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Original article

Early stage of intraperitoneal rupture of Hepatocellular Carcinoma: CT and MRI evaluation

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SUMMARY

The purpose of this study is to describe CT and MR findings of early stage intraperitoneal rupture of Hepatocellular Carcinoma (HCC). Nine patients (5 men, 4 women), with known HCC, displayed suspicious CT findings of early intraperitoneal rupture during routine follow up. These included a local fluid collection creating dentation on tumor surface, mimicing capsular retraction. Six of the patients were further evaluated with MRI. Collection was aspirated and cytological analysis was positive for malignant cells in all cases. All patients were under chemotherapy for unresectable, large HCC's, but none had ascites. They all died within a year for reasons uncelked to tumor rupture. In conclusion, we believe that this type of intraperitoneal rupture, which has never been proposed before, represents a local, extra-capsular extension of HCC, with micro-ruptures of liver capsule and local peritoneal infiltration and thickening that confine the collection locally preventing from massive intraperitoneal hemorrhage. The dentation of the tumor surface, in our opinion, represents pressure from the collection rather than true capsular retraction ("pseudo-retraction sign"). In conclusion, we believe that this type of rupture does not predispose to massive intraperitoneal hemorrhage and is a sign of advanced disease with poor prognosis.

Key Words: Hepatocellular Carcinoma, Hemoperitoneum, Rupture.

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INTRODUCTION

Hepatocellular carcinoma (HCC) is the commonest primary malignant tumor of the liver. Spontaneous intraperitoneal rupture of HCC is a life threatening condition which is rare in whites, and commoner in Asians, with a reported rate of 10,3-14,5%.[1-3] Though there are many studies describing image findings of intraperitoneal rupture of HCC, there is no available literature indexed in Medline describing early signs of intraperitoneal rupture of HCC. The purpose of the current study is to describe the CT and MR findings in 9 patients, with proven, local, encapsulated spontaneous intraperitoneal rupture of HCC with no clinical or radiological evidence of hemoperitoneum.

MATERIALS AND METHOD

Over a 7 year period (1998-2005), 963 patients (638 men, 325 women, mean age:68,48 years) with known, unresectable HCC, were submitted to CT in our department, on one or more occasions, during routine follow up. All HCC's had been histopathologically confirmed by CT guided percutaneous biopsy, and all patients were under chemotherapy for unresectable tumors.

Among them, 9 patients (0,93% of the total, 5 men, 4 women, mean age: 68,55 years) displayed CT findings suspicious of infiltration of the liver capsule with local intraperitoneal rupture of the tumor, creating a small encapsulated intraperitoneal collection mimicking capsular retraction. None of them had clinical or laboratory evidence of massive blood loss, and CT did not reveal signs of hemoperitoneum. Six of the patients were further evaluated with MRI and all of them were finally scheduled for CT guided aspiration of the collection. Three of the 9 patients were seropositive for hepatitis B virus, 1 for hepatitis C virus and 1 for both viruses, while the other 4 were sero-

negative for both viruses. Seven patients had a history of liver cirrhosis (77,7%) (Table 1).

CT scans were obtained with a Picker PQ 5000 CT scanner device with slice thickness 5mm, pitch 1, reconstruction interval 5mm, with a FOV ranging from 320-400 mm, depending on the patient's size. Images were obtained before and after contrast agent administration, during arterial phase (25-30 seconds after injection) and portal phase (60-70 seconds after injection), while in some instances images were obtained during the equilibrium phase (100-120 seconds after injection). A bolus injection of 120-150 ml (3-4 ml/sec) of non-ionic contrast medium (Ultravist 300, Shering, Germany) was given.

