

Unusual Presentation of Hepatocellular Carcinoma with Peritoneal Carcinomatosis: Importance of Abdominal Distension as a Clinical Indicator

Mariam Shahid, Marya Hameed, Syed Maaz Tariq, Ameet Kumar Jesrani, Ashok Kumar, Suneeta Bansari

ABSTRACT:

Hepatocellular carcinoma (HCC) is a common malignancy of the liver. It is frequently diagnosed in the male gender with a racial predilection towards Asian and African populations. In addition to distant metastasis, large tumors can result in direct extrahepatic metastasis to the peritoneum and diaphragm through rupture of exophytic tumor hepatocellular carcinoma in peritoneal cavity. We report a case of a 55-year-old male having hepatocellular carcinoma secondary to hepatitis C with peritoneal metastasis. The CT abdomen with contrast triphasic study was suggestive of alarming features of chronic liver disease with multicentric hepatoma formation predominantly in segment VIII with the localized subcapsular collection. Additionally, an extensive omental thickening and nodularity were also seen in subhepatic space. Multiple nodules were seen in right cardiophrenic angle, right lower abdomen, and rectovesical pouch. In contrast to conventional chemotherapy with sorafenib, cytoreduction surgery with hyperthermic intraperitoneal chemotherapy has been shown to dramatically improve survival in patients.

Keywords: MeSH: Hepatocellular carcinoma, Liver, Metastasis

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INTRODUCTION:

Hepatocellular Carcinoma (HCC) is the most frequently diagnosed malignancy of the liver and is one of the leading causes of cancer-related death globally. HCC is often diagnosed in the male gender with a high incidence in the Asian and African populations. The most significant risk factor for HCC is cirrhosis and chronic liver disease which

are mostly caused by excessive alcohol and viral hepatitis. It classically presents as a localized tumor in the liver but can metastasize to distant sites. Imaging detects 13-36% of patients with metastases at the time of diagnosis. Imaging is prone to underestimate the metastases as according to autopsy it can be as high as 68%.¹ There are several mechanisms which promote metastasis such as aggressive tumor biology and molecular alterations. In the case of HCC factors such as the larger size of the tumor, infiltration, satellite nodules and high alpha-fetoprotein levels have been shown to correlate with metastatic potential.² Large tumors can result in direct extrahepatic invasion and commonly abdominal wall diaphragm and peritoneum are involved. Peritoneal carcinomatosis can occur through the rupture of exophytic HCC into the peritoneal cavity resulting in a massive seeding of cancer. The prevalence of peritoneal carcinomatosis secondary to hepatocellular carcinoma has reported incidence of 2-6%, however the exact incidence in Pakistan is not known.³ Spontaneous rupture of HCC is a dreadful complication having an incidence of 5-26% and mortality ranging from 25% to as high as 75%.⁴ Hepatectomy is considered as a feasible option for spontaneous HCC ruptures which offers long-term survival in a selected group of patients with 1 and 3-year survival rates being 60%-77% and 42%-54% respectively. Despite favorable outcomes, the relationship between surgery timing in patients with HCC rupture and peritoneal carcinomatosis is a matter of debate. Herein, we report a case of a 55-year-old patient with HCC, secondary to hepatitis C with peritoneal carcinomatosis.

Mariam Shahid

Consultant, Department of Radiology
Jinnah Postgraduate Medical Centre
Email: Mariam.shahid_100@hotmail.com

Marya Hameed

Assistant Professor, Department of Radiology
National Institute of Child Health
Email: drmash84@gmail.com

Syed Maaz Tariq

House Office, Department of Medicine
National Institute of Child Health
Email: maaztariqsyed@gmail.com

Ameet Kumar Jesrani

Assistant Professor, Department of Radiology
Sindh Institute of Urology and Transplantation
Email: ameet.jesrani@yahoo.com

Ashok Kumar

House Office, Department of Medicine
National Institute of Child Health
Email: ashok.duhs@gmail.com

Suneeta Bansari

Resident, Department of Radiology
House Office, Department of Medicine
National Institute of Child Health
Email: suneetabansari@gmail.com

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CASE PRESENTATION:

A 55-year-old male, known case of Hepatitis C reported to the emergency department with the complaints of worsening abdominal pain and indigestion. At the time of presentation to the emergency department, the patient's vital signs were within normal limits, with a blood pressure of 130/80 mmHg, a heart rate of 90 beats per minute, a respiratory rate of 18 breaths per minute and temperature of 37°C (98.6°F), which was also within the normal range. Initial assessment included a thorough medical history followed by physical examination. The abdominal examination revealed a tender right upper quadrant with abdominal distension and dullness to percussion. The initial management included the administration of intravenous fluids and analgesics to relieve the patient's pain and maintain hydration. The patient was also advised to fast and was started on proton pump inhibitors to manage the indigestion.

