SAR·DFP
Society of Abdominal Radiology
Disease-Focused Panels
Primary Hepatic Neuroendocrine Tumour

Presented By: Dr. Kedar G Sharbidre M.D
Case history: 49 year old female with incidentally discovered liver mass during workup for back pain following a fall.

Multiphasic Contrast enhanced CT study of the abdomen (A: Non-contrast, B: Arterial, C: Portal venous and D: delayed) showing large right hepatic mass with predominantly cystic areas(White arrow). Arterial phase hyperenhancement(yellow arrow heads)is notably seen along the margins and in solid components with delayed iso to hypoenhancement.
A whole body PET scan from the skull base through the mid-thigh after administration of 5.71 mCi GA-68 Dotatate NET Spot. IV. MIP coronal (A), Fused Coronal (B) and Fused Axial(C) showing markedly tracer avid, large, mixed (solid and cystic) mass in the right lobe and medial hepatic segment. No other suspicious tracer avid finding elsewhere in the chest, abdomen or pelvis.
**Diagnosis:** Primary hepatic neuroendocrine tumour

**Imaging:** Incidentally detected hepatic mass with nonspecific imaging findings on cross sectional imaging as above. No other lesions were seen elsewhere in the abdomen or CT on multiphasic CT performed on two separate occasions. PET-Dotatate scan revealed intense activity within the hepatic lesion and absence of uptake elsewhere in chest, abdomen or pelvis. Upper GI endoscopy was negative.

**Pathology:** Well differentiated neuroendocrine neoplasm (grade 1). Core biopsy of the hepatic mass: Polygonal, monomorphic cells containing granular nuclear chromatic with small nucleoli.

Immunohistochemical stains with appropriate positive controls:
- Positive for chromogranin, synaptophysin, cytokeratin (CAM5.2). Negative for PAX8, TTF-1, Arginase-1
- Ki67 labeling index: <2% (approximately 1,000 cells were counted).
DISCUSSION:

• Primary hepatic neuroendocrine tumours (PHNET's) are not only rare (with less than 150 cases reported worldwide) but also present with non-specific clinical and radiographic presentation, and histologically heterogeneous entity.

• As metastatic neuroendocrine tumours to the liver are much more common, extensive investigations are crucial to exclude a primary tumour elsewhere since the therapeutic options and prognoses differ between them. Only once a primary extrahepatic source is excluded after investigations, can the diagnosis of PHNETs be made confidently.

• Mostly discovered incidentally, without endocrinological symptoms compared to the hepatic metastases from enteropancreatic NETs. Clinically patient is asymptomatic or symptoms secondary to mass effect of the tumour on the hepatic parenchyma and adjacent structures (abdominal pain, weight loss, palpable mass, gastric outlet obstruction).

• The pathognomonic features of carcinoid syndrome associated with metastatic neuroendocrine tumours to the liver, occur infrequently (despite evidence showing the presence of bioactive amines) with primary hepatic neuroendocrine tumours (5-10%).

• They show slow growth and have low malignancy potential presenting a 10-year survival as high as 73%.
**IMAGING:**

1. Variable and lacks specificity, often misdiagnosed as other hypervascular benign lesions like hepatic adenoma or hemangioma or hepatic malignancy such as HCC or cholangiocarcinoma.

2. Tumours usually arise in a background of non-cirrhotic liver and may vary in size from a few centimeters to the largest reported as being 26 cm. On MRI, both primary tumors and NET metastases appear T1 hypointense and T2 hyperintense and demonstrate intense enhancement in hepatic arterial dominant phase with washout in portal venous and delayed phases, reflecting hypervascularity on multiphase CT and MRI.

 Kellock et al reported that G1 PHNETs usually have single lesion in the right lobe whereas G3 PHNETs commonly have multiple diffuse lesions or one large tumor accompanied by several satellite lesions. In a case series Huang et al. found that many of these tumors had cystic changes or necrosis present on ultrasound, CT, and MRI as seen in our case and this feature may be helpful in differentiating them from HCC. In a recent case report by Krohn et al. PHNET mimicked an Echinococcus cyst on CT and MRI.

<table>
<thead>
<tr>
<th>PHNET’s or metastatic NET’s</th>
<th>HEPATOCELLULAR CARCINOMA (HCC)</th>
<th>CHOLANGIOCARCINOMA</th>
<th>BENIGN HEPATIC LESIONS</th>
<th>METASTASIS</th>
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<tbody>
<tr>
<td>PHNETs: Arterial hyper or hypoenhancement with variable washout.</td>
<td>Marked solid arterial hyperenhancement, delayed washout pattern and associated pseudo capsule.</td>
<td>Progressive delayed phase enhancement on multiphase study.</td>
<td>FNH and adenoma: Arterial hyperenhancement with portal venous phase enhancement equal to or slightly higher than normal liver tissue.</td>
<td>Rim arterial hyperenhancement, peripheral washout and delayed central enhancement.</td>
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<td>Metastatic Hepatic NET’s: Arterial hyperenhancement.</td>
<td>Cirrhotic liver or h/o hepatitis.</td>
<td>Scar</td>
<td>Scar +</td>
<td></td>
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<tr>
<td>Non cirrhotic liver. No hepatitis.</td>
<td>Scar/Calcifications: In Fibrolamellar HCC</td>
<td>Calcification+</td>
<td>Calcifications/Fat/Blood/cystic changes: Variable, depending on primary tumour.</td>
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<tr>
<td>Cystic/necrotic changes: Esp in PHNET’s.</td>
<td>Capsule+</td>
<td>Fat : absent</td>
<td>Diffusion Restriction +</td>
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<tr>
<td>Scar/calcifications: Absent.</td>
<td>Fat/Hemorrhage: +</td>
<td>Increased serum levels of alpha-feto protein (AFP).</td>
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<tr>
<td>Capsule: Absent</td>
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<td>Fat: Absent</td>
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<tr>
<td>Hemorrhage: Variable</td>
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<td>Symptoms of carcinoid tumour: Variable</td>
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<td>Immunoreactivity for chromogranin A, neuron specific enolase, and synaptophysin.</td>
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PATHOLOGY:
• The assessment of cellular proliferation appears as a reliable tool to determine the malignancy potential of these tumors, and lower cellular proliferation is linked to better survival rates. However it is difficult to distinguish between primary or secondary hepatic NETs based on the histopathologic findings only.

• The cellular origin of PHNETs remains unclear, however possible sites of origin include (1) from neuroendocrine cells scattered in the epithelium of the intrahepatic biliary tract; (2) from heterotopic pancreatic or adrenal tissue located in the liver; (3) or the neuroendocrine differentiation of a single malignant stem cell that is the precursor of other hepatic tumors.

• Immunohistochemistry is performed as the definitive diagnosis for PHNETs, typically after they have already been resected. NETs have previously been shown to be associated with immunoreactivity for chromogranin A, neuron specific enolase, and synaptophysin.

MANAGEMENT:
• Surgical resection with clear margins is the mainstay treatment for single isolated PHNETs with long-term survival rates.
• For unresectable tumours confined to liver, treatment options include transcatheter arterial chemoembolization (TACE) or liver transplantation. Chemotherapy can be considered for treatment of PHNETs with multiple masses or distant metastases; however, its benefit remains questionable.
REFERENCES: