between July 2001 and March 2011. Acute phase CT-scan and MRI imaging in patients diagnosed with non-traumatic liver hematomas were interpreted with particular attention to the radio-semiotic characteristics of hematomas and liver lesions. Those findings were then confronted to the patients’ final diagnoses.
Results: Twelve patients were included (mean age of 42 years). In seven of them a suspect liver lesion was discovered in the acute CT-Scan or MRI imaging. All lesions were strongly hyper vascular. The haemorrhage revealed hepatocarcinoma in four patients, liver adenoma in two and focal nodular hyperplasia in another.
Conclusion: It is important in spontaneous liver haemorrhage to consider the high probability of hepatocarcinoma or potentially malignant lesions even when the patient has no known hepatic disorders, and especially in young patients. The results of this study show that imaging is a key issue at the acute phase of inaugural non-traumatic hepatic haemorrhages and requires a simple but complete triphasic injected protocol.
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Spontaneous liver haemorrhage is defined as any hepatic haemorrhage occurring without any traumatism. It is a rare disorder, potentially fatal, associated with a high morbidity [1].

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Non-traumatic intrahepatic haemorrhages can occur in the natural history of any liver tumor but hepatocellular carcinomas and hepatic adenomas widely dominate the other histological types. [2–4].

Exceptionally, focal nodular hyperplasia [5], liver metastases [4] and, to a lesser extent, any type of intrahepatic tumoral processes (angiomyolipoma…) are likely to give rise to spontaneous liver haemorrhages.

Beyond the tumoral causes, other pathological conditions, whether local or general, isolated or associated, are likely to be the cause of hepatic bleeding. They are summed up by the HELLP syndrome [6,7], all congenital, acquired or iatrogenic coagulation anomalies, amylosis [8], hepatic peliosis [9], and certain connective tissue diseases [10]. Diagnostic work-up of spontaneous intrahepatic haemorrhage is easy when there is an underlying tumoral lesion or known pathological condition at a risk of haemorrhage [11,12] although, for some patients, haemorrhage is the first clinical manifestation [13] hence aetiological diagnostic work-up is critical, especially at the acute phase as the heavy therapeutic solutions are associated with high morbidity [1,14,15]. This retrospective, single centre case study aims at:

- determining efficiency of CT and MRI imaging in acute phase diagnosis work-up of spontaneous inaugural hepatic haemorrhages (that is, occurring without any traumatism in patients until then free of any known situation involving a risk of liver hemmorrhage);
- specifying the radio-semiological elements at stake in the diagnosis work-up of this clinical situation.

Materials and methods

This study is a retrospective analysis of cases between July 2001 and March 2011.

During this time period, all patients presenting with spontaneous liver haemorrhage, for which CT and MRI imaging during the acute phase (i.e., the first 15 days) was available in digital format, were included. Patients were recruited by using a keyword search in all CT or MRI imaging reports.

The medical file of each patient was then studied to exclude patients presenting at least one of the following criteria:

- peripartum patients, with a HELLP syndrome, whether or not confirmed;
- patients with a history of liver lesion, whatever the type;
- patients with a recent history of abdominal surgery;
- patients that recently underwent a traumatism, surgical intervention, biopsy or any invasive hepatic procedure;
- patients without follow-up information after baseline imaging.

Imaging data of the acute phase was examined blind to the final diagnosis and the following elements of radiosemiological interest were assessed:

- haematoma: location, size (greatest axial diameter), attenuation before and after contrast injection, homogeneity, hepatic capsule’s rupture, haemoperitoneum;
- hepatic lesions (when visible): number, size, location, MRI signal, intralesional vascularisation;

- hepatic parenchyma: signs of chronic liver condition (steatosis, cirrhosis, other), permeability of the afferent and efferent vessels, haemodynamic disorders (localized or extensive);
- any other abdominal lesion discovered on the baseline imaging.

The last phase of the analysis consisted, in a confrontation between the CT and MRI imaging in the acute phase with the final diagnosis determined for each patient.

Results

Thirty-five patients were eligible for inclusion between January 2001 and March 2011. Among them, eight presented with known hepatic lesions with (adenoma, hepatocellular carcinoma, hepatic actinomycosis), three were in a peripartum context (including two with a confirmed HELLP syndrome), two had a post-traumatic liver haemorrhage, and one underwent a cholecystectomy a month prior to the diagnosis. Imaging data was not available in digital format for six patients and three patients only had one imaging examination without any follow-up. Therefore, 12 patients were recruited since they did not present any of the exclusion criteria.

Among them, 10 benefited from an abdominal CT with injection of contrast (83.3%) at the acute phase and five (41.7%) of an MRI.

The mean age at the time of diagnosis was 41.9 years (SD = 17.1 years), with a mean age of 43.5 years for the women (SD = 16.9 years) and 34.4 years for the men (SD = 15.5 years). There were 10 women and two men.

