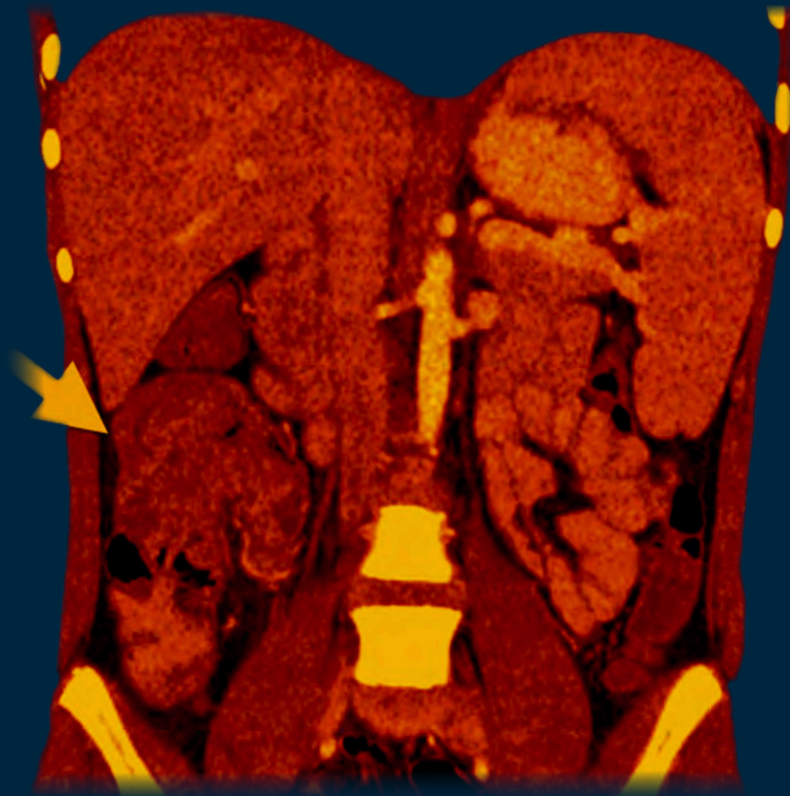


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Frontoethmoidal Encephalocele

Jasmine M. Haraburda, BS; Alexander J. Towbin, MD; Richard B. Towbin, MD

Abstract

Encephaloceles are rare congenital malformations characterized by a herniation of brain tissue and meninges through a skull defect. While clinical presentation and severity can vary widely depending on the size, location, and contents of the encephalocele, early diagnosis is critical for management and outcome planning. Imaging, particularly MRI, plays a central role in delineating the extent of the defect and identifying associated abnormalities. Definitive treatment involves surgical repair, which can significantly improve both functional and cosmetic outcomes. Long-term prognosis depends on the presence of associated anomalies, involvement of functional brain tissue, and development of complications such as hydrocephalus.

Keywords: neuroradiology, brain, congenital anomaly

Case Summary

A G1P0 woman presented for advanced fetal imaging after a second-trimester US identified a frontoethmoidal encephalocele. The neonate was delivered at 36 weeks and 3 days via cesarean section due to the encephalocele, preterm premature rupture of membranes, and the onset of preterm labor. Postnatally, an external ventricular drain and ventriculo-peritoneal shunt were placed.

Imaging Findings

Fetal MRI (Figure 1) showed an anterior midline defect in the frontoethmoidal region at the level of the orbits extending from the nasal bone superiorly to the frontal area. A sac containing dysmorphic brain tissue with a small volume of cerebrospinal fluid extended from the bony defect of the skull. Postnatal head US (Figure 2) showed an enlarged, distorted ventricular system

and dysmorphic cerebral tissue. Postnatal brain MRI (Figure 3) and head CT (Figure 4) confirmed the findings and identified intracranial hemorrhage.

Diagnosis

Frontoethmoidal encephalocele.

The differential diagnosis includes nasal glioma, dermoid cyst, nasal polyp, meningocele, mucocoele, neurinoma, and vascular malformation.

Discussion

Encephaloceles are rare neural tube defects characterized by a sac-like protrusion of brain tissue and meninges covered by skin (or at least an epithelial layer) through a skull defect.^{1,2} Encephaloceles have a global prevalence between 0.8 and 4 per 10,000 live births, representing 10-20% of all craniospinal dysraphisms.³ Frontoethmoidal encephaloceles are more common in Southeast Asia, where the incidence is as high as 1 in 5000

live births. The etiology underlying this geographic predisposition is unknown, but likely multifactorial.¹

Although encephaloceles can occur as isolated defects, they are associated with additional central nervous system or extracranial anomalies in 23-37.5% of patients.³ For example, herniation of the ventricular system into the encephalocele sac can lead to hydrocephalus. Encephaloceles have also been linked to genetic syndromes such as Meckel-Gruber syndrome, trisomy 13, and trisomy 18.³

Encephaloceles are classified by the location of herniation and may be anterior, occipital, basal, or involve the cranial vault.⁴ Occipital encephaloceles are the most common, accounting for approximately 75% of cases, followed by the frontoethmoidal (15%) and basal (10%) types.⁵ While typically considered neural tube defects, the exact pathophysiology remains unclear. Anterior encephaloceles are thought to result from abnormal neural crest cell development, whereas occipital encephaloceles are believed to arise from defective segmentation of the posterior cranial bones.³

Frontoethmoidal encephaloceles involve anterior herniation of brain tissue, typically from the frontal lobe, and meninges through a defect in the frontoethmoidal region. The nasofrontal subtype occurs at the junction between

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Figure 1. (A) Sagittal and (B) axial T2-weighted fetal MRI images showing an anterior midline defect in the frontoethmoidal region at the level of the orbits extending from the nasal bone superiorly to the frontal area. There is a well-defined external sac containing dysmorphic brain tissue with a small volume of cerebrospinal fluid. There is asymmetric enlargement of the right lateral ventricle.

