Imaging of non-neoplastic liver lesions in infants

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- Non-neoplastic liver disease in infancy is rare and can present as a focal lesion or an infiltrative process.

- While some liver lesions are benign and incidental findings, others may progress rapidly to end stage liver disease and eventually death.

- Early recognition of these lesions may avoid prolonged morbidity and facilitate timely management.
Clinical findings seen in 16 infants with non-neoplastic liver lesions

- Abdominal distention
- Hepatomegaly
- Jaundice
- Abnormal liver function
- Incidental liver abnormality found on abdominal or renal ultrasound
Results

Non-neoplastic liver processes were divided into 5 etiological categories:

- Ischemia
- Infection
- Vascular lesions
- Traumatic lesions
- Biliary abnormalities
Normal infantile liver features

- Average liver span (longitudinal midclavicular) in infants ~ 6 cm
- Ultrasound (US)- homogeneous echotexture
  - At birth the liver parenchyma and renal cortex (red arrow) have similar echogenicities, the liver can be more echogenic than the kidney at 6 months
  - The caudate lobe can appear slightly hypoechoic secondary to acoustic shadowing from fat or fibrous tissue within the fissure of the ligamentum venosum
Normal infantile liver features

- Computed tomography (CT)- homogeneous in attenuation, 40-70 Hounsfield units on noncontrast images
  - Unenhanced liver density is greater than or equal to the spleen
  - Enhanced liver density is similar to the density of the spleen
Normal infantile liver features

- Magnetic resonance imaging (MRI)
  - Signal intensity (SI) of the liver is similar to the SI of spleen on T1-weighted images (A)
  - SI of the liver is low compared to the spleen on T2-weighted images (B)
Case 1

- Female full term infant with hepatomegaly and cutaneous hemangioma on the right upper back.

- AP radiograph of the abdomen demonstrates an abnormal soft tissue mass in the right upper quadrant (arrow) displacing the bowel loops inferiorly and the stomach to the left.
Case 1

- A longitudinal ultrasonogram shows a well-defined heterogeneous and mainly hypoechoic mass lesion (arrow) within the right lobe of the liver.
Case 1

- An aortic angiogram to rule out the possibility of a bleeding liver hemangioma shows an abnormal collection of vessels in the back within the subcutaneous hemangioma of the back (arrow).
Case 1

- AP image from a celiac angiogram shows displacement of the hepatic arteries by a space-occupying mass in the liver.
- There is no evidence of a liver hemangioma or abnormal vessels suggestive of a neoplasm.
Axial enhanced CT of the abdomen shows a well-circumscribed hypodense mass within the liver.
Case 1

The liver mass (arrow) is hypointense on coronal T1-weighted (A) and axial T2-weighted images (B) compared to the normal liver (L). This is consistent with intralesional hemosiderin.

Collectively the US, CT, and MRI findings in this case are consistent with a liver hematoma.

Follow-up US after 6 months showed complete resolution of the hematoma.
Case 2

- A full term male infant presented with abdominal distention.
- (A) Initial ultrasound demonstrates a round, echogenic lesion in the liver (arrow).
- (B) On a follow-up ultrasound 5 days later, the lesion has decreased in echogenicity and appears hypoechoic.
- These findings are consistent with a resolving hematoma.
Infantile liver hematomas

- Infantile liver hematomas are usually small and not symptomatic
- Typically subcapsular in location
- Infantile liver hematomas may be secondary to trauma, coagulopathy, or sepsis
- US is performed initially to evaluate the extent of injury and later to follow healing
- US findings - acute hematomas are hyperechoic or nearly isoechoic due to fibrin or clot
  - Hematomas become more liquefied resulting in subacute hematomas appearing more hypoechoic and cystic
- CT findings - acute or subacute hematomas have irregular high density fluid (fibrin or clot) surrounded by low attenuation
  - Chronic hematomas are primarily low attenuation lesions
Case 3

A male infant born at 36 weeks of gestation presented with 3 weeks of increasing abdominal distention. Laboratory tests revealed elevated liver function tests (LFTs).