MR scans were obtained with a Siemens 1 T scanner (Siemens Expert Plus). Before contrast administration, axial and coronal Haste T2WI and Flash T1WI images were obtained, with a slice thickness of 8mm, FOV 340-400 mm, depending on patient's size and a matrix of 256X192. FSE T2WI images with Fat Sat (TE; 85 and 165) were also obtained, with a slice thickness of 8mm, interslice gap of 0,3 and a matrix of 256X168. After administration of 15-20 ml of contrast agent (Magnevist, Shering, Germany), axial Flash T1WI images were obtained with identical parameters as before the administration of contrast agent.

All patients were informed about the purpose of the study and gave their written consent before CT guided aspiration. Aspirations were performed using 18-20 gauge fine aspiration needles, under local anaesthesia with lidocaine, and aspirates were sent to the cytologist the same day.

RESULTS

All patients with suspicion of local, encapsulated, intraperitoneal rupture of HCC, displayed a similar imaging pattern in CT and MR examinations: a small concave to triangular peripheral dentation of the tumor surface, mimicking capsular retraction, which appeared hypoattenuating and non-enchasing in CT, with high signal intensity in T2-WI and low signal intensity in both T1-WI and T1-WI after gadolinium administration (Fig 1-2).

All patients had widespread tumorous infiltration of liver parenchyma, which involved 4 to 6 liver segments (mean: 4,33). Maximal tumor diameters were 9,3-24,1 cm(mean size:14,5 ±4,26 cm). Five of the HCC's displayed necrotic areas and none of them protruded out of the liver contours. None of the patients had ascites. Cytological analysis of the aspiration was positive for malignant cells in all cases. All patients died within a year following the diagnosis of localized intraperitoneal rupture of HCC (93-331 days, mean survival time:216,8 days). Etiology of death was hepatic coma in 4 patients, intestinal bleeding in 3 patient and malignant malaise in the remaining 2 patients. None of the patients manifested hemoperitoneum from massive intraperitoneal rupture of the mass.

DISCUSSION

Spontaneous rupture of HCC is a life threatening condition with a reported rate of 10,3-14,5 % in Asians, while it is rarer in whites.[1-3] Most of the patients present with acute abdomen and die within a small time interval after rupture due to massive blood loss into the peritoneal cavi-

Table 1. Patients' demographic data and HCCs' characteristics.

PATIENT	SEX	AGE (Years)	CT	MRI	HBV / HCV	CIRRHOSIS	LIVER SEGMENTS	MAX SIZE (cm)	SURVIVAL (Days)
1	M	62	+	+	HBV+	N	2(7,8)	9,3	331
2	F	74	+	+	-	N	4(1,4,5,8)	11,6	263
3	M	77	+	+	HBV+	Y	6(1,4,5,6,7,8)	24,1	93
4	M	75	+	-	HCV+	Y	4(1,4,5,8)	14,3	183
5	F	77	+	-	-	Y	5(4,5,6,7,8)	13,9	212
6	F	53	+	+	HBC+ HCV+	Y	4(1,4,5,8)	13,4	265
7	M	60	+	+	-	Y	4(5,6,7,8)	14,1	202
8	M	83	+	-	-	Y	6(1,4,5,6,7,8)	17,7	111
9	F	56	+	+	HBV+	Y	4(5,6,7,8)	12,1	291
Mean		***68,55***					***4,33***	***14,5***	***216,8***