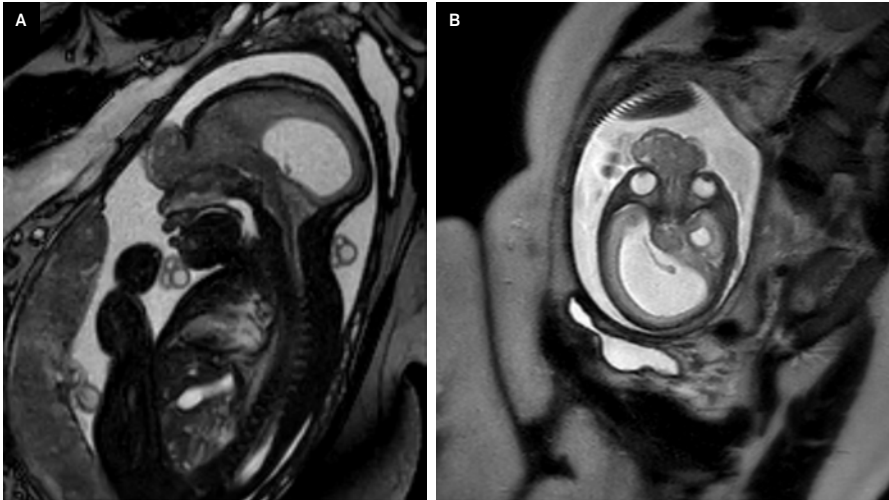


Figure 2. Coronal head US images performed on the day of birth showing an enlarged, distorted right lateral ventricle. Because the left frontal lobe is herniated into the encephalocele (not visible on the US), the right hemisphere appears larger, and there is leftward midline shift.

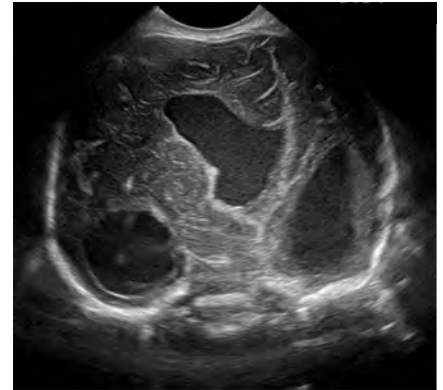
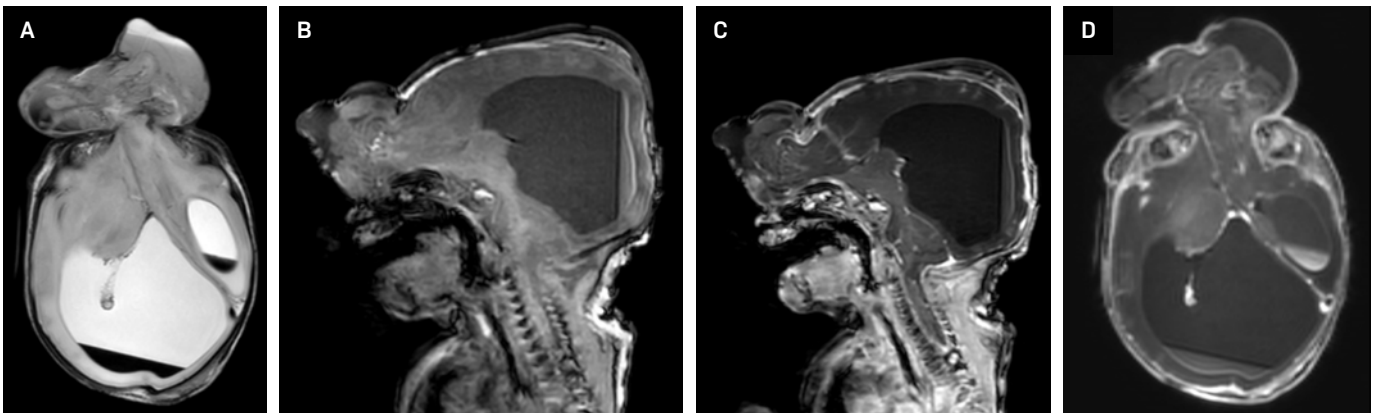


Figure 3. (A) Axial T2 and (B) sagittal T1 MRI performed at 1-day of life showing a large frontoethmoidal encephalocele with brain parenchyma, meninges, and CSF herniating through a midline defect at the level of orbits. (C) Axial and (D) sagittal T1 post contrast MRI shows the anterior aspect of the superior sagittal sinus and other venous structures extending into the encephalocele. The herniated brain parenchyma includes more of the left cerebral hemisphere and appears grossly dysplastic. There is resultant distortion of the brain parenchyma, leftward deviation of midline, and asymmetric enlargement of the right lateral ventricle. Blood/CSF levels are seen in both lateral ventricles.



the frontal and nasal bones, usually near or through the foramen cecum.⁶ This generally results in a small anterior cranial fossa. Frontal encephaloceles almost always contain olfactory tissue.⁷ Clinically, they usually present at birth as a visible midline mass, which may enlarge with crying (a positive Furstenberg sign) and may be associated with cerebrospinal fluid rhinorrhea or recurrent meningitis.⁸

Multiple imaging modalities can aid in characterizing encephaloceles. MRI helps localize the defect, characterize the

hernial sac contents, and identify other associated defects. Notably, defect size and hydrocephalus are key prognostic factors. Meanwhile, CT can better characterize bony anatomy. MR venogram or CTA are helpful in identifying venous abnormalities. Imaging of suspected encephaloceles is useful in ruling out other differential diagnoses. For instance, an encephalocele may appear similar to a nasal glioma, but present with intracranial extension and/or communication with the subarachnoid space on MRI.^{1,2,9}

Prenatally, termination of a pregnancy may be chosen if the encephalocele is large or has a poor prognosis to minimize maternal risk. Larger encephaloceles with improved prognoses may require cesarean section to minimize birth trauma. For relatively small encephaloceles, vaginal delivery may be possible.¹⁰ Definitive postnatal treatment involves surgical intervention to remove the encephalocele and repair the associated dural and bony defects. In cases where hydrocephalus is present, placement of a

Figure 4. (A) Axial and (B) sagittal CT performed at 6 days of life showing the anterior midline defect and the large frontoethmoidal encephalocele and lateral ventriculomegaly with layering hemorrhage.



ventriculoperitoneal shunt may be necessary.¹ Surgical repair can lead to significant improvements in both functional and cosmetic outcomes. When the encephalocele is covered by intact skin, surgery may be safely delayed until early infancy to reduce the risks associated with anesthesia and excessive blood loss.¹¹

Prognosis is variable depending on size, contents, infection, and associated defects. The mortality rate of encephaloceles is 29%. One study demonstrated that 83% of patients with encephaloceles developed mental and/or physical impairment. Approximately 20% of infants with congenital encephalocele have seizures.¹¹

herniation of brain tissue and meninges through a skull defect. While clinical presentation and severity can vary widely depending on the size, location, and contents of the encephalocele, early diagnosis is critical for management and outcome planning. Imaging, particularly MRI, plays a central role in delineating the extent of the defect and identifying associated abnormalities. Definitive treatment involves surgical repair, which can significantly improve both functional and cosmetic outcomes. Long-term prognosis depends on the presence of associated anomalies, involvement of functional brain tissue, and development of complications such as hydrocephalus.

Conclusion

Encephaloceles are rare congenital malformations characterized by a

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Overlap Syndrome

Jesus Macias, BS; Richard B. Towbin, MD; Yinan Li, MD; Carrie M. Schaefer, MD; Alexander J. Towbin, MD

Abstract

Autoimmune hepatitis with primary sclerosing cholangitis, also known as overlap syndrome, is a rare occurrence in the pediatric population. Children with overlap syndrome present with findings related to each disease. In addition, there is a high association with coexisting inflammatory bowel disease. Imaging, particularly MRI with MR cholangiopancreatography, pre- and post-hepatobiliary contrast administration imaging, and MR elastography, allows for a complete assessment of the liver and can be used in the diagnosis and surveillance of each component of liver disease.

Keywords: gastrointestinal, intestine, autoimmune

Case Summary

A teenager with a history of ulcerative colitis, autoimmune hepatitis (AIH), and sclerosing cholangitis presented with jaundice and hyperbilirubinemia. He had previously had symptoms related to liver failure and portal hypertension with low platelet levels, esophageal varices, and variceal bleeding.

Imaging Findings

An endoscopic retrograde cholangiopancreatography (ERCP) (Figure 1) demonstrated diffuse irregularity of intra- and extrahepatic bile ducts, pruning of intrahepatic bile ducts, narrowing of the distal common bile duct, and filling defects within the right central intrahepatic ducts consistent with primary sclerosing cholangitis (PSC).

MR cholangiopancreatography (MRCP) (Figure 2) showed the liver to be small, with a macronodular contour and wispy

increased T2 signal consistent with fibrosis. There was a large volume of ascites. Intrahepatic bile ducts were not well visualized. The common bile duct was relatively enlarged, and the gallbladder was dilated.

Diagnosis

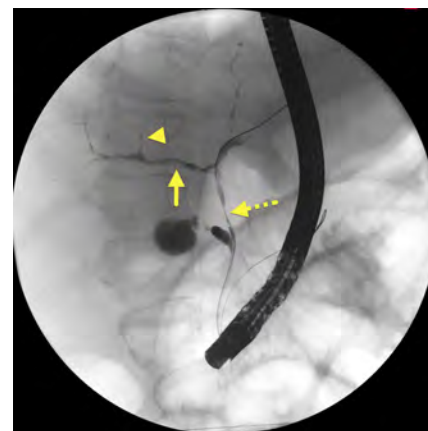
Overlap syndrome.

The differential diagnosis includes viral hepatitis, choledocholithiasis, ascending cholangitis, and primary biliary cirrhosis.

Discussion

AIH is a liver disease characterized by lymphoplasmacytic infiltration, lobular inflammation, and damage.¹ It occurs in 1 in 200,000 people in the general United States population and is strongly associated with HLA DR3 and DR4 alleles.^{1,2} Patients present with findings of liver failure: thrombocytopenia, coagulopathy,

Figure 1. Endoscopic retrograde cholangiopancreatography image showing narrowing (dashed arrow) of the distal common bile duct, debris (arrow) within the right hepatic duct, and pruning (arrowhead) of intrahepatic ducts typical of advanced primary sclerosing cholangitis.



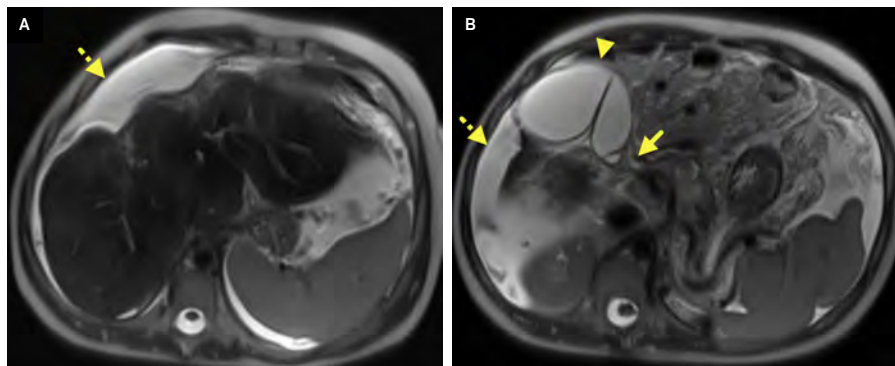
jaundice, abdominal pain, and elevated serum transaminases.² AIH can be categorized into AIH type 1 (positive for ANA and smooth muscle antibody) or type 2 (positive for liver kidney microsomal antibody) disease. Immunosuppression is the mainstay of treatment. Those with acute liver failure and encephalopathy will need a liver transplant. The risk for recurrence of AIH in transplanted patients is 16-43%.^{1,2}

Over the past decade, there have been significant advances in the imaging and

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Figure 2. MR cholangiopancreatography image at the level of the (A) liver and (B) gallbladder showing the liver to have an undulating macronodular contour with wispy increased T2 signal. There is a large volume of ascites (dashed arrow). The gallbladder (arrowhead) is distended, and the common bile duct (arrow) is relatively enlarged. Note that intrahepatic bile ducts are not visible.



quantification of liver fibrosis. US and MR elastography have been used to measure liver stiffness, a value used as a surrogate for liver fibrosis. In patients with known hepatic fibrosis, routine screening with MRI using a hepatobiliary agent is recommended.³ Studies in children have shown that hepatobiliary agents help to improve lesion detection and improve the diagnostic confidence when a liver lesion is identified.⁴

PSC occurs in 0.2-1.5 per 100,000 children.² Its presentation is insidious, with signs and symptoms of growth delay, fat-soluble vitamin deficiencies, jaundice, and pruritus.² PSC can be diagnosed via cholangiogram. MRCP is currently the test of choice due to its noninvasive nature. All types of cholangiograms can show multiple dilations and strictures, giving the bile ducts a beaded appearance.^{2,5} ERCP allows for biopsy and the therapeutic dilation of strictures with stenting to slow the development of end stage liver disease. On biopsy, periductal onion skin fibrosis is seen in 40% of cases.² Treatment of PSC is usually supportive.

Overlap syndrome occurs in 6-11% of patients with AIH.¹ These patients

have characteristics of both AIH and PSC. Additionally, inflammatory bowel disease is present in 41% of patients with overlap syndrome.¹ Immunosuppression combined with ursodeoxycholic acid has demonstrated improvement in serum transaminase levels but has not been associated with improved patient outcomes.^{1,2} AIH patients with elevated GGT or poor response to immunosuppression warrant screening with MRCP to evaluate for PSC and overlap syndrome.² Characteristic imaging findings of overlap syndrome include macro-regenerative nodules, peripheral liver atrophy, and biliary ductal irregularity.¹

Patients with sclerosing cholangitis are at risk for developing cholangiocarcinoma at some time in their life. This risk increases from the time of diagnosis and is said to occur in 9% at 10 years and 19% of patients at 20 years from diagnosis.² While this risk is high, cholangiocarcinoma is still rare in the pediatric population, occurring in 1% of pediatric patients with PSC. Because of the elevated risk, patients require frequent monitoring with MRCP, especially as they age.^{2,5,6}

Conclusion

AIH with PSC, also known as overlap syndrome, is a rare occurrence in the pediatric population. Children with overlap syndrome present with findings related to each disease. In addition, there is a high association with coexisting inflammatory bowel disease. Imaging, particularly MRI with MRCP, pre- and post-hepatobiliary contrast administration imaging, and MR elastography, allows for a complete assessment of the liver and can be used in the diagnosis and surveillance of each component of the liver disease.

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Colorectal Adenocarcinoma in an Adolescent with Lynch Syndrome

Shivatej Dubbaka; Alexander J. Towbin, MD; Richard B. Towbin, MD

Abstract

Hereditary nonpolyposis colorectal cancer (HNPCC) is a heritable disease that significantly increases the risk of colorectal cancer. Risk assessment should be considered in pediatric patients with a family history of colorectal cancer, followed by appropriate screening with routine colonoscopies. Cross-sectional imaging is a valuable adjunct to colonoscopy, helping to identify complications and stage disease. Thanks to surgical advances and rigorous screening programs, colorectal cancer associated with HNPCC often carries a favorable prognosis.

Keywords: gastrointestinal, intestine, neoplasm, syndrome

Case Summary

A teenage male with a family history of colon cancer originally presented with anemia and weight loss. A colonoscopy was performed, which revealed a large fungating mass of the right colon.

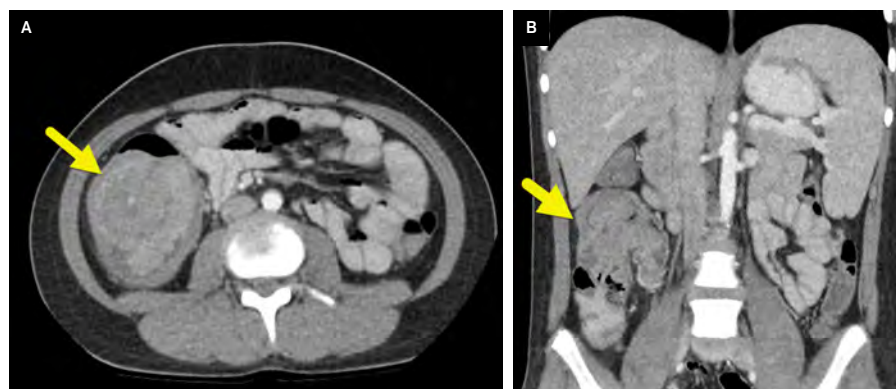
Imaging Findings

Contrast-enhanced CT of the abdomen (Figure 1) showed a large enhancing intraluminal mass within the mid-ascending colon. There was no appreciable colonic wall thickening. However, the mass was acting as a lead point, causing a colocolonic intussusception. Subsequent F18 fluorodeoxyglucose PET/CT (Figure 2) showed uptake within the colonic mass.

Diagnosis

Colonic adenocarcinoma in the setting of Lynch syndrome.

Figure 1. (A) Axial and (B) coronal CT images showing a large soft-tissue mass (arrow) within the ascending colon. The mass causes a colo-colonic intussusception.



The differential diagnosis of a colonic mass in an adolescent includes Burkitt lymphoma, adenocarcinoma, gastrointestinal stromal tumor, and carcinoid tumor. Due to the patient's family history of colon cancer, colorectal adenocarcinoma in the setting of a cancer predisposition syndrome was suspected.

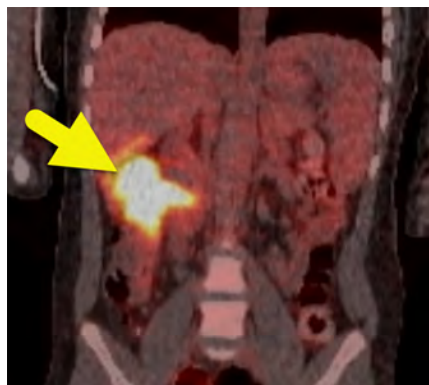
Discussion

Lynch syndrome, or hereditary nonpolyposis colorectal cancer (HNPCC), is the most common inherited cause of colorectal cancer. It follows an autosomal-dominant inheritance pattern and results from mutations in DNA mismatch repair genes, which are responsible for correcting base-pairing errors during DNA replication. Deficiency in these genes leads to microsatellite instability and the accumulation of genetic errors, thereby increasing cancer risk.¹ While colorectal cancer is the most common malignancy associated with HNPCC, affected individuals also have elevated risks

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Figure 2. Coronal image from fused F18 fluorodeoxyglucose PET/CT showing intense uptake within the colonic mass (arrow). The mass had a maximum standardized uptake value of 18.2. There was no metastatic uptake.



for endometrial, ovarian, upper urinary tract, upper gastrointestinal, brain, and prostate cancers.²

Individuals at high risk for HNPCC, including those with a positive family history, are advised to follow specific screening guidelines. Colorectal cancer screening typically begins with colonoscopy between 20 and 25 years of age, or 2–5 years earlier than the youngest age of colorectal cancer diagnosis in the family. Colonoscopy should then be repeated every 1–2 years. Although there are currently no formal surveillance protocols for other associated malignancies, high-risk individuals may benefit from additional screening for endometrial and upper gastrointestinal cancers.³

In pediatric patients, HNPCC is typically diagnosed only after the development of malignancy. While colorectal adenocarcinoma is the most common presentation, other associated cancers such as renal cell carcinoma and cerebral malignancies have also been reported. Although HNPCC-associated colorectal cancer is rare in children, these patients are often diagnosed at advanced stages.^{4,5} Given the increased cancer risk in pediatric patients

with HNPCC, it is essential to obtain a thorough family history in children with potential hereditary cancer risk.

Current staging of colorectal cancer includes colonoscopy and biopsy. Cross-sectional imaging modalities play a complementary role in determining disease extent and staging. On CT, colorectal cancer typically appears as a soft-tissue mass that causes luminal narrowing or colonic wall thickening. Complications such as obstruction, perforation, or fistula formation may also be identified. Tumor extension beyond the colon may present as an extra colic mass. This finding is often associated with infiltration and thickening of the pericolic fat or loss of the normal fat plane.⁶

Treatment guidelines for colorectal cancer in patients with HNPCC typically involve segmental resection or subtotal colectomy, depending on tumor extent and degree of invasion. Available chemotherapeutic agents for colorectal cancer include 5-fluorouracil, oxaliplatin, and irinotecan; however, their effectiveness in tumors associated with HNPCC remains uncertain.^{7,8}

Although colorectal cancer has a high recurrence rate in patients with HNPCC, overall survival rates remain favorable, with approximately 90% at 5 years, 80% at 10 years, and 70% at 15 years following diagnosis. These positive outcomes have been attributed to the use of extended colectomies and rigorous surveillance protocols.⁹

Conclusion

HNPCC is a heritable disease that significantly increases the risk of colorectal cancer. Risk assessment should be considered in pediatric patients with a family history of colorectal

cancer, followed by appropriate screening with routine colonoscopies. Cross-sectional imaging is a valuable adjunct to colonoscopy, helping to identify complications and stage disease. Thanks to surgical advances and rigorous screening programs, colorectal cancer associated with HNPCC often carries a favorable prognosis.

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Trilateral Retinoblastoma

Alexander J. Luna, MD; Richard B. Towbin, MD; Alexander J. Towbin, MD

Abstract

Trilateral retinoblastoma is a rare condition occurring in the setting of retinoblastoma with an associated pineal or suprasellar mass. Baseline brain MRI at the time of retinoblastoma diagnosis is recommended to identify synchronous intracranial tumors. Ongoing surveillance may be warranted for intracranial cystic lesions with suspicious features, such as wall irregularity, nodularity, or atypical size. While isolated retinoblastoma carries a favorable prognosis with curative potential, the development of trilateral retinoblastoma is associated with significantly poorer outcomes, even with aggressive treatment.

Keywords: orbit, brain, neoplasm, genetic

Case Summary

A male infant presented with signs of cellulitis of the right eye and parental concerns of worsening vision. On ophthalmoscopic examination, leukocoria was present in the right eye.

Imaging Findings

MRI (Figure 1) obtained at the time of diagnosis showed a large heterogeneous mass occupying the right globe. The mass covered the optic disk, and there was mild enhancement of the optic nerve near its insertion at the disk. Small nodules were visible within the right anterior chamber. 2 small nodules were visible within the left globe. In addition to the masses of each globe, there was a 1.9 cm mass of the pineal gland. The mass was slightly hyperintense to the adjacent deep white matter structures on T2-weighted images and hypointense on T1-weighted images. It had several small internal cystic spaces

and enhanced avidly. The lateral and 3rd ventricles were dilated.

CT (Figure 2) performed after right eye enucleation showed the pineal mass to be partially calcified.

Diagnosis

Retinoblastoma in both eyes with a pineoblastoma—so-called trilateral retinoblastoma.

The differential diagnosis for leukocoria in an infant includes congenital cataracts and Coats disease.

Discussion

Trilateral retinoblastoma is a rare malignancy defined by the presence of a midline intracranial primitive neuroectodermal tumor in patients with unilateral or bilateral retinoblastoma. A germline mutation in the *RB1* gene plays a central role in the pathogenesis of retinoblastoma,

including trilateral retinoblastoma. In one study, *RB1* mutations were identified in all patients with trilateral retinoblastoma. In 70-75% of patients with trilateral retinoblastoma, the intracranial tumor arises from the pineal gland. In the remaining patients, tumors develop in the suprasellar or parasellar region.¹ When both pineal and suprasellar tumors are present alongside ocular retinoblastoma, the condition is referred to as quadrilateral retinoblastoma, although this presentation is exceedingly rare.^{2,3}

The reported incidence of trilateral retinoblastoma varies across studies of patients with retinoblastoma.^{4,7} In an analysis of large cohorts of patients with bilateral retinoblastoma, de Jong et al identified an overall incidence of 3.8%. Of these, 82% had pineal trilateral retinoblastoma and 18% had nonpineal tumors. Among patients with hereditary retinoblastoma—defined as all bilateral cases and unilateral cases with either a family history or a germline *RB1* mutation—the incidence of trilateral retinoblastoma was slightly lower at 3.5%.⁴

Historically, the pineal tumor component of trilateral retinoblastoma was detected metachronously, often months or years after the initial diagnosis of retinoblastoma. However, with the widespread adoption of routine baseline brain imaging, particularly MRI,

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Figure 1. MRI performed in an 8-month-old male infant with leukocoria. (A-C) Axial three-dimensional fast imaging employing steady-state acquisition showing a large heterogeneous lobulated lesion (arrow) within the right globe. Nodules extend to the anterior chamber (arrowhead). 2 small lesions are present in the left globe (dashed arrows). (D) Axial T1-weighted postcontrast sequence with fat saturation showing mild enhancement of the retina (arrow) and optic nerve (arrowhead) near its insertion at the optic disk. (E) Sagittal T1-weighted image at midline showing the hypointense pineal mass (arrow). (F) Axial T2-weighted image showing the mass (arrow) to be slightly hyperintense to the adjacent thalamus. The lateral ventricles are enlarged. (G) Sagittal T1-weighted postcontrast image at midline showing diffuse enhancement of the pineal mass (arrow).

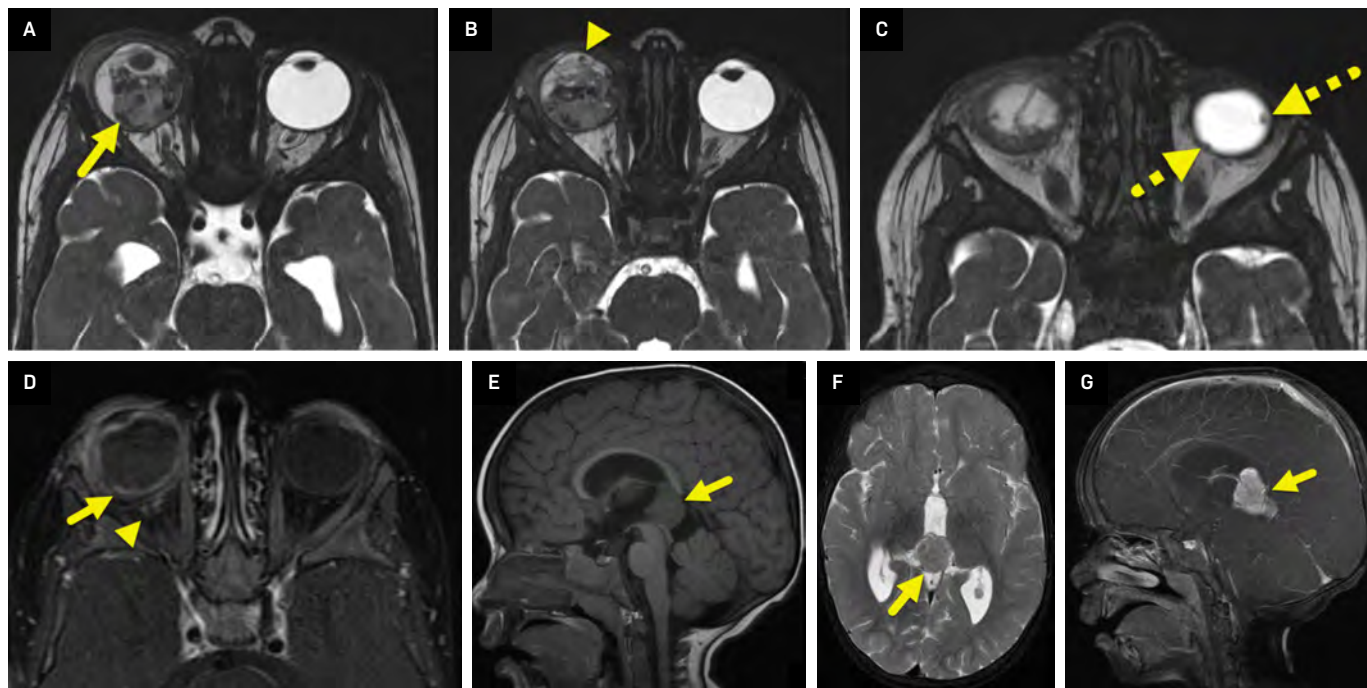
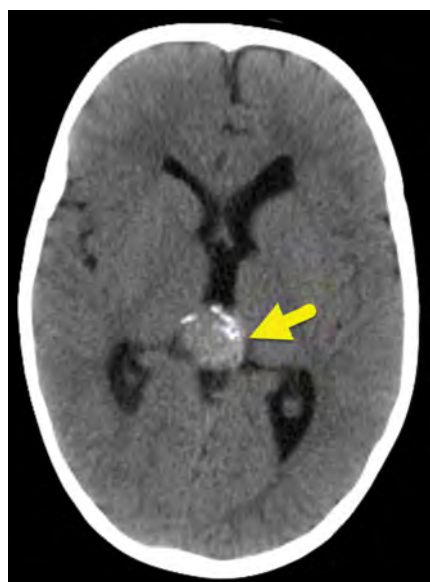


Figure 2. Axial CT of the head showing the pineal mass (arrow) with peripheral calcification. The lateral and 3rd ventricles are enlarged.



synchronous detection of intracranial tumors has become more common. These synchronous tumors are often

asymptomatic and smaller in size at the time of diagnosis, enabling earlier intervention. Notably, survival has been reported in cases of asymptomatic pineoblastoma less than 15 mm in diameter, as well as in nonpineal trilateral retinoblastoma regardless of tumor size or the presence of symptoms.^{1,4}

The historical incidence of synchronous trilateral retinoblastoma may have been underestimated due to inconsistent use of baseline neuroimaging. In a study by Rodjan et al, patients who underwent baseline brain MRI were diagnosed with trilateral retinoblastoma at a median age of 12 months, typically before the onset of intracranial symptoms. In contrast, patients who did not receive baseline imaging were diagnosed an average of 27 months after retinoblastoma diagnosis and often presented with signs of intracranial hypertension. Tumors in the baseline imaging group were significantly smaller (mean diameter 18 mm, range 9-34 mm) compared with those without baseline

imaging (mean diameter 35 mm, range 11-59 mm). Hydrocephalus and positive cerebrospinal fluid cytology were also more common in the latter group.

On MRI, intracranial tumors in trilateral retinoblastoma, whether pineal or suprasellar, typically demonstrate well-defined borders and heterogeneous enhancement due to cystic components or necrosis. These lesions are generally isointense to gray matter on both T1- and T2-weighted sequences. Cystic components are seen in up to 57% of pineal tumors.⁵⁻¹¹ The increased detection of smaller cysts in more recent studies may reflect advances in MRI resolution and technique.¹

Because trilateral retinoblastoma is a rare malignancy, there is no uniform consensus regarding follow-up frequency for cystic pineal lesions. Recommendations often depend on lesion characteristics. Rodjan et al advised repeat MRI 6 months after detection of “probably benign pineal cysts,” which they defined

as cystic lesions with thin, smooth walls and discrete rim enhancement. In contrast, de Bloeme et al recommended a more selective approach, reserving follow-up imaging for lesions with suspicious features such as irregular wall thickening greater than 2 mm, nodularity, or when the size of the solid or cystic component exceeds the 99th percentile for age-based norms. Even when using baseline screening and selective surveillance for suspicious lesions, a high number of follow-up MRIs may still be required to detect malignant transformation. This strategy increases the burden of imaging, contributes to patient and caregiver anxiety, and introduces risks associated with repeated anesthesia exposure.¹

Once diagnosed, trilateral retinoblastoma typically requires aggressive treatment. Intensive chemotherapy followed by autologous stem cell rescue has been associated with longer survival compared with conventional chemotherapy alone.⁶ Despite these efforts, overall prognosis remains poor. In one study that included patients with metastatic retinoblastoma, the 1-year event-free survival rate following treatment was 28.3%.¹² Another study reported a 5-year mortality rate of 56% for patients with pineal trilateral retinoblastoma.⁶

Our patient was successfully treated with chemotherapy, right eye enucleation,

left eye thermotherapy, and pineoblastoma resection.

Conclusion

Trilateral retinoblastoma is a rare condition occurring in the setting of retinoblastoma with an associated pineal or suprasellar mass. Baseline brain MRI at the time of retinoblastoma diagnosis is recommended to identify synchronous intracranial tumors. Ongoing surveillance may be warranted for intracranial cystic lesions with suspicious features, such as wall irregularity, nodularity, or atypical size. While isolated retinoblastoma carries a favorable prognosis with curative potential, the development of trilateral retinoblastoma is associated with significantly poorer outcomes, even with aggressive treatment.

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Steatohepatitis

Nadir Khan Yusufzai, BS; Richard B. Towbin, MD; Carrie M. Schaefer, MD; Alexander J. Towbin, MD

Abstract

Steatohepatitis in children most commonly arises in the setting of metabolic dysfunction-associated steatotic liver disease (MASLD) but can also occur in association with other conditions, including Wilson disease, Reye syndrome, cystic fibrosis, viral hepatitis, and inherited metabolic disorders. While liver biopsy remains the diagnostic gold standard, noninvasive imaging techniques such as US and MRI-proton density fat fraction play an important role in screening and monitoring disease progression. Lifestyle modification remains the cornerstone of therapy for MASLD, although adherence challenges persist. Early recognition and management are essential to prevent potential progression to advanced fibrosis, cirrhosis, and hepatocellular carcinoma.

Keywords: gastrointestinal, liver, inflammation

Case Summary

An adolescent with a heterozygous cystic fibrosis transmembrane conductance regulator mutation and a history of recurrent pancreatitis presented for imaging during workup for total pancreatectomy with islet autotransplantation.

Imaging Findings

Abdominal MRI (Figure 1) showed hepatic steatosis with a fat fraction of 21%. Hepatic steatosis was also visible on CT (Figure 2) and US (Figure 3).

Diagnosis

Steatohepatitis.

The differential diagnosis is broad and includes metabolic dysfunction-associated steatotic liver disease (MASLD), linked

to conditions such as type 2 diabetes, insulin resistance, hypertension, obesity, and dyslipidemia. The differential further encompasses genetic disorders such as Wilson disease, Reye syndrome, cystic fibrosis, alpha-1 antitrypsin deficiency, and hereditary hemochromatosis, as well as viral hepatitis (A, B, C), pediatric autoimmune liver diseases, drug-induced liver injury, malnutrition, and inherited metabolic disorders.

Discussion

Steatohepatitis is characterized by the accumulation of fat in the liver, leading to inflammation and hepatocellular injury. In children, the primary cause is MASLD, previously known as nonalcoholic fatty liver disease. MASLD begins with steatosis. Over time, inflammation may develop, causing steatohepatitis. In some patients, this can progress to fibrosis, cirrhosis, and ultimately hepatocellular carcinoma.

The progressive form of MASLD is termed metabolic dysfunction-associated steatohepatitis (MASH).¹

MASLD should be suspected in children and adolescents with persistently elevated liver enzymes and established risk factors, such as male sex, obesity, central adiposity, insulin resistance, and dyslipidemia. The diagnosis is made after exclusion of other liver diseases, including inborn errors of fatty acid metabolism, peroxisomal disorders, and lysosomal storage disorders, or it may be identified incidentally. Other chronic liver diseases that can present with steatohepatitis in children include Wilson disease, Reye syndrome, hemochromatosis, viral hepatitis, autoimmune hepatitis, and alpha-1 antitrypsin deficiency.^{2,3}

The prevalence of MASLD has increased substantially over the past decade, making it the leading cause of chronic liver disease in children and adolescents worldwide. In the general pediatric population, MASLD affects an estimated 7% of children and adolescents, with rates exceeding 34% among children with obesity.⁴ The development of MASLD is influenced by a complex interplay of genetic, epigenetic, environmental, and gut microbiome factors. Additional risk factors include maternal obesity, perinatal exposure to antibiotics, and an intestinal microbiota

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Figure 1. Axial multiphase Dixon MRI of the liver showing (A) in-phase, (B) opposed-phase, and (C) fat-only (water-saturated) images. There is marked signal dropout on the opposed-phase image, consistent with hepatic steatosis. The fat-only image shows mild parenchymal signal, confirming excess hepatic fat. The hepatic fat fraction was measured at 21%.