Characteristics of the haemorrhage

The largest haemorrhage measured 28 cm and the smallest 4.5 cm (mean: 11.7 cm; SD = 5.8 cm). They all appeared very heterogeneous on the CT-scan, with distinctly hyperdense portions and more hypodense zones.

In nine patients (75%), the haemorrhage was at least in part of liver segment VI or VII.

Characteristics of the intrahepatic lesions discovered

In seven patients, at least one lesion was visible at the acute phase (66.7%). The mean size of the nodules was 78.2 mm (SD = 85.5). The mean enhancement, after injection of contrast agent, of the visible nodules directly in contact with the haematoma [5] was 66% (59–74%) at the arterial time, attesting to the highly hypervascular nature (wash-in) of these lesions with a sharp tendency to early wash-out (Fig. 1).

Five patients (41.7%) underwent a liver MRI during the acute phase. This helped specify the characteristics of the nodules that seem to be iso or discretely hyper-T1 (no hypo-T1) and all were distinctly hypervascular.


Hepatic parenchyma and intrahepatic vessels

Hypervascularisation of the hepatic parenchyma was noted in 11 patients (84.6%). In eight patients (61.5%), this was limited to direct contact with the haemorrhage, and in three patients (23.1%) it extended to an entire lobe (Fig. 2).

Evolution, diagnosis and confrontation to the imaging findings

A suspect lesion was visible in seven patients (58.3%) at the acute phase.

Among them, the diagnosis of hypervascular tumour indicated in the initial imaging was quickly invalidated for one patient and its absence was confirmed after a 32-month follow-up.

Among the five patients where a lesion was not visible at the acute phase, the follow-up helped objectify a lesion in one patient. There was a 12-week period from the first clinical signs to the detection of the nodule (hypervascular tumour in contact with the haemorrhage). At the end of our study, a definite diagnosis was made in 10 patients (83%), confirmed by anatomopathology in nine of them (75%). At the end of the diagnosis work-up, liver haemorrhages revealed, in the seven patients with a suspect lesion:

- two adenomas (Fig. 3);
- four hepatocellular carcinomas, including one multifocal (Figs. 4 and 5);
- one focal nodular hyperplasia.

In three other patients for which a final diagnosis was made, without any suspect or detected lesion, we found:

- one haemorrhagic cyst confirmed by the anatomopathologist;
- one non specific necrotico-haemorrhagic lesion;
- another patient was diagnosed with haemopathy associated with major coagulation disorders, which was held for for the causal aetiology of the non-traumatic liver haemorrhage.

No diagnosis was made after a mean follow-up of 26 months for the last two patients.
One patient benefited from selective arterial embolisation at the acute phase for haemostatic purposes due to haemodynamic instability. The final diagnosis in this patient, in whom the causal nodule was visible as of the acute phase, was hepatocellular carcinoma. This was pathologically confirmed. In 75% of the patients, where the final diagnosis was hepatocellular carcinoma, the diagnosis was made at the acute phase (<1 week) leading to tumour surgery within a mean period of 1.5 weeks.

All of the histologically proven adenomas had beta-catenine mutation and were inflammatory. One of the hepatocellular carcinomas was developed on a beta-catenine mutated and inflammatory adenoma. In the three patients presenting with detectable lesion(s) at the acute phase, follow-up showed that the lesional burden was underestimated with numerous lesions detected afterwards.

**Efficacy of the CT and MRI imaging**

Fig. 6 sums up the contribution of the imaging in the early diagnosis of hepatic lesions discovered along with an inaugural non-traumatic haemorrhage.

**Discussion**

Spontaneous liver haemorrhage is a rare disorder and its aetiology is widely dominated, outside of the peripartum, by tumoral lesions, among which are extensively found adenomas and hepatocellular carcinomas [3,16–19].

The clinical presentation of these patients is not very specific, most often associating intense abdominal pain, sudden onset and severe hypovolemia possibly involving
haemorrhagic shock, all motivating heavy care, in an adapted department that may require emergency haemostatic procedures.

The diagnostic work-up for these patients, until then free of any liver disease and presenting with an inaugural non-traumatic haemorrhage remains important and is a tough challenge for the radiologist and the clinician, especially during the acute phase.

Almost 60% of the patients in our series were detected, at the time of onset of a spontaneous intrahepatic haemorrhage, with a tumoral lesion that was visible as of the acute phase in 86% of them.

Among them, more than half (57%) had hepatocellular carcinomas and more than one quarter (28%) had beta-catenine mutated and inflammatory hepatic adenomas, known to be major risk factors of carcinomatous degeneration [20].

To summarize, in these patients until then free of any liver disease, over 85% of the documented tumoral lesions were malignant or involved a high risk of malignant degeneration.

The very early mean age of occurrence (33.7 years) of hepatocellular carcinomas and the fact that they develop on healthy liver in all of the patients in our cohort reveals the key issue raised by this clinical situation, and the importance of an aetiologically fast, oriented, histologically documented diagnosis as there is a risk of misjudging a malignant or potentially malignant tumoral lesion leading to a prejudicial delay in care.

Moreover, the detection of focal nodular hyperplasia in one patient illustrates the fact that, even though adenomas and hepatocellular carcinomas are responsible for the greatest number of non-traumatic intrahepatic haemorrhages in our cohort, as well as in the literature,
they may complicate the evolution of any liver tumour [21,22], especially when it is hypervascular and hepatocytic.

The key role of the radiologist in the diagnostic process involves, beyond a good understanding of the nosology of this disorder, use of adapted and optimised imaging to detect any possible tumoral lesion. In our series, suspect lesion(s) was/were diagnosed as of the acute phase in six out of seven patients, by applying imaging protocols with complete and oriented sections.

In this situation, CT-scanner plays a major role: easily accessible, it is fast and sensitive for the detection of liver tumours.

In this situation, CT protocol should be simple but complete, systematically including a phase without injection, completed by an injection of multiphase contrast agent to try and detect a lesion, assess its vascularization characteristics, look for an extensive haemodynamic abnormality and possibly detect active arterial bleeding, that would be a strong argument for an urgent invasive treatment.

The role of a systematic late sequence is debatable since it involves additional exposure to radiation and provides little additional information, in particular as to the causal aetiology of the spontaneous haemorrhage, especially when a lesion is not visible. It should be considered on a
case-by-case basis to characterise a lesion detected on other acquisition phases. An MRI may also be carried out in the acute phase of spontaneous intrahepatic haemorrhages. This requires the implementation of a full protocol, including diffusion sequences and an injection of gadolinium contrast agent. The reduced accessibility, the importance of rapid care for patients in the acute phase and the specialised interpretation required do not preclude in favour of this isolated technique for the initial diagnosis of spontaneous liver haemorrhages in everyday practice. In addition, it may be hindered by the haemodynamic instability of the patient or the impossibility of having the patient hold his breath as required for the formation of quality images. Finally, it is less sensitive for the diagnosis of active haemorrhages [23]. However, MRI, is extremely helpful for the follow-up as it helps limit the repetition of irradiating examinations and provides important information for the possible characterisation of the lesions seen by the scanner.

In addition to the aetiological diagnosis, severity diagnosis is essential during the acute phase of an intrahepatic haemorrhage as the consequences may be deadly, especially in case of active arterial bleeding or intraperitoneal rupture [24].

Moreover, in most patients, the haemorrhage justifies heavy, intensive care [1,15], often associated with transfusion procedures involving their own risks. The abundance of the bleeding may sometimes include invasive endovascular or even surgical haemostatic treatment.

In case of haemodynamic instability not responding to medical treatment, selective embolisation is on of the standard of care for the haemorrhagic complications of liver tumours due to its efficacy on the bleeding and the low rate of complications compared with emergency surgery [15,25]. In most cases, this technique stops the bleeding and gives enough time to perform "delayed" surgery whose results are much better than first intention surgery [26]. However, this therapeutic procedure involves specific risks that, although rare, should be noted in this situation. In fact, in the acute phase of intrahepatic tumours, vasculisation disorders are very common as demonstrated by almost one quarter of the patients presenting extensive "arterialisation" of the hepatic parenchyma (related to the compression of the portal system and the sinusoidal capillaries [27] with a risk of ischemia in case of embolisation of the parenchyma that is only fed by the arterial system [28]). Therefore, the diagnostic phase should dwell upon the vascularisation disorders if they are extensive and if an endovascular procedure is considered due to haemodynamic instability.

In short, the problem for the radiologist confronted with a spontaneous intrahepatic haemorrhage during the acute phase in a patient until then free of liver disease or a liver lesion is twofold: evaluation of the initial gravity of the haemorrhage and aetiological diagnosis as of the acute phase.

During the acute phase, multiphase CT-scan seems to sufficiently answer these two questions with a full protocol comprising, in particular, a phase without injection and an arterial phase.

The protocol is capital since, in almost all of the patients in which a lesion was detected, it was seen as of the acute phase. An incomplete protocol would involve another CT-scan with additional exposure and another injection of contrast agent.

MRI plays a more important role afterwards, to specify the type of any lesions found and in the patient follow-up to limit the exposure.

The prevalence of carcinomatous lesions or lesions with a risk of malignant degeneration in our series and the early age of occurrence of these lesions reveals the central role of imaging in patients presenting an inaugural non-traumatic hepatic lesion and that of the radiologist who has to apply an optimum (complete and oriented) imaging protocol, as of the acute phase, to answer the aetiological question and assess the gravity of the haematoma. Due to its availability, the three-phase CT-scan appears to be the technique to favour.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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