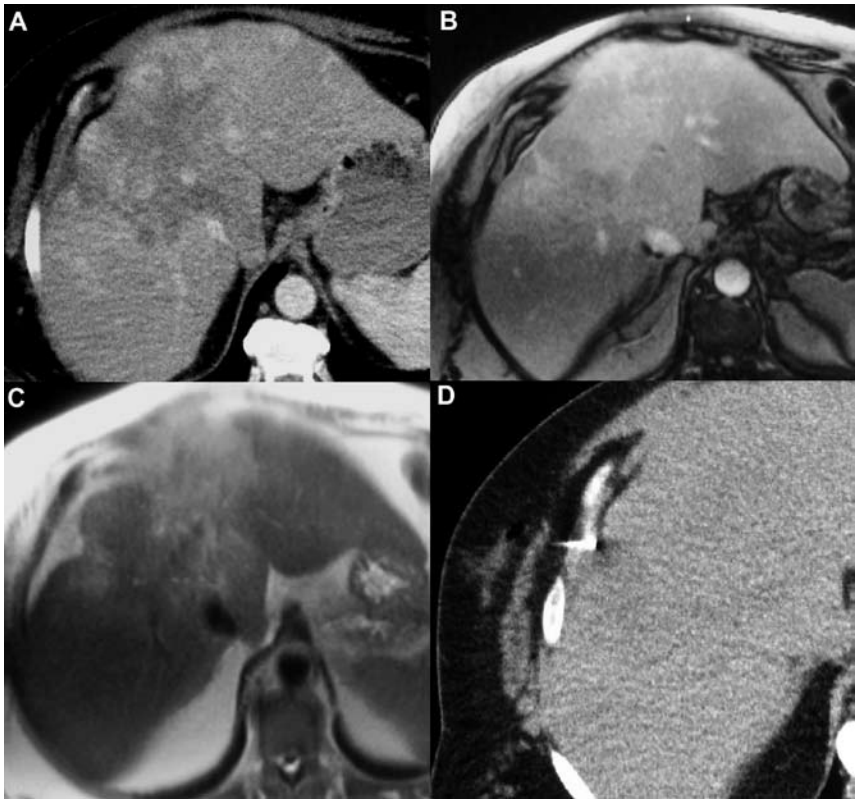
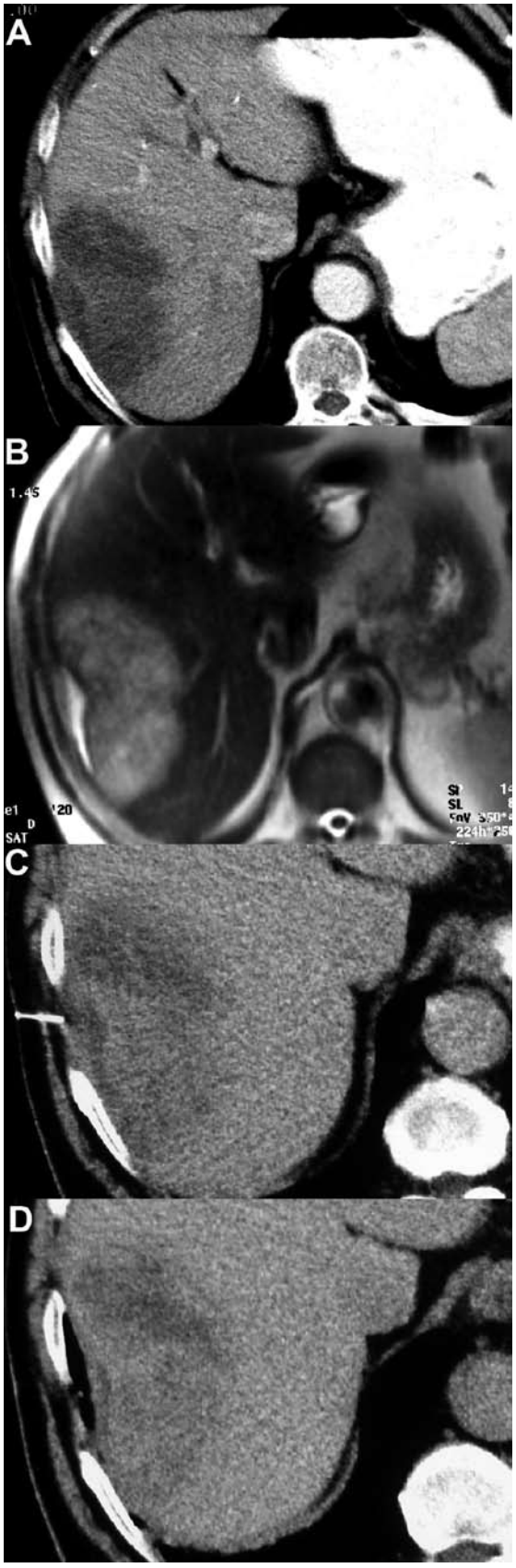


