Clinical Case Report

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Hepatocellular carcinoma with thoracic metastases presenting as hemothorax

A case report and literature review

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Abstract

Rationale: Hemothorax caused by metastasis or direct invasion of hepatocellular carcinoma (HCC) in the chest is rare. We report a case of hemothorax caused by metastasis in the mediastinum and treated with transcatheter arterial embolization (TAE).

Patient concerns: A 60-year-old woman with HCC was admitted to receive chemotherapy. Two days after admission, she complained of dyspnea, and a chest X-ray revealed right pleural effusion. Thoracentesis confirmed the diagnosis of hemothorax. Computed tomography (CT) angiography showed lung, pleural, and mediastinal metastases and contrast extravasation from the right lower mediastinal mass.

Diagnoses: Hemothorax caused by spontaneous rupture of mediastinal metastasis of hepatocellular carcinoma.

Interventions: During emergent angiography, contrast extravasation from the right T10 intercostal artery was observed and we performed embolization with lipiodol and gelatin sponge particles. After embolization, no active bleeding was observed.

Outcomes: The patient died because of sepsis and multiple organ failure 22 days after admission.

Lessons: We reviewed 21 cases of HCC with metastasis or direct invasion in the chest presenting hemothorax. The results revealed that male sex and right hemothorax were predominant in these cases. The average age of the patients was 61.24±10.82 years. The most common symptoms were dyspnea, chest wall pain, and shock. Thoracentesis can confirm the diagnosis, and CT angiography can help identify the location of contrast extravasation before TAE. The reported bleeding arteries were the intercostal, inferior phrenic, bronchial, hepatic, and superficial cervical arteries. TAE with embolic agents is a feasible treatment. The overall outcomes in these cases were poor.

Abbreviations: ADI-PEG20 = pegylated arginine deiminase, CT = computed tomography, FMP = fludarabine, mitoxantrone, and prednisone, FOLFOX = folinic acid, fluorouracil, and oxaliplatin, HCC = hepatocellular carcinoma, TACE = transcatheter arterial chemoembolization, TAE = transcatheter arterial embolization.

Keywords: computed tomography, hemothorax, hepatocellular carcinoma, thoracic metastasis, transcatheter arterial embolization

1. Introduction

Hepatocellular carcinoma (HCC) sometimes causes hemoperitoneum. However, hemothorax caused by metastasis or direct invasion of HCC is rare.[1] We report a case of hemothorax caused by mediastinal metastasis and treated with transcatheter arterial embolization (TAE). We also review and summarize the previously reported cases of hemothorax caused by metastasis or direct invasion of HCC.

2. Case presentation

A 60-year-old woman with progression of HCC and lung metastasis was admitted to our hospital for her 12th cycle of chemotherapy with a folinic acid, fluorouracil, and oxaliplatin (FOLFOX) regimen on March 2, 2016. She had a history of HCC in segments 7 and 8 of the liver and received segmental hepatectomy in September 2009; tumor recurrence in segments 5 and 6 with tumor rupture and hemoperitoneum postemergent embolization and segmental hepatectomy in March 2011; local recurrence in the liver dome and lung metastasis after receiving sorafenib from March 2012 to February 2013; pegylated arginine deiminase (ADI-PEG20) treatment for 12 cycles (March to May 2013); fludarabine, mitoxantrone, and prednisone (FMP) therapy for 4 cycles (June to October 2013); transcatheter arterial chemoembolization (TACE) 4 times (November 2013 to July 2014); and 11 cycles of chemotherapy with the FOLFOX regimen (December 2014 to January 2016). She also had diabetes mellitus, chronic hepatitis C, liver cirrhosis, and hypertension.

On admission, physical examination revealed a body temperature of 36.6°C, a pulse rate of 106 beats/min, blood pressure of 118/80 mm Hg, and a respiration rate of 18 breaths/min.

