

Dotted Fried Egg Pan Appearance: A Sign of Aggressive Intrahepatic Mass Forming Cholangiocarcinoma

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Abstract

Background: Intrahepatic Cholangiocarcinomas (ICC) are the second most common primary malignant liver tumors after Hepatocellular carcinomas (HCC). They pose a diagnostic challenge, and often it becomes difficult to distinguish these from metastases, particularly adenocarcinomas from the gut, pancreas, and gall bladder. In some patients, atypical presentations on imaging also make it difficult to distinguish them from HCC lesions.

Case presentation: Authors present one such case of a 60-year female with history of nausea with weight loss of recent onset for ultrasound examination which revealed multiple hypoechoic nodules in the liver. A CECT and Plain MRI examination confirmed the same. A triple phase CE MRI was done which revealed a large heterogenous liver mass with satellite nodules in the remaining liver with a dotted fried egg pan appearance".

A guided Fine needle aspiration and biopsy was done which showed adenocarcinoma metastasis.

Conclusions: Authors describe a new sign not described earlier "Dotted fried egg pan sign" which is a sine qua non of an aggressive mass forming ICC and differentiates it from other mimicking lesions of the liver.

Keywords: Cholangiocarcinoma; Hepatocellular carcinoma; Metastasis; Malignant; Adenocarcinomas; Hypoechoic nodules.

Abbreviations: MF-ICC: Mass Forming Intrahepatic Cholangiocarcinoma; HCC: Hepatocellular Carcinoma; MRI: Magnetic Resonance Imaging; CECT: Contrast Enhanced Computed Tomography; PD-L1: Programmed Death-Ligand1.

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Introduction

Intrahepatic cholangiocarcinoma (ICC) is the second most common primary malignant liver tumor after hepatocellular carcinoma (HCC) [1]. It represents around 20% of cholangiocarcinomas and develops within liver from the second-order bile ducts, peribiliary glands, hepatic stem cells and are usually in peripheral locations of liver [2-3]. According to its macroscopic appearance, the Liver Cancer Study Group of Japan [4-8] has subdivided ICC into four categories: (I) the mass-forming (MF) type, well-defined, solid, non-encapsulated, poly lobulated mass within the liver at distance from the hilum with normal main bile ducts. (II) the periductal infiltrating type (PI), characterized by a tumoral growth pattern spreading along intrahepatic portal tracts and causing biliary stenosis of the involved ducts with upstream biliary dilatation (III) the intraductal growth (IG) type, typified by a polypoid or papillary tumor mass growing within the lumen of a dilated large BD; (IV) the mixed pattern. MF type is the most prevalent, accounting for about 65% of all ICCs, while PI and IG type are much less common, representing 6% and 4% of all ICCs, respectively [9-12]. At advanced stages, intrahepatic metastases occur consisting of varying size nodules, which may coalesce to form larger masses which are indistinguishable from the primary lesion; regional lymph nodes and lung metastasis may also arise in late stage of disease [13]. Preoperative diagnosis of MF, PI and mixed type is always a challenge especially to differentiate them from other hepatic malignant lesions especially metastasis and

HCC nodules and is usually achieved by combining clinical, radiological, serological, and histological information. Authors present one such case and discuss the usefulness of triple phase contrast MRI study, and also describe a new sign “Dotted fried egg pan appearance” which is a diagnostic of aggressive MF-ICC and has not been described so far.

Case presentation

A 60-year female with history of weight loss and nausea since past three weeks presented for ultrasound examination of abdomen. The patient had a past history of cholecystectomy 20 years ago and was HCV, HBV nonreactive. ESR was 20mm in the first hour. All routine hematological and biochemical examinations were normal. Routine ultrasound examination of liver showed multiple hypoechoic rounded solid lesions in both the lobes (Figure 1). A contrast enhanced computed tomography of the abdomen and chest revealed multiple non-enhancing nodules in both lobes of liver with upper abdominal nodes with bilateral small lung nodules (Figure 2). Plain MRI of the abdomen showed solid hyperintense infiltrative and well-defined rounded lesions in both lobes (Figure 3A-B) with a normal MR cholangiogram (Figure 3 C). A FDG -PET scan also revealed hypodense avid lesions in the liver and in the lungs with few FDG positive nodes in the upper abdomen and mediastinum. A guided fine needle aspiration cytology with core biopsy of liver was done which revealed pleomorphic cells with areas of small cell acinar pattern.