- (A) AP view of the abdomen shows multiple air-filled loops of bowel centered in the midabdomen with bulging of the flanks consistent with ascites.

- (B) Ultrasound image demonstrates a heterogeneous liver.
Case 3

Axial enhanced CT of the abdomen shows a nonenhancing low attenuation lesion within the liver with surrounding ascites.

Hypodense liver lesion on CT appears hyperintense on a coronal SSFSE MR image.
Case 3

- **Differential Diagnosis**: metastatic neuroblastoma, diffuse hepatic necrosis from infection or ischemia. Neoplastic processes such as hepatoblastoma or hamartoma were considered less likely secondary to the diffuse appearance and lack of enhancement.

- Liver biopsy confirmed multifocal parenchymal necrosis, focal portal and lobular inflammation, and moderate portal fibrosis. Mild cholestasis and proliferation of ductal structures were believed to be due to a nonspecific reactive process secondary to liver ischemia.
Case 3 diagnosis: Liver necrosis secondary to ischemia

Liver necrosis

- Liver ischemia in infants may be secondary to intraoperative ligation of the hepatic artery, vasculitis, or hypercoaguable states
- US findings - acute infarction appears as a peripheral hypoechoic area
  - Late infarction may appear as a cystic lesion of bile
- CT findings - typically wedge-shaped hypodense lesions, however can be centrally located with indistinct margins without significant enhancement
Case 4

- Female infant who was found to be hypertensive at birth and had elevated LFTs.
- Noncontrast CT of abdomen shows linear calcification in the hepatic artery (red arrow) as well as curvilinear calcification of the aorta (white arrow).
A female infant with elevated blood pressure and respiratory distress at birth also presented with gross hematuria.

Coarse calcifications of the aorta and renal arteries (black arrows) are seen on an axial noncontrast CT section of the upper abdomen (A). Additional images reveal calcifications of the celiac axis, hepatic, splenic, and brachial arteries (B).
Case 5

- On the 19th day of life, the patient developed abdominal distention and necrotizing enterocolitis leading to death on the 21st day from extensive hemorrhagic bowel infarction with purulent peritonitis.

- On autopsy the diagnosis of idiopathic infantile arterial calcification was confirmed.
Cases 4 & 5 diagnoses:
Idiopathic infantile arterial calcification

Idiopathic infantile arterial calcification
- Known as generalized arterial calcification of infancy or occlusive infantile arteriopathy
- Congenital disorder characterized by calcification of the muscularis media, intimal proliferation, and fibrosis of the elastic and muscular arteries
- Clinical presentation- respiratory distress, weakness, tachycardia, hypertension, end organ ischemia, and sudden death
- Survival depends on the severity of vascular compromise by intimal proliferation and treatment given
- Imaging findings - calcification of the aorta and arteries can be seen on plain radiographs and better on non-contrast CT
Full-term female infant with Down’s syndrome found to have hyperbilirubinemia and elevated LFTs underwent an abdominal ultrasound. An incidental finding is described below.

Longitudinal ultrasound image demonstrates a hypoechoic tubular structure extending from the umbilical vein (red arrow) to the portal vein (white arrow) draining into the IVC (blue arrow). Flow is noted within this structure (B). This imaging is typical for a patent ductus venosus connecting the portal vein to the hepatic vein and draining into the IVC.
A premature female infant found to have right upper quadrant calcifications on an abdominal radiograph underwent an abdominal ultrasound.

Ultrasound shows an echogenic focus with posterior shadowing in the right hepatic lobe on transverse (A) and longitudinal (B) images.

As with case 6, based on the location of the calcification, a calcified ductus venosus was diagnosed.
Case 8

- A premature male infant presented with vomiting and abdominal distention.