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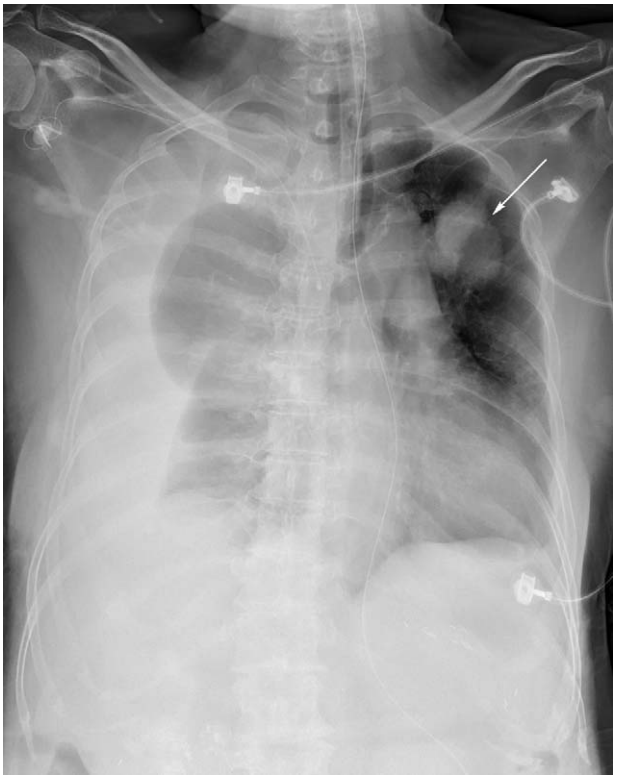

Figure 1. Chest radiography after intubation revealed right pleural effusion and left upper lung metastasis (arrow).

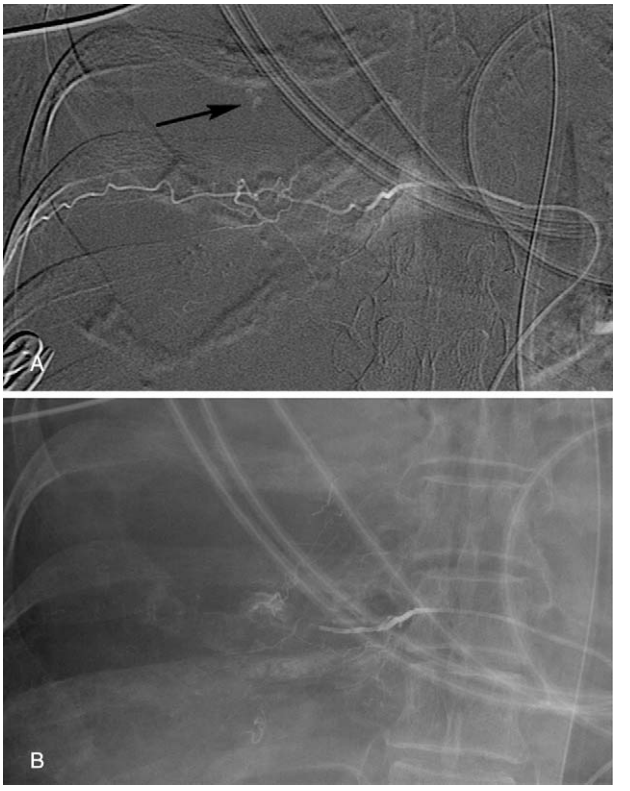

Figure 3. Angiography of the right T10 intercostal artery showed (A) contrast extravasation (arrow) (B) and total occlusion after embolization with lipiodol and gelatin sponge particles.

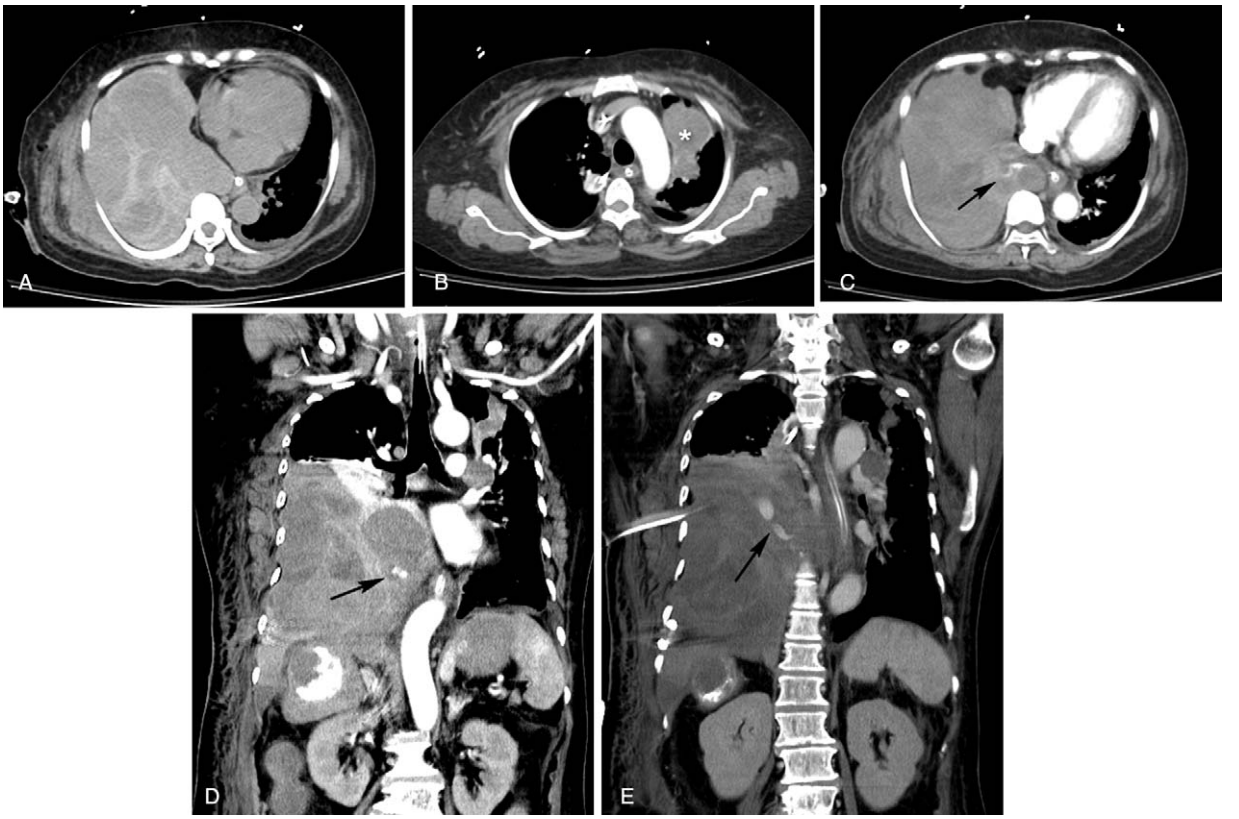

Figure 2. Computed tomography (CT) of the abdomen. (A) Axial noncontrast-enhanced CT revealed a hyperdense lesion in the right pleural space, consistent with hemothorax. (B) Lung metastasis was observed in the left upper lobe of the lung (*). (C and D) Contrast extravasation was observed on axial and coronal CT angiography (arrows in C and D). (E) Coronal contrast-enhanced CT showed contrast extravasation (arrow).

Table 1

All published cases of metastasis or direct invasion of hepatocellular carcinoma in the chest presenting hemothorax (n=21).

	Sex	Age, y	Symptoms	Side	Metastatic sites	Hepatitis	Treatment	Cause of death	Outcome
Case 1, Hino[12]	M	71	Dyspnea	R	Mediastinum (lymph node)	ALC	Supportive care	RF, HF	Dead (1 d)
Case 2, Sato et al[13]	F	71	Shock	R	Thoracic vertebrae	Non-B	Supportive care	Shock	Dead (within 1 d)
Case 3, Kohno et al[14]	M	53	Chest pain, dyspnea	L	Rib	N/A	TAE (superficial cervical artery) with gelatin sponge	Cancer death	Dead (5 mo)
Case 4, Lin et al[15]	M	31	Dyspnea, shock, chest wall bulging	L	Chest wall, rib, pleura	B	C/T	Cancer death	Dead (2 mo)
Case 5, Sekiya et al[16]	M	79	Chest wall pain, shock, dyspnea	R	Rib	ALC	Supportive care	Shock	Dead (17 h)
Case 6, Akimaru et al[17]	M	67	Dyspnea, shock, palpitation	L	Lung	B	Supportive care	Shock	Dead (36 h)
Case 7, Takagi et al[18]	F	55	N/A	L	Pleura	Non-B	Supportive care	RF	Dead (2 wk)
Case 8, Kanou et al[19]	M	65	Cough, fatigue	R	Direct invasion of diaphragm	C	TAE (right hepatic artery) with ethanol and lipiodol	Rupture of EV	Dead (40 d)
Case 9, Masumoto et al[20]	M	64	Dyspnea	R	Direct invasion of diaphragm, pleura	C	TAE (right inferior phrenic artery) with gelatin sponge	Cancer death	Dead (3 mo)
Case 10, Ogata et al[21]	M	64	Chest pain	R	Rib	B and C	Supportive care	RF, HF	Dead (26 h)
Case 11, Sohara et al[22]	F	59	Shock	R	Lung, pleura	C	Supportive care	Shock	Dead (within 1 d)
Case 12, Ishikawa et al[23]	M	55	Dyspnea	R	Direct invasion of the diaphragm	C	TAE, but failed; RFA	Cancer death	Dead (4 mo)
Case 13, Shiozawa et al[24]	M	68	Chest pain, shock	R	Mediastinum, pleura	B	TAE (left inferior phrenic artery)	N/A	Alive (>12 mo)
Case 14, Tanioka et al[25]	M	59	Dyspnea	R	Pleura	C	Supportive care	RF	Dead (2.5 mo)
Case 15, Wei et al[1]	M	42	Chest pain	L	Chest wall	B	Surgery	MOF	Dead (6 d)
Case 16, Tan et al[26]	M	62	Chest pain	R	Rib	N/A	N/A	Shock	N/A
Case 17, Ono et al[11]	F	56	Shock, epigastric pain	R	Direct invasion of the diaphragm	B	TAE (right hepatic and left hepatic arteries) with coil and gelatin sponge. Surgery	N/A	Alive (>2 y)
Case 18, Nagao et al[27]	M	71	Shock	R	Chest wall	N/A	TAE (right intercostal artery) with gelatin sponge	N/A	Alive (>15 mo)
Case 19, Oh et al[28]	M	60	Dyspnea, chest pain	L	Lung, mediastinum	B	TAE (left bronchial artery) with lipiodol, adriamycin and polyvinyl alcohol	N/A	Dead (4 mo)
Case 20, Okamoto et al[29]	M	74	N/A	R	Pleura, lung	B	Surgery	N/A	Alive (>13 mo)
Case 21, present case	F	60	Dyspnea	R	Lung, pleura, mediastinum	C	TAE (right intercostal artery) with lipiodol and gelatin sponge	Sepsis, MOF	Dead (20 d)

ALC=alcoholic, C/T=chemotherapy, EV=esophageal varices, F=female, HF=hepatic failure, L=left, M=male, MOF=multiple organ failure, N/A=nonavailable, R=right, RF=respiratory failure, RFA=radiofrequency ablation, TAE=transcathete.

Laboratory investigations showed the following: hematocrit, 34.4%; hemoglobin, 11.2 g/dL; red blood cell count, 3.76 million/mm^3; white blood cell count, 2600/mm^3; platelet count, 55,000/mm^3; blood urea nitrogen, 89.4 mg/dL; creatinine, 4.17 mg/dL; sodium, 131 mEq/L; and potassium, 4.0 mEq/L.

Two days after admission, she complained of dyspnea, and a chest radiography revealed right pleural effusion (Fig. 1). Thoracentesis confirmed the diagnosis of hemothorax. Computed tomography (CT) angiography showed lung, pleural, and mediastinal metastases and contrast extravasation from the right lower mediastinal mass (Fig. 2). During emergent angiography, contrast extravasation from the right T10 intercostal artery was observed and TAE with lipiodol and gelatin sponge particles was performed. After the procedure, no active bleeding was observed (Fig. 3). However, she died because of sepsis and multiple organ failure 22 days after admission.

The case report has been approved by the Chang Gung Medical Foundation Institutional Review Boards (IRB), Taipei, Taiwan. The patient consent was waivered by the IRB.

3. Discussion

HCC is usually hypervascular and spontaneous rupture is not uncommon. Metastatic lesions of HCC, like their primary lesions, have the tendency to rupture.[2] Rupture of metastatic lesions have been reported in the adrenal gland,[3,4] kidneys,[5] mandible,[6] peritoneum,[7,8] and spleen,[9,10] besides chest lesions, which will be discussed below.