Fig. 1. 53 year old woman with HCC occupying parts of the left and right liver lobes.
A. CT, portal venous phase.
B. MRI, T1WI, axial plane after i.v. gadolinium administration.
C. MRI, T2WI, axial plane.
Note the small, triangular encapsulated fluid collection in the surface of the lesion with the apparent liver capsular retraction.
D. Aspiration of this fluid under CT guidance with an 18 gauge aspiration needle. Cytological analysis of the sample was positive for malignant cells.

ty.[4,5] There are a lot of studies describing pathogenesis and imaging findings of ruptured HCC in the peritoneal cavity.[1-13] These include a peripherally located tumor in contact with liver capsule with a protruding contour, discontinuity of hepatic surface, haematoma at the site of rupture, hemoperitoneum, contrast extravasation and separation of tumor content from a peripheral enhancing rim ("enucleation sign").[5] However, early, confined stage of intraperitoneal rupture of HCC has not been described before. To all of our patients, cytology of the aspirated fluid from the site of suspected rupture was positive for malignant cells. Care was taken during CT guided percutaneous fluid aspiration to avoid penetrating the liver surface and aspirating cells from the underlying tumor, which would give false positive results. These findings are strong evidences that HCC's in all of our patients had infiltrated liver surface, creating small micro-ruptures in liver capsule that enabled malignant cells to enter the peritoneal cavity locally. This stimulated the creation of a small, encapsulated, localised fluid collection over the site of rupture, within an area of apparent liver capsular retraction. Previouse serial CT imaging of our patients, revealed poor response of the HCC's to chemotherapy, with a tendency to enlarge over time. Additionally, before the appearance of this encapsulated, small collection, the liver surface was smooth, with no capsular irregularity. Therefore, capsular retraction cannot be attributed, to tumor shrinking during chemotherapy, since there was no response to it, or to a fibrotic nature of the lesion, which is considered uncommon in HCC's,[14] and presupposes gradual presentation over serial imaging during enlargement of the primary lesion. Therefore, we believe that this notch of the periphery of the HCC, is not a real capsular retraction, but compression of the underlying liver lesion from the localized ascetic collection. None of our patients had ascetic collection anywhere else in the peritoneal cavity, except for the small, local collection and there was no clinical or laboratory evidence of intraabdominal haemorrhage.

Imaging findings were highly suggestive of localised intraperitoneal rupture in all of our patients. The triad of a large peripherally located HCC with a small intraperitoneal, localized collection and apparent capsular retraction of the liver capsule underneath the collection were present in all cases, with a sensitivity of 100% for early intraperitoneal rupture of HCC. The proposed mechanism of this type of extracapsular extension of HCC is as follow: a peripherally located HCC, during growth, comes in touch with the liver surface. Infiltration and micro-ruptures of the liver capsule permit some malignant cells to



escape locally, stimulating the formation of a small local collection, confined due to the high viscosity of this cellular fluid which is admixed with blood, necrotic material and bile and due to the local peritoneal adhesions. Compression of the underlying lesion by the fluid, simulates liver capsular retraction, which is a "pseudo-retraction", differing pathogenetically from the true fibrotic retraction of a peripheral cholangiocarcinoma or fibrolamellar hepatocellular carcinoma,[14,15] or from the retraction created by a regressed peripherally located hepatic metastasis after treatment[14,16] (Fig 3).

No protrusion of HCC out of the liver contour and absence of ascetic collection, prevented massive intraperitoneal rupture of HCC. Under these circumstances, chronic infiltration of the capsule creates adhesions between peritoneal layers that encyst small accumulations of ascetic fluid. Implantation of malignant cells is restricted by the peritoneal adhesions and stimulates the production of local fluid collection. There is no evidence from our series that this type of confined intraperitoneal rupture of HCC predisposes to real intraperitoneal rupture with the typical findings of hemoperitoneum, since all patients died within a short period of time from reasons irrelevant to massive blood loss. The pathogenesis of hemoperitoneum after spontaneous rupture of HCC is considered the disruption of tumor surface or tearing of a feeding artery that causes rupture of HCC.[5] This, seems to be rather difficult to occur when peritoneal layers are fixed from tumor infiltration, as in our patients, confining locally an otherwise fatal rupture of a peripherally located HCC in the peritoneal cavity.

From our data, it emerges that this type of rupture is a rare manifestation of HCC's, correlating with exten-

Fig. 3. Schematic presentation of growth and confined intraperitoneal rupture of a HCC.
A. Small HCC that does not touch the liver capsule.
B. The HCC has grown, abuts on liver capsule without infiltrating it.
C. HCC has grown even more, capsular infiltration and micro-ruptures have occurred and some malignant cells have locally entered the peritoneal cavity, stimulating the development of a small local fluid collection. In this phase, pressure from the collection removes liver capsule away from lesion surface (arrows), but the pressure is not enough yet to create a dentation on tumor surface.
D. The pressure of the collection has increased and compresses tumor surface, simulating liver capsular retraction (arrows). Adhesions of the peritoneal layers prevent the rupture to expand over the whole peritoneal cavity, and malignant implantations are confined within the area of the collection. This stage of confined intraperitoneal rupture has typical CT and MR imaging findings that were demonstrated in all of our patients.

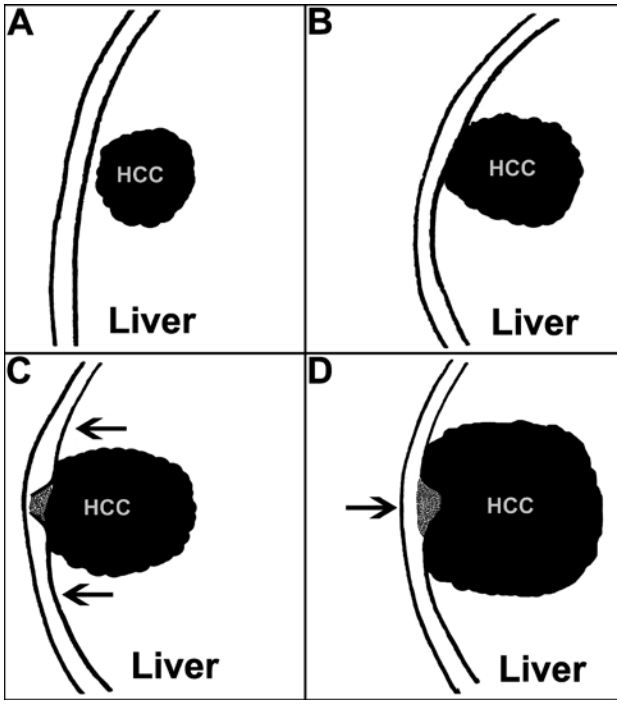


Fig. 2. 62 year old man with HCC of the right liver lobe.
A. CT, late arterial phase.
B. MRI, T2WI, axial plane.
C. CT guided aspiration of the local extracapsular fluid collection with an 18 gauge aspiration needle.
D. CT immediately after aspiration of the fluid.
Note the presence of air after the aspiration of the fluid, which is confined locally within the area of the pre-existing local fluid collection, an evidence of the infiltration and the development of adhesions between the peritoneal layers. Cytological analysis of the sample was positive for malignant cells.

sive liver disease, not responding to chemotherapy and is a marker of poor outcome. Consequently, prophylactic surgery or hepatic arterial embolization is not proposed in this group of patients, since there is no evidence of increased risk of massive intraperitoneal bleeding and prognosis is already aggravated due to advanced liver disease.

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