FOR YOUR EYES ONLY:
A Guide to Accurate Detection of Diffuse Infiltrators in the Liver

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Target Audience

- Practicing Radiologists
- Fellows
- Residents
Learning Objectives

• Overview of infiltrative diseases of the liver
  • Sarcoidosis
  • Amyloidosis
  • Hematologic disorders
  • Infiltrative neoplasms

• Review cases of infiltrative liver disease to recognize findings that allow differentiation between these disorders
  • CT, MRI, PET
Infiltrative Liver Diseases

- Diseases in which abnormal cells or proteins deposit around hepatocytes
- Occur secondary to a broad host of causes
  - Inflammation
  - Neoplasm
  - Overproduction of protein
Infiltrative Liver Diseases

A word about “fatty infiltration”...

Hepatic steatosis is not a truly infiltrative process because it is fat deposition within hepatocytes rather than surrounding hepatocytes.

Consider reporting: “Diffuse hepatic steatosis” rather than “Diffuse fatty infiltration”
Sarcoidosis

Multisystem granulomatous disease thought to be a result of immune response to a yet unknown stimulus, affecting patients worldwide.

Noncaseating granulomas (as seen in biopsy specimens, top right) most frequently found in the lymphoid tissue of lungs/mediastinum, liver, spleen and skin, though other areas are also possible.

• Diagnosis of exclusion (infection, granulomatous process of known etiology, lymphoma), typically requiring biopsy
• Therapy typically involves corticosteroids and cytotoxic agents, accurate diagnosis is essential to avoid medication side effects
Sarcoidosis

Imaging features

- Deposition may result in organomegaly
- Granulomas are microscopic and therefore often not visible as focal lesions at the resolution of medical imaging
  - Patchy areas of relative hypoenhancement at CT/MR and inflammation (+DWI and increased T2 on MRI)
  - Accumulate in the periportal region (lymphatics)
- May result in chronic inflammation causing fibrosis
  - Cirrhosis is end stage
Hepatic Sarcoidosis

51 year-old woman with known sarcoid:

MRI Abdomen:
- Diffuse hepatosplenomegaly
- Innumerable ill-defined, hypoattenuating lesions with enhancing cores present throughout the liver and spleen
- T2 Imaging demonstrates a “periportal halo” of decreased signal compatible with periportal infiltration

US Guided core biopsy:
- Diffuse heterogeneous echotexture
- Non-caseating granulomas (brackets)
Hepatic Sarcoidosis

52 year-old man:

MRI Abdomen:
- Nodular liver contour
- Focal fibrosis in segment VII (arrows)
- No focal lesions
- Findings compatible with cirrhosis of the liver

Liver Explant:
- Cirrhosis with focal non-necrotizing granulomatous inflammation (sarcoid)
Hepatic Sarcoidosis

36 year-old man:

MRI Abdomen:
- Nodular liver contour compatible with cirrhosis
- Scattered T2 hyperintense, enhancing foci throughout the liver (arrows)
- Hypointense splenic lesions
- Enhancing, T2 hyperintense osseous lesions (arrowheads)

Liver biopsy:
- Granulomatous inflammation compatible with sarcoid
44 year-old man with biopsy proven pulmonary and osseous sarcoid, with rising LFTs:

MRI Abdomen:
- Mild hepatomegaly
- Multiple subtle punctate areas of reduced diffusion, T2 hyperintensity and faint arterial hyperenhancement (arrows)
- Mildly increased liver stiffness
- Normal spleen
- Enhancing osseous lesions
Amyloidosis

- Abnormal deposition of proteins in the extracellular space
- Apple green birefringence on congo red stain

WHO classification
- Amyloid light chain (AL) – Primary type
- Amino acid (AA) – Secondary type, acute phase reactant from chronic inflammation
- Other types including transthyretin-related amyloidosis (ATTR) which can be hereditary or secondary to dialysis, thyroid carcinoma, or diabetes

Amyloid may involve any part of the body but most commonly the GI tract (bowel, liver), spleen, kidneys, heart, and genitourinary system.
**Amyloidosis**

**Hepatic Imaging Features:**
- May be diffuse (most common) or localized (less common)
- Hepatomegaly
- Low density at CT
- Reported High T1, low T2 signal
- Findings are nonspecific

**Systemic vs. Localized Amyloid:**
- Systemic amyloid results from deposition of light chains in tissue – no FDG uptake
- Localized amyloid typically results in local giant cell reaction – + FDG uptake

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Amyloidosis

60 year old woman with abdominal pain:

CT +C:
• Massive hepatomegaly
• Diffuse hypoattenuation

Liver Biopsy: Amyloidosis with extensive replacement of hepatic parenchyma.

69 year old man:

CT +C:
• Moderate hepatomegaly
• Heterogeneous attenuation of hepatic parenchyma

Liver Biopsy: AL type amyloidosis.
63 year-old man with AL Amyloidosis diagnosed by bone marrow biopsy, treated with autologous stem cell transplant. Bone marrow analysis after transplant was negative for residual disease, however, the patient remained symptomatic. PET/CT and MRI were performed:

**MRI Abdomen:**
- Multiple non-circumscribed T2 hyperintense lesions in both lobes of the liver
- Enhance less avidly than liver on arterial and portal-venous phases

**PET/CT:**
- Focal FDG uptake within lesions
63 year old man with abdominal pain found to have diffuse hepatic amyloidosis at biopsy

CT Abdomen without contrast:
- Heterogeneous hepatic density, most pronounced in the right hepatic lobe

MRI Abdomen:
- Subtle T2 hyperintense enhancing foci in both lobes
- Markedly heterogeneous enhancement of the right lobe
Hematologic Disorders

Extramedullary hematopoiesis:
Production of RBCs outside bone marrow
Result of myelofibrosis, diffuse osseous metastases, leukemia, thalassemia, sickle cell
Occurs throughout body: Chest, liver, spleen, retroperitoneum, presacral, epidural space

Imaging appearance in the liver:
Most commonly: Organomegaly
Sometimes discrete masses and/or periportal/peribiliary involvement

CT images from an 83 year old woman with myelofibrosis show diffuse hepatosplenomegaly without focal lesions. Planar images following injection of $^{99m}$Tc-Sulfur Colloid show diffusely increased hepatic and splenic uptake compatible with extramedullary hematopoiesis

Hematologic Disorders

Images from a 29 year old woman found to have low platelets ($50 \times 10^9/L$) and initially treated with splenectomy without improvement.

CT Abdomen:
Marked atrophy of the right hepatic lobe, and abnormal heterogeneous enhancement of an enlarged left lobe. Delayed images show contrast uptake compatible with fibrosis.

Liver Biopsy:
Patchy changes including evidence of venous outflow impairment (sinusoidal dilatation with hepatic atrophy), extramedullary hematopoiesis and nodular regenerative hyperplasia with patchy periportal fibrosis.
Lymphoma/Leukemia:
Typically secondary hepatic involvement (Non-Hodgkins)
Primary hepatic lymphoma is extremely rare

Imaging appearance in the liver:
Focal liver masses are most common, however infiltrating pattern may be seen
80 year old woman with history of multiple myeloma and newly abnormal liver function tests:

CT with contrast:
• Heterogeneous enhancement

MR with contrast:
• Patchy peripheral low T1 signal, with corresponding increased T2 signal and reduced diffusion
• Relative hypoenhancement is seen on contrast enhanced images

Liver Biopsy: Large B-cell lymphoma
65 year old woman with history of cutaneous T-cell lymphoma and a cholestatic picture on laboratory testing:

CT with contrast:
- Massive hepatomegaly
- No focal lesions
- Small ascites

Liver biopsy:
- Extensive sinusoidal and parenchymal involvement of liver by confluent nests of large lymphoma cells
- Immunohistochemical staining compatible with large B-cell lymphoma
Infiltrative Metastases

33 year old woman with breast cancer and known liver metastases:

- Infiltrative metastases typically arise from breast, lung or melanoma primary.
- When confluent or after treatment may result in the appearance of "pseudocirrhosis" with capsular nodularity and retraction.
- Elevated portal pressures may also be present due to portal obstruction by metastases or architectural distortion from desmoplastic reaction.

Initial Staging CT 6 mo Follow-up exam after chemotherapy
Infiltrative Metastases

64 year old woman with infiltrating ductal carcinoma of the breast:

Pre-treatment CT:
- Innumerable hypodense lesions consistent with metastases
- Otherwise normal liver morphology

3 months Chemotherapy

Post-treatment CT:
- Pseudocirrhosis characterized by:
  - Bilobar atrophy
  - Contour nodularity
  - Bands of fibrosis
  - Splenomegaly and ascites (portal HTN)
Infiltrative Metastases

74 year old woman with history of pancreatic neuroendocrine tumor:

MR Abdomen:
Ill defined enhancing and infiltrating mass with reduced diffusion located in the posterior right hepatic lobe.

Liver Mass Biopsy:
Findings compatible with high grade/de-differentiated metastatic neuroendocrine tumor.
Infiltrative Metastases

58 year old man with right chest melanoma and known metastatic axillary nodes.

**Abdominal sonogram:**
Sonogram obtained for abdominal pain and elevated LFTs shows multiple hypoechoic nodules throughout the liver as well as contour irregularity of the liver capsule.

**FDG PET/CT:**
Patchy hypermetabolism throughout the left lobe of the liver. Nodular liver contour.

**Liver biopsy:**
Positive for metastatic melanoma.
59 year old man with metastatic small bowel neuroendocrine tumor:

CT Abdomen:
Geographic area of hypoenhancement within segments II/IVa. Associated capsular retraction. Additional geographic mass in the tip of segment II well defined hypodensities in the posterior right lobe of the liver.

68-Gallium DOTA-TATE PET/CT performed 24 hours later:
Marked DOTA-TATE uptake in the region of both geographic infiltrative appearing masses as well as within other normal appearing areas of the liver. Findings suggest more diffuse metastatic involvement of the liver than is seen on anatomic imaging alone.
Mimics – Focal fatty deposition

44 year old man with remote history of testicular cancer being evaluated for abdominal pain and distension:

CT Abdomen:
Low density involving the majority of the left hepatic lobe and the medial posterior right hepatic lobe.

MR Abdomen:
In-phase (IP) and opposed-phase (OP) images demonstrate loss of signal on opposed-phase images (arrowheads) corresponding to area of concern on CT. Contrast enhanced MR sequences performed later in the exam demonstrate a similar appearance to that of CT.

Liver biopsy: Hepatic steatosis
Mimics – Perfusional Abnormality

44 year old woman with history of pancreatitis:

MR Abdomen:
Markedly heterogeneous arterial phase enhancement throughout the liver normalizes on portal venous phase images. Findings compatible with a transient hepatic intensity difference (THID).
Summary

- Infiltrative diseases of the liver encompass a wide spectrum of causes with often overlapping imaging appearance.

Clinical Relevance

- Imaging appearance may be nonspecific, making diagnosis challenging.
- Patterns and clinical information may help with more accurate diagnosis.
~ Thank you ~

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