The initial blood workup included a complete blood count (CBC), liver function tests (LFTs), and other relevant laboratory investigations. The CBC showed a hemoglobin level of 12.2 g/dL (reference range: 13.5-17.5 g/dL), a total white blood cell count of $9.4 \times 10^3/\text{iL}$ (reference range: $4.0-11.0 \times 10^3/\text{iL}$), and a platelet count of $200 \times 10^3/\text{iL}$ (reference range: $150-450 \times 10^3/\text{iL}$). The LFTs revealed slightly deranged liver enzymes, with an alanine aminotransferase (ALT) level of 68 U/L (reference range: 7-56 U/L) and an aspartate aminotransferase (AST) level of 80 U/L (reference range: 10-40 U/L). The patient's anti-HCV test was positive, indicating a previous or ongoing hepatitis C infection. The current HCV viral load was also elevated at 150,000 IU/ml, which suggested ongoing viral replication. Moreover, the alpha-fetoprotein level was markedly raised, indicating a potential malignancy. These findings prompted the need for further investigation, which included a CT abdomen with contrast triphasic study that showed features of chronic liver disease with multicentric hepatoma formation predominantly in segment VIII with the localized subcapsular collection (Figure 1). Extensive omental thickening and nodularity were also seen in subhepatic space. Multiple nodules were seen in the right cardiophrenic angle, right lower abdomen, and rectovesical pouch. Mesenteric and retroperitoneal lymphadenopathy (Figure 2) along with splenomegaly and varices formation was also identified. The patient was advised of urgent surgical and oncological review.

A 55-year-old male with known hepatitis C came to the emergency department with worsening abdominal pain & indigestion. The physical examination revealed a tender right upper quadrant, initial blood workup showed slightly deranged liver enzymes. His anti-HCV test was positive and his current HCV viral load was 150,000 IU/ml. Alpha-fetoprotein level was markedly raised. CT abdomen with contrast triphasic study showed features of chronic liver disease with multicentric hepatoma formation predominantly

in segment VIII with the localized subcapsular collection (Figure 1). Extensive omental thickening and nodularity were also seen in subhepatic space. Multiple nodules were seen in the right cardiophrenic angle (Figure 3), right lower abdomen, and rectovesical pouch. Mesenteric and retroperitoneal lymphadenopathy (Figure 2) along with splenomegaly and varices formation was also identified. The patient was advised of an urgent oncological and surgical consultation.

Figure 1: Axial and coronal CECT abdomen shows arterially enhancing tumor in a cirrhotic liver with multiple peritoneal deposits and portal hypertension.

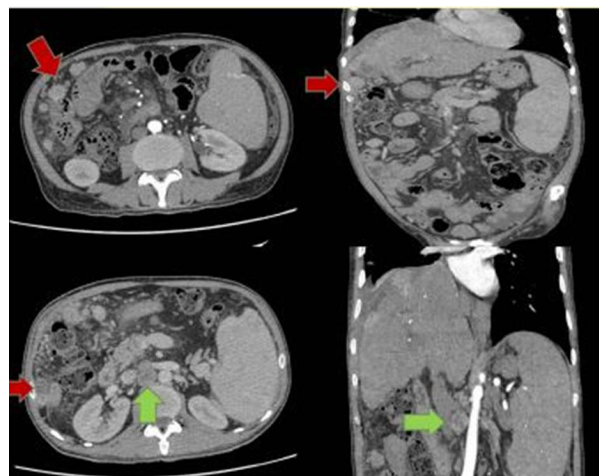
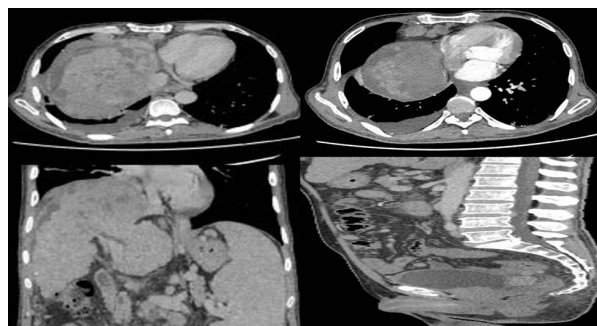


Figure 2: CECT abdomen with reformatted images. Note a collection in right perihepatic space secondary to tumor rupture and multiple cardio phrenic and peritoneal deposits



DISCUSSION:

Peritoneal carcinomatosis is a manifestation of several gastrointestinal malignancies. It is characterized by the deposition of tumors in the peritoneum. It has a variable presentation and can present from asymptomatic to as severe as debilitating pain, diarrhea, bloating, and weight loss. Colorectal cancer, the third most common cancer in the world is usually diagnosed with synchronous peritoneal carcinomatosis and provides a good case study for it. The peritoneal manifestation in tumors is rare. Its incidence is reported in 12% of the ruptured hepatocellular carcinoma cases in a large French cohort.⁵ Mostly the patients with HCC rupture subsequently present with intrahepatic

recurrence, the treatment options then are repeated hepatectomy and transarterial chemoembolization. Primary cancer of the peritoneum is even rarer. The usual imaging such as CT and MRI lack sensitivity to detect and assess for disease burden in peritoneal carcinomatosis. The usual CT scan findings such as omental caking, thickening of omentum, and nodules are not common, especially in the earlier stages of the disease. Several studies have determined that a CT scan can underestimate the disease present in the peritoneal cavity and is not reliable for estimating the tumor burden. Compared to CT, MRI and especially diffusion-weighted images have been shown to have better detection accuracy. However, in resource-deficient settings, it comes with the challenge of high cost, motion artifacts, and radiologists not being adequately trained with sophisticated imaging. Peritoneal carcinomatosis was considered to be a lethal disease with limited surgical acceptance until the advent of cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (HIPEC) which has dramatically improved survival in patients. In cytoreduction surgery (CRS), the gross viable tumor is removed, followed by heated cytotoxic chemotherapy for unresectable residual disease. This method has the remarkable capability to not only limit systemic toxicities but also increase the exposure of tumors to chemotherapy.⁶ In one of the largest cohorts investigating aggressive surgical management of peritoneal metastasis of HCC, it was found that the overall survival from surgery is 46.7 months. This result is highly variable to the medical management which includes Sorafenib and/or systemic chemotherapy, where overall survival is 6 and 14 months.⁷ Despite advantages there is a significant morbidity and mortality burden attached to CRS/HIPEC treatment modality and this option is also limited to a highly specific group of patients with favorable tumor characteristics and a low burden of co-morbidities. Pressurized intraperitoneal aerosol chemotherapy (PIPAC) is a newer novel and minimally invasive therapeutic option for patients having peritoneal carcinomatosis. PIPAC is mostly effective in military peritoneal carcinomatosis as drug penetrates more into small nodules rather than bulky tumor mass.⁸ In a pooled analysis of 16 studies it was concluded that PIPAC resulted in a 69% tumor regression rate as assessed by peritoneal sampling during repeated PIPACs. It is worth mentioning that several studies have investigated a combination of systemic chemotherapy and PIPAC and in another study, CRS was also concomitantly performed. The burden of side effects was low even when PIPAC was combined with systemic therapy which had a positive effect on the quality of life. The data suggests there is no significant hepatic or renal toxicity involved allowing the inclusion of patients with an extraperitoneal disease or who might be at significant risk of developing it. Further studies are still required before it can be a treatment of choice. In patients with peritoneal carcinomatosis, the evidence is limited for the benefit of chemotherapy and according to trials, the

benefit is minimal to none when going further than third-line chemotherapy. Considering the side-effect profile and quality of life, alternative therapies are an essential need of patients. PIPAC is indeed an option for such patient groups.

CONCLUSION:

Hepatocellular carcinoma is the most common primary malignancy of the liver. It has a gender predilection for males and is frequently linked to alcohol and hepatitis B and C viruses. We report a case of a 55-year-old patient with peritoneal metastasis of HCC. The peritoneum is a rare location of HCC metastasis with only 12% incidence. Proper imaging is crucial to detect peritoneal carcinomatosis. The advent of CRS with HIPEC has dramatically changed the course of the disease with an improved overall survival rate as compared to systemic/ palliative chemotherapy based on sorafenib and other chemotherapeutic agents. A significant burden of mortality and morbidity is associated with CRS/HIPEC treatment. A newer modality of PIPAC which is minimally invasive is emerging to be another option for patients who may not qualify for HIPEC. PIPAC has been shown to cause significant tumor regression. The side-effect profile of PIPAC is also favorable, having a positive effect on the quality of life. More clinical trials are required to investigate PIPAC further to consider it as a gold standard treatment.

Authors Contribution:

Mariam Shahid: Data Collection, Drafting
Marya Hameed: Study Concept
Syed Maaz Tariq: Statistical Analysis
Ameet Kumar Jesrani: Drafting, Study Design
Ashok Kumar: Critical Review
Saneeta Bansari: Proof Reading

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