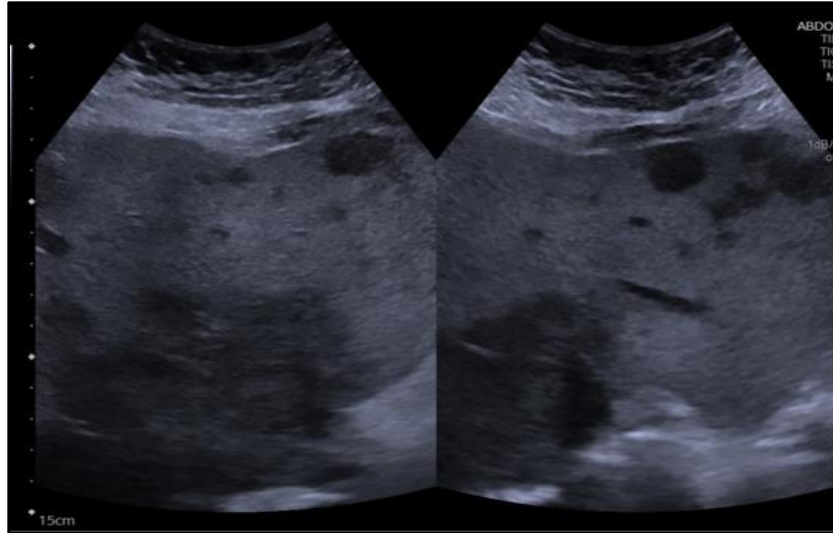


Figure 1: Ultrasound of the liver showing multiple hypochoic rounded lesions in both the lobes.



Figure 2: Contrast enhanced CT image of the liver showing non enhancing hypodense lesions.

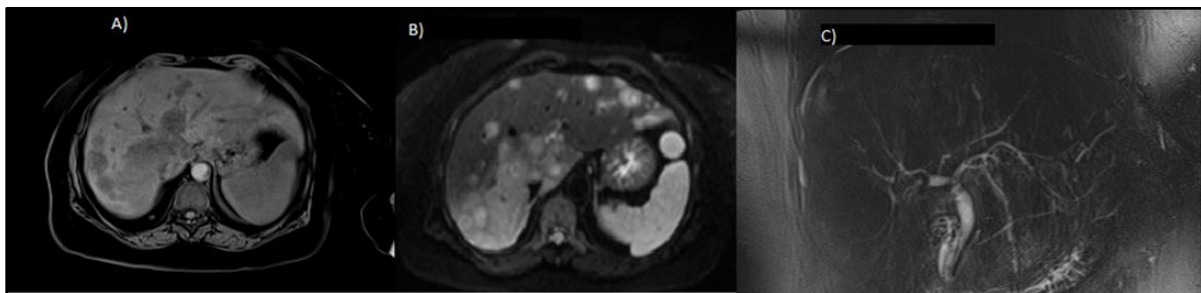


Figure 3: A) Plain MR axial T1W image showing hypointense rounded lesions in liver. B) T2W image with hyperintense mass forming and rounded nodular lesions. C) MRCP showing normal cholangiogram.

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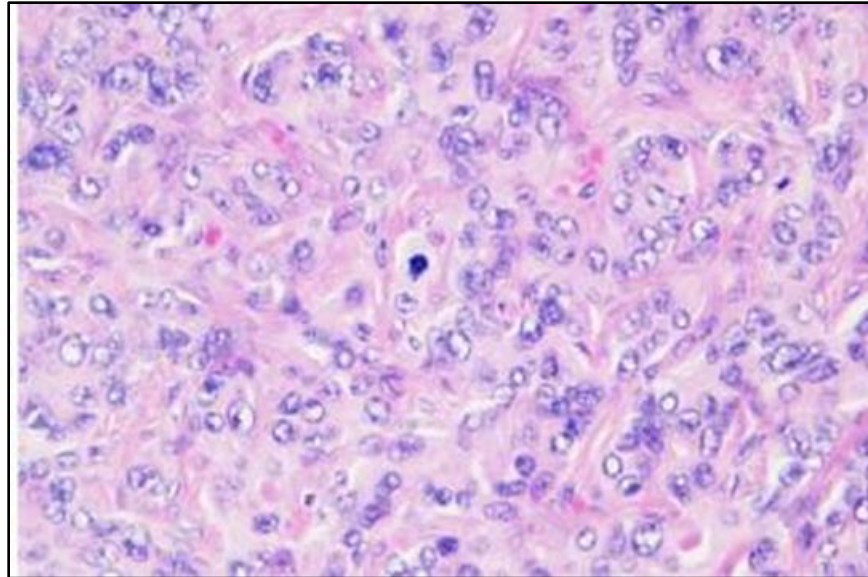


Figure 4: Hematoxylin and Eosin high power histology image showing infiltrative small round cells with poor acinar pattern and increased stroma.

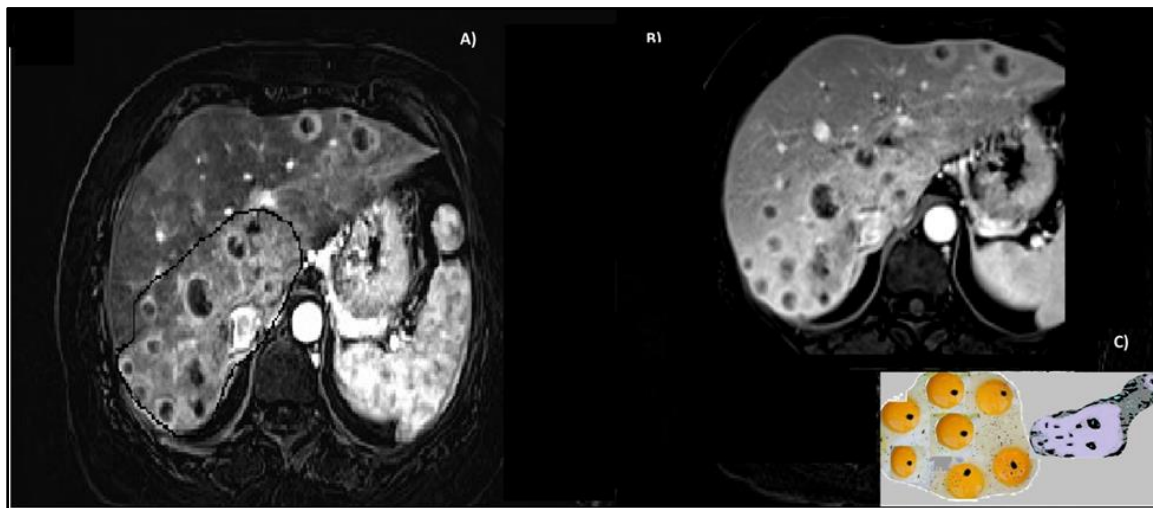


Figure 5A: Arterial phase contrast enhanced MR showing dotted fried egg appearing mass in right lobe (marked with black line drawing) B. Portal Phase of contrast enhanced MR of liver showing persistent dotted fried egg with some rim thickening. C) Line drawing and photo depiction of the above appearance of MF-ICC.

On histology infiltrating small cells with poorly differentiated acinar pattern with abundant stroma was seen (Figure 4) which was suggestive of poorly differentiated metastasis from adenocarcinoma. Various

tissue biomarkers were done i.e. CA19-9, CEA, AFP, IDH₁, IDH₂, CK19, MP-7 isocitrate dehydrogenase (IDH₁, IDH₂), Cytokeratin 19 and Metalloproteinase-7 were positive. Next generation sequencing was done which

showed a FGR2-BICC1 fusion mutation. A triple phase contrast enhanced MRI was done which showed a 11x8 cm heterogeneously enhancing mass in the right lobe of liver with central rounded hypo enhanced lesions with an enhancing dot in them. Few similar scattered nodules were seen in both lobes in arterial phase (Figure 5A-C) which show partial progressive filling by contrast a sign we labeled as dotted fried egg in pan appearance. After reviewing all the clinical, histological, biomarker, molecular and radiological findings the diagnosis of MF-ICC was made. Patient was put on intravenous gemcitabine and Cisplatin along with immunotherapy durvalumab (a programmed death-ligand1 (PD-L1) inhibitor) six cycles and is on follow up.

Discussion

MF-ICC lesions usually are clinically silent in the early stages of disease and once they increase in size or metastasize, they pose a diagnostic challenge especially to differentiate them from primary lesions like HCC and other metastatic hepatic lesions. The diagnosis is usually achieved by combining clinical, radiological, serological, and histological information. No single biomarker is diagnostic to point towards biliary origin. Radiological features of MF-ICC also vary with the histological features i.e. the degree of cell differentiation in the tumor and the degree of desmoplasia, tumoral fibrosis and mucin formation. MF-ICC lesions usually have a more densely fibrotic component with sparse tumoral cells while the periphery has more abundant and proliferating tumoral cells, that infiltrate the surrounding parenchyma either by compression,

infiltration along the sinusoids or replacement of hepatocytes. On plain MRI MF-ICC appears a hypointense lesion on T1w with a variable increased T2 signal which depends on degree of tumor fibrosis, mucoid change, and necrosis and hence most of MF-ICC present as a heterogeneous lesion on T2 both areas of hyperintensity and areas of hypo intensity [11-13]. On triple phase MRI there is a peripheral rim enhancement of the lesion in the early arterial phase with gradual filling of central component giving a classic cloud like appearance which differentiates it from HCC and other metastatic liver nodules on a triphasic contrast study [14]. Diffusion imaging may show target sign i.e. Diffusion restriction at the peripheral part and low DWI in central part and is also characteristic of MF-ICC [15]. There may be ancillary findings like capsular retraction, lymphadenopathy, biliary dilatation, vascular encasement, satellite nodules and lung metastasis. However, in atypical cases these classic features may not be present as was seen in the present case. MF-ICC lesions may appear hyper vascular or there may be lack of progressive enhancement or even be hypo vascular on arterial phase due to mucin secretion and it becomes impossible to differentiate it from solitary hypo vascular metastasis or HCC. Authors describe a classic “dotted fried egg pan appearance” of MF-ICC in triple phase contrast enhanced MR study in this patient where in the arterial phase there is diffuse mass like enhancement of the lesion interspersed with multiple non enhancing rounded hypointense nodules with enhancing rims like a fried egg and with a central dot. This is explained by the presence of central fibrin/mucin collections in the hepatic lobules with the dot being

compressed hepatic venule. The enhancing rim being due to hyperemic tumor cells and the stroma of the tumor matrix showing collagenous enhancement. This appearance remains unchanged in the portal phase while in the late phase there may be some central filling or thickening of the rims. Authors feel that this is sine qua non of an aggressive MF-ICC and has not been described in literature. It not only helps to differentiate the lesion from metastatic liver nodules but also differentiates it from atypical liver HCC.

Conclusion

The diagnosis of intrahepatic MF-ICC is very challenging both on imaging as well as on histopathology examination and the appearances mimic those of metastasis from adenocarcinoma as well as atypical HCC. The combined use of histology with biomarkers and radiological examination is important to reach a final diagnosis. The case highlights the importance of triple phase contrast enhanced MRI which shows a dotted fried egg

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Consent for publication

Yes.

Availability of data and material

Yes.

Competing interests

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Authors' contributions

Atul Kapoor and Aprajita Kapur-Manuscript preparation, Rishiv Kapur-bibliography search and figure and art.

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