- A transverse ultrasound image of the liver shows a curvilinear echogenic focus with posterior shadowing. This structure represents a calcified ductus venosus.
Cases 6, 7, & 8 diagnoses: Ductus venosus remnants/calcification

Ductus Venosus remnants/calcification

- Ductus Venosus (DV)- connects the umbilical vein to the inferior vena cava to shunt oxygenated blood from the placenta to the fetal systemic circulation
- DV normally closes by thrombosis during the 1st week of life, however flow has been noted in 11% of neonates on days 17 and 18 of life
  - Patent DV
    - US findings - the patent DV appears as a hypoechoic vascular structure extending from the left portal vein to the hepatic vein/IVC confluence
  - Calcification of the DV may occur within a thrombosed DV
    - Radiographic findings - “tram-track” calcifications in the right upper quadrant
    - US findings - intrahepatic linear or curvilinear calcifications in the region of the DV
Case 9

- A 37 week gestation neonate with prior umbilical vein catheter placement developed abdominal distension, abdominal wall erythema, tachypnea, and anemia.

- Longitudinal sonograms through the liver show a multiseptated fluid collection in the subcapsular region of the inferior aspect of the right lobe of the liver (A). An additional well-marginated, heterogeneously hypoechoic parenchymal lesion with a hyperechoic rim (arrow) was seen in the dome of the right lobe of the liver (B).
A premature infant with TPN (total parenteral nutrition) infusion through an umbilical vein catheter developed hepatomegaly on the 7th day of life followed by hypotension, anemia, abdominal distention, and rigidity with fullness of right upper abdomen.

(A) Transverse sonogram shows a multilobular heterogeneous intraparenchymal lesion in the right lobe that is mainly hypoechoic anteriorly and slightly hyperechoic posteriorly with a distinct echogenic rim (arrow).

(B) Follow-up longitudinal sonogram through the right lobe of the liver at 1 month of age shows the same lesion anterior to the IVC (arrow) smaller in size and with new shadowing calcifications.
Cases 9 & 10

- Differential diagnosis for hepatic lesions with heterogeneously hypoechoic centers and hyperechoic rims in neonates:
  - Abscesses
  - Hemangioendotheliomas
  - Hematomas from birth trauma
  - Hamartomas
  - Hepatic erosion by umbilical catheter

Clinical history correlation can exclude the possibility of a hematoma from lack of birth trauma and an abscess from lack of history of necrotizing enterocolitis. Lack of peripheral hypervascularity on sonography can exclude the possibility of a hemangioendothelioma and an abscess.
Umbilical vein catheter trauma

- Early diagnosis can prevent life-threatening complications caused by hepatic necrosis and hemorrhage
- Liver capsular rupture can cause TPN ascites
- Therapeutic aspiration of the TPN ascites may be needed in some, but therapeutic intraperitoneal drainage tubes should be avoided
- Neonates with a history of umbilical vein catheter erosion do well clinically after the removal of the catheter
- US findings are nonspecific with lesions appearing similar to hematomas
  - The lesions in the acute/subacute phase can appear as a complex cystic collection within the liver or hepatic subcapsular space
  - Chronic lesions may have dystrophic calcifications
- Follow-up sonograms can document the decrease in liver lesions and ascites
Case 11

- A healthy full-term male infant with maternal history of herpes simplex developed fever and progressive tachypnea 1 week after birth. Blood cultures were negative. Laboratory studies revealed thrombocytopenia and elevated LFTs.

- Abdominal US on day 12 of life demonstrates a diffusely hyperechoic liver (red arrow). Note the increased echogenicity of the liver compared to the renal cortex (white arrow).
Case 11

- Sagittal ultrasound image of the brain shows abnormally echogenic, well-defined gyri. The thalamus is diffusely increased in echogenicity.
- Due to the prenatal clinical history, CSF analysis, and imaging findings in the liver and brain, disseminated herpes simplex virus was diagnosed.
Case 11 diagnosis: Disseminated Herpes Simplex Virus

**Herpes Simplex Virus**

- May be acquired congenitally however most infections are transmitted at birth during vaginal deliveries
- Can present as a primarily CNS disease or disseminated infection
- Clinical presentation: respiratory distress, hypotension, jaundice, seizures, DIC, and shock
- Radiographic findings are nonspecific and similar to other types of hepatitis
- US findings - usually normal
  - Acute severe hepatitis: hepatomegaly, hypoechoic liver parenchyma with increased echogenicity of portal triads “starry-sky”
  - Chronic: heterogeneous echogenic hepatic parenchyma
- CT findings - heterogeneous parenchymal enhancement
Case 12

- Premature male infant who presented with jaundice was found to have elevated LFTs shortly after birth.

- The liver is heterogeneous with innumerable hypodense foci primarily in the left lobe on an enhanced axial CT of the abdomen. Note small bilateral pleural effusions.
Case 12

- Differential diagnosis for multiple nonenhancing, low attenuation lesions in the liver include:
  - infectious etiologies (bacterial, viral, or fungal)
  - infiltrative lesions (metabolic disorders)
  - diffuse neoplastic processes (hepatoblastoma, metastatic neuroblastoma, congenital histiocytosis, or leukemia)

- Liver biopsy was obtained which confirmed the diagnosis of hepatic cytomegalovirus.
Case 12 diagnosis: Cytomegalovirus

Cytomegalovirus

- Cytomegalovirus (CMV) is a double-stranded DNA virus in the herpes family
- CMV can be transmitted transplacentally, during delivery, or via breast milk ingestion
- Clinical Presentation - most are asymptomatic at birth
  - 5-20% are symptomatic - jaundice, hepatosplenomegaly, petechiae
- Imaging findings are generally nonspecific and similar to other viral infections that cause hepatitis
Case 13

- A premature infant born at 24 weeks of gestation was treated with ampicillin and gentamicin for possible bacterial sepsis. On day 17 of life, the patient developed bilious vomiting and abdominal distention.

- Abdominal radiograph reveals a large loculated collection of air in the right upper quadrant (arrow).

- Differential includes loculated free air, distended bowel, or an abscess.
Case 13

- Enhanced CT of the abdomen demonstrates a large hypodense lesion (arrows) with an enhancing rim containing air and fluid in the right lobe of the liver (L).

- Ultrasound-guided percutaneous aspiration confirmed the liver lesion to be a hepatic abscess. Cultures were positive for E. coli.
Liver Abscess

- Common etiologic agents in infants are E. coli, Staphylococcus spp., Streptococcus spp., Pseudomonas aeruginosa, Haemophilis parainfluenzae, and Klebsiella
- Occur secondary to hematogenous spread of bacteria from infection such as omphalitis, thrombophlebitis after umbilical vein catheterization, and sepsis
- Clinical presentation - fever, RUQ pain, hepatomegaly, elevated LFTs
- Radiograph findings - may see an abnormal collection of gas within the abscess cavity
- US findings - irregular, thick walls which may show hypervascularity and hypoechoic centers with through transmission; abscesses containing a large amount of air will demonstrate increased echogenicity with posterior shadowing
- CT findings - hypodense mass with thickened, enhancing walls, ± foci of gas
Case 14

- Full-term male infant who presented with jaundice at 1 month of life. Laboratory studies revealed conjugated hyperbilirubinemia. Abdominal ultrasound was initially performed and was normal.

- Hepatobiliary iminodiacetic acid scan taken at 30 min (A) and 4 hours (B) demonstrates normal hepatic uptake however no biliary excretion. Tracer is not visualized within the biliary tree or small bowel.
Case 14

- The differential diagnosis of conjugated hyperbilirubinemia with absent or delayed biliary excretion includes biliary atresia and neonatal hepatitis as the primary considerations. Other rarer causes of neonatal cholestasis include primary sclerosing cholangitis and Alagille syndrome.

