Radiology Case Reports 16 (2021) 550–554

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Case Report

Gastric wall metastases from hepatocellular carcinoma: case report and review of the literature

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ARTICLE INFO

Article history:
Received 24 September 2020
Revised 16 December 2020
Accepted 16 December 2020

Keywords:
Gastric wall metastases
HCC
18F-Choline

ABSTRACT

A 69-year-old male patient who had a history of well-differentiated hepatocellular carcinoma (HCC) post right hepatectomy presented a year later with iron-deficiency anemia. His anemia work-up included upper endoscopy that revealed multiple gastric polyp a biopsy from the largest demonstrated metastatic hepatocellular carcinoma. His magnetic resonance imaging (MRI) showed a gastric "polyp" without evidence of local HCC recurrence within the liver. His subsequent dual imaging with Choline/fluorodeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) confirmed the gastric metastases and in addition revealed other sites of unexpected metastatic disease in the right adrenal and the bone that was asymptomatic.

Patient was started on sorafenib and currently he is alive one-and-half-year postdetection of his metastatic disease under palliative care.

This case showed that the possibility of gastric metastases should be kept in mind when confronted with anemia in HCC patient and also highlight the complementary role of molecular imaging modality along with MRI in the metastatic work-up for hepatocellular carcinoma postcurative resection.

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https://doi.org/10.1016/j.radcr.2020.12.047

Introduction

Extrahepatic metastases (EHM) of hepatocellular carcinoma (HCC) are now observed frequently because of improved diagnostic methods and prolonged survivals.

The most frequent metastatic sites of HCC are lungs, bone, lymph nodes, and adrenal glands. However, gastrointestinal tract involvement is a rare entity with a poor prognosis that should be kept in mind particularly in patient with unexplained anemia; it can occur via hematogenous route or direct invasion. Here we report a case with HCC after liver resection who presented with unexplained anemia and was found to have gastric metastases.

Molecular imaging modality namely ^{18}F-Choline/PET CT played a major role along with magnetic resonance imaging (MRI) and upper endoscopy to properly evaluate the patient and assess the burden of his recurrent disease.

Case presentation

A 69-year-old male patient who presented with large liver mass involving segment VIII that was consistent with HCC and appeared to be a non-AFP producing HCC. According to Barcelona-Clinic Liver Cancer Staging system (BCLC Staging of Liver Cancer) he fits the intermediate stage (stage B) at presentation since he has large tumor more than 3 cm, good liver function (Child-Pugh classification: A) with good performance status (ECOG score is 0).

Right hepatectomy was performed; the pathological examination revealed a 10 cm well-differentiated hepatocellular carcinoma; the surrounding liver parenchyma revealed mild steatosis.

One year later during the surveillance follow-up post his liver resection, he was noted to have generalized weakness and anemia. His follow-up MRI showed a gastric "polyp" without evidence of local HCC recurrence within the liver (Fig. 1). Subsequently; he underwent upper endoscopy that revealed multiple gastric polyps in the body of the stomach; 2.5 cm polyp in the greater curvature was removed and sent for histopathology. Another gastric body polyp measuring 3 cm was found with evidence of bleeding. Epinephrine injected (2 mL) and bleeding stopped.

The biopsy demonstrated metastatic hepatocellular carcinoma. His alphafetoprotien (AFP) at that time was 3.3 μg/L, which is normal, his lab was only remarkable for iron-deficiency anemia.

Further staging work-up included dual imaging with ^{18}F-Choline/fluorodeoxyglucose (^{18}FDG) positron emission tomography (PET)/CT. In addition to the gastric metastasis; he had PET findings of a right adrenal metastasis, as well as bone metastases involving multiple sites at L4-L5, and the right parietooccipital region of the skull (Fig. 2). His bone metastases were asymptomatic. Patient was started on sorafenib and currently he is alive one–and-half-year postdetection of his metastatic disease under palliative care.

Discussion

HCC is the most prevalent primary malignancy of the liver account for 85%-90% of primary liver cancer that has a poor prognosis owing to its frequent intrahepatic recurrence and EHM [1].

However, with newer treatment modalities including liver transplant, together with advances in imaging techniques, survival from hepatocellular carcinoma have improved, patients might achieve long term survival that is substantially longer than before [2].

Furthermore; EHM of HCC are now observed more frequently because of improved diagnostic methods and prolonged survival.