In 2012, Ono et al[11] reviewed 17 cases of hemothorax caused by either metastasis or direct invasion in the chest. We further reviewed previous literature and found 21 cases (including the present case) of HCC with metastasis or direct invasion in the chest presenting hemothorax (Table 1); these cases are summarized in Table 2.

According to Table 2, these cases predominantly involved men (76.2%) and right hemothorax (71.4%). The average age of affected patients is 61.24 ± 10.82 years. The most common symptoms are dyspnea (52.6%), chest pain (36.8%), and shock (42.1%). Patients may have acute onset of pleural effusion and symptoms. Pleural tapping can confirm the diagnosis.

Nine patients (45.0%) were treated with TAE, and procedural failure occurred in one case. The reported bleeding arteries were the intercostal, inferior phrenic, bronchial, hepatic, and superficial cervical arteries. These arteries were related to the locations of contrast extravasation. The patients who exhibited bleeding in 2 cases with direct diaphragmatic invasion involved bleeding from the hepatic arteries. To identify the bleeding arteries, CT angiography can be helpful. A gelatin sponge was most commonly used, and other embolic agents, including ethanol, lipiodol, and polyvinyl alcohol particles were also used. Other treatment modalities, including chemotherapy, surgery, and radiofrequency ablation have been adopted. However, there are too few cases to analyze and more cases are needed for further evaluation.

Regarding the outcomes, 45% of patients died within a month, 80% died within 6 months, and only 20% of cases survived for more than 6 months. Most deaths within a day were caused by shock, and the causes of deaths from several days to 6 months included respiratory failure, hepatic failure, multiple organ failure, and cancer death. The outcomes of 8 patients undergoing successful TAE varied greatly; the survival time ranged from 40 days to more than 15 months. One patient who received combined TAE and surgery even survived for more than 2 years.

Table 2

Summary table of all published cases.

Sex (n = 21)	Male = 16 (76.2%)
Age (n = 21)	61.24 ± 10.82 y
Side of hemothorax (n = 21)	Right = 15 (71.4%)
Symptoms (n = 19)	Dyspnea = 10 (52.6%)
	Chest wall pain = 7 (36.8%)
	Shock = 8 (42.1%)
	Chest wall bulging = 1 (5.3%)
	Cough = 1 (5.3%)
	Fatigue = 1 (5.3%)
	Epigastric pain = 1 (5.3%)
Treatment (n = 20)	TAE = 9 (45.0%)
	Surgery = 3 (15.0%)
	C/T = 1 (5.0%)
	RFA = 1 (5.0%)
	Supportive care = 8 (40.0%)
Tumor supply arteries of angiography (n = 8)	Intercostal artery = 2 (25.0%)
	Inferior phrenic artery = 2 (25.0%)
	Hepatic artery = 2 (25.0%)
	Bronchial artery = 1 (12.5%)
	Superficial cervical artery = 1 (12.5%)
Outcome (n = 20)	Dead within 1 d = 3 (15.0%)
	Dead within 1 wk = 7 (35.0%)
	Dead within 1 mo = 9 (45.0%)
	Dead within 6 mo = 16 (80.0%)
	Alive for more than 6 mo = 4 (20.0%)

C/T = chemotherapy, RFA = radiofrequency ablation, TAE = transcatheter arterial embolization.

In conclusion, thoracic metastasis or direct invasion of HCC presenting with hemothorax is rare, and cases involving men and right hemothorax are predominant. If a patient with thoracic metastasis of HCC has acute pleural effusion, dyspnea, chest pain, or shock, tumor bleeding should be taken into consideration. CT angiography can identify the locations of contrast extravasation. The bleeding arteries that have been reported are the intercostal, inferior phrenic, bronchial, hepatic, and superficial cervical arteries. TAE with embolic agents is a feasible treatment. The overall outcomes of these cases are poor.

Author contributions

Writing – original draft: Chih-Wei Yen.
Writing – review & editing: Li-Sheng Hsu, Chien-Wei Chen, Wei-Hsiu Lin.

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