- Liver biopsy confirmed the diagnosis of neonatal primary sclerosing cholangitis.
Case 14 diagnosis:
Neonatal primary sclerosing cholangitis

Neonatal primary sclerosing cholangitis

- Neonatal primary sclerosing cholangitis is a rare entity
  - The cause is unknown however genetic and immunological factors may play a part in the etiology
- Characterized by inflammation of the bile ducts resulting in fibrosis, obstruction, cholestasis, and biliary cirrhosis
- Clinical presentation - cholestasis, hepatomegaly, jaundice, elevated LFTs occur in the first week of life
  - In all reported cases, jaundice resolved by the first year of life however the disease progressed to cirrhosis
- HIDA scan findings - normal hepatic uptake of radiotracer however excretion into the intestine is severely delayed or absent
- Cholangiography findings - irregularity of the bile ducts with areas of stenosis, dilatation, and beading
- CT findings - bile duct segmental strictures with wall thickening
A 3 month old male with history of CMV infection at birth presented with dehydration and elevated LFT’s. Ultrasound showed a heterogeneous liver with a suggestion of portal venous air vs calcifications.

Axial enhanced CT section of the upper abdomen demonstrates abnormal, nodular contour of the liver with hypodense nodules. Splenomegaly was also noted. These findings are consistent with cirrhosis secondary to chronic CMV hepatitis.
Case 16

- A full term male infant presented with jaundice at birth. HIDA scan demonstrated severely delayed excretion of radiotracer. The patient was suspected to have biliary atresia however dilated ducts were not seen intraoperatively.

- Follow-up imaging 2 months later shows multiple cysts (arrows) in the porta hepatis region on US (A) and CT (B) images. Splenomegaly was also noted.

- Liver biopsy was performed which showed fibrosis with ductal destruction consistent with biliary cirrhosis, primary etiology was unclear.
Infantile cirrhosis

- End stage liver disease characterized by chronic destruction of the liver parenchyma with fibrotic replacement and nodular regeneration
- May be secondary to chronic hepatitis, congenital hepatic fibrosis, biliary atresia, cystic fibrosis, Budd-Chiari syndrome, disorders of metabolism, medications, or TPN
- Primary biliary cirrhosis - cholestatic liver disease with destruction of the interlobular bile ducts
- US findings - atrophy of the right hepatic lobe and medial segment of the left lobe with hypertrophy of the caudate lobe and lateral segment of the left lobe, nodular contour, diffuse heterogeneity of the liver parenchyma
- CT findings - nodular contour, may see regenerating nodules, ± ascites
Summary

- Differential Diagnosis of diffuse liver lesions in infants
  - Viral hepatic infections
  - Diffuse hepatic necrosis from infection or ischemia
  - Metastatic neuroblastoma
  - Neoplastic processes such as hepatoblastoma
  - Cirrhosis
  - Primary sclerosing cholangitis
- Differential diagnosis of focal liver lesions in infants
  - Abscess
  - Hematoma
  - Hamartoma
  - Hemangioendothelioma
  - Vascular malformations
  - Lymphangioma, hemangioma
  - Liver cyst
  - Iatrogenic trauma from umbilical venous catheters
Summary

- Non-neoplastic liver lesions presenting in the neonate/infant can be difficult to diagnose as they are rare and can have overlapping clinical and radiographic features.
- The lesions can be categorized into ischemia, infection, vascular lesions, traumatic lesions, and biliary abnormalities.
- While a few of these lesions can be incidental findings, others will progress to end-stage liver disease without treatment.
- Specific findings on ultrasound, CT, and MRI can be helpful in narrowing the differential in a timely manner.
- Tissue biopsy may be necessary in some cases to make the final diagnosis and determine treatment.
References

References