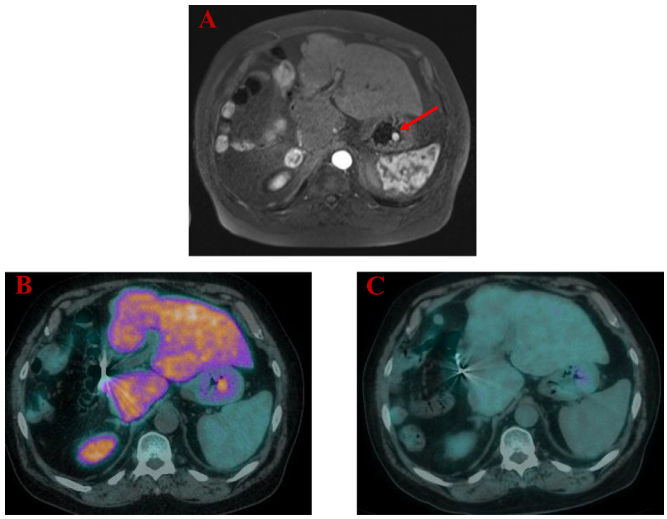

Fig. 1 – Enhancing gastric polyp arising from the greater curvature of the stomach (red arrow) seen in the T1 weighted MRI early arterial image (A) that shows intense choline uptake with minimal FDG uptake on fused ^{18}F Choline PET-CT (B) and ^{18}F FDG PET-CT (C).

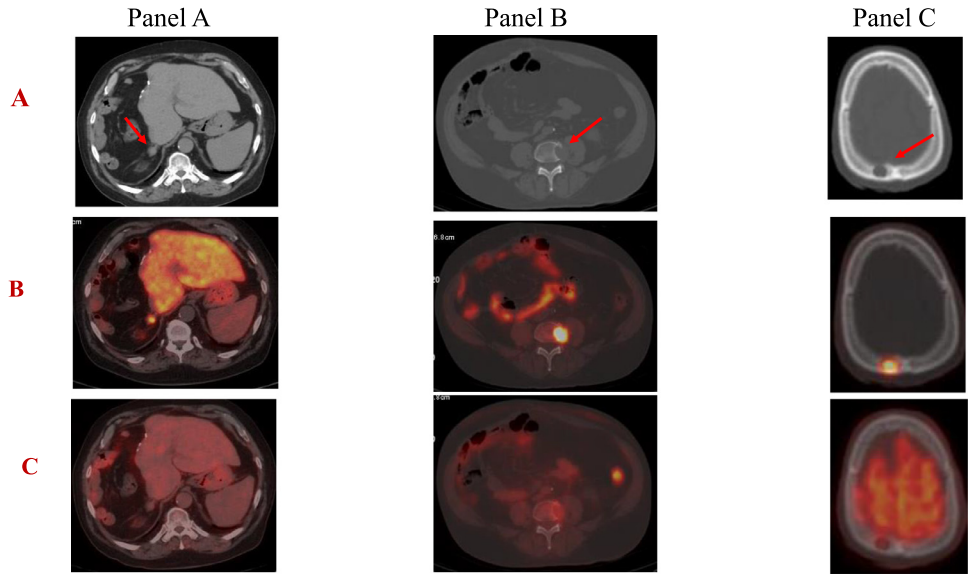

Fig. 2 – Right adrenal metastases, L-2, and right parieto-occipital lytic bone metastases (red arrows) in panel A, B, and C respectively; top raw represents CT, middle raw represents fused ^{18}F Choline PET-CT and the bottom raw represents fused ^{18}F FDG PET-CT.

Because of better control of the primary tumor, the significance of distant metastases to patient management has increased.

Approximately, 13.5%-36.7% patients with HCC will develop EHM particularly in advanced stage disease according to the Barcelona clinic liver cancer (BCLC) staging system; lung is the most common site of metastasis in HCC, followed by lymph nodes, bones and the adrenal glands [3,4].

Gastric metastasis from HCC is extremely rare; in a series of 8267 patients with HCC, only 7 cases (0.08%) were found to have gastric metastases [5]. Additionally, among 31 autopsied cases of HCC, gastric metastasis was found in only one case [6].

Metastases are usually concurrent with intrahepatic lesions, but can occur alone in the absence of intrahepatic recurrence. It usually occurs by the direct invasion of a contiguous neoplasm, or by hematogenous spread [7].

Portal-systemic circulation and the retrograde portal vein are mainly the possible routes of hematogenous metastasis to the stomach. Portal vein tumor thrombi lead to releasing cancer cells in the portal vein draining retrograde into the gastric venous system and then becoming implanted into the intramural vein of the stomach [8,9]. In our case, the patient did not have portal vein tumor thrombus; however, he had a sizable tumor measuring 10 cm that is alone considered a risk factor for recurrence or distant hematogenous metastases.

The proper evaluation and detection of intrahepatic spread, involvement of vascular structures and diagnosis of EHM is crucial to optimize potential therapy for patients.

CT/MRI are not recommended as the primary imaging modality for surveillance; except in patients whom ultrasound is limited by body habitus, hepatic steatosis, or severe parenchymal heterogeneity from advanced cirrhosis.

Our patient had steatosis which limit the sensitivity of US therefore MRI of the abdomen with AFP were initially requested when he presented with anemia to exclude recurrent disease.

AFP alone is not recommended because of its poor sensitivity and specificity [10]. The combination of AFP plus US/MRI increase the detection rate compared with US/MRI/CT alone [10]; that was observed in our patient whom AFP was normal at the time of initial recurrence.

His subsequent dual imaging with Choline/FDG PET/CT confirmed the gastric metastases and in addition revealed other sites of unexpected metastatic disease in the right adrenal and the bone.

Role of conventional and molecular imaging in HCC

Conventional CT/MRI

CT and MRI remain the main stay of oncologic imaging of the liver.

In the presence of chronic liver disease, HCCs can be diagnosed on dynamic contrast CT/MR if they display characteristic features like arterial enhancement and portal venous washout regardless of the size [11]. MRI has been shown to be more sensitive than CT scan in a per lesion comparison (80% vs 68%) [12].

Molecular imaging

Molecular imaging particularly with the hybrid imaging technique that combines positron emission tomography and CT/MRI is playing evolving and growing rules in oncological imaging. The forefront and the most widely used radio-

tracer for PET imaging is FDG. It reflects intracellular glucose metabolism which is usually increased in malignant tissue, known as Warburg effect.

^{18}F-FDG is administered intravenously and is then transported into cells by glucose transporter proteins in a fashion similar to that for unlabeled D-glucose. Subsequently, ^{18}F-FDG is then phosphorylated by hexokinase to form ^{18}F-FDG-6-phosphate. The cell membrane is impermeable to both glucose 6-phosphate and FDG-6-phosphate. However, the latter cannot be further degraded via the glycolysis pathway nor can it easily undergo dephosphorylating by glucose-6-phosphatase. Ultimately, ^{18}F-FDG-6-phosphate remains trapped within the cell and the more ^{18}F-FDG within the cells the more increased uptake within the tumor itself [13].

Low level of glucose-transporter-1 and high glucose-6-phosphatase expression within HCC cells are causing reduced FDG uptake within HCC lesions [14].

The overall detection rate for HCC is ranging from 50% to 65% [15,16]. However; with regard to detection of metastases from HCC, FDG perform reasonably well with 77% sensitivity and 98% sensitivity [17].

Several other radiotracers have been evaluated in HCC to overcome the limitations of FDG PET/CT such ^{11}C-acetate and ^{11}C/^{18}F-Choline.

^{11}C-Acetate

Acetate is a precursor of Acetyl-CoA needed for the synthesis of fatty acids and cholesterol to build up the cell membrane [18]. Unlike ^{18}F-FDG PET, the detection rate of well-differentiated type of HCC is high; several authors evaluated the role of dual-tracer PET with ^{18}F-FDG/^{11}C-Acetate in patients with HCC lesions. ^{11}C-Acetated achieved a sensitivity of 70%-80% that can easily exceed 80% to approach nighties when the dual imaging technique (FDG/Acetate) is being performed [19–21].

The main limitation of ^{11}C-Acetate is represented by the ultra-short half-life of C-11 radionuclide of about 20 minutes so that the use of ^{11}C-Acetate is possible only in PET centers with an on-site cyclotron. To overcome these limitations, a derivative of acetate labeled with ^{18}F-fluorine, which has a significantly longer half-life (110 minutes), has been developed.

^{18}F-Choline

Choline is a precursor of phospholipids, such as sphingomyelin and phosphatidylcholine (lecithin), which is essential for cell membrane synthesis during the cell proliferation process, the event that is augmented in malignant tissues [22].

^{18}F-fluorocholine (FCH) PET/CT seems to be a promising modality in the evaluation of HCC, with a sensitivity and specificity of 88% and 100%, respectively [23]. It is more sensitive than ^{18}F-FDG PET/CT in the detection of this malignancy, particularly the well-differentiated type [23].

Again; the dual imaging tracer modality (FDG/Choline PET) yielded a higher overall sensitivity exceeding 90% in the detection with much improved specificity [24,25]. It was shown to be superior to CT or MRI for the detection of extrahepatic HCC, with an accuracy of 99% vs 32%, respectively [26].

Interestingly, all the sites of metastases in our patient were choline avid while showing no significant FDG activity.

In conclusion, the possibility of gastric metastasis should be kept in mind particularly in patients with advanced HCC when presenting with unexplained anemia; surveillance work-up should include conventional MRI/CT in combination with AFP and molecular imaging study namely ^{18}F-Choline PET/CT to exclude local recurrence within the liver and distant metastases.

Acknowledgments

The authors gratefully acknowledge the support of the King Faisal Specialist Hospital and Research Center (KFSH&RC) (RAC # 2151 003 and RAC # 2130 022). This work was funded in part by King Abdualaziz City for Science & Technology (14-MED 1963-20). Thanks also to the Cyclotron and Radiopharmaceutical Department for the support in providing the needed radiotracer for this study.

Consent for gastric wall metastases from HCC

Authors are confirming that the presented study is under an approved project by the research ethical committee and research advisor board at the institutions. Furthermore, no patient's identification been presented in this manuscript. Yet original consent and permission was signed by the patient for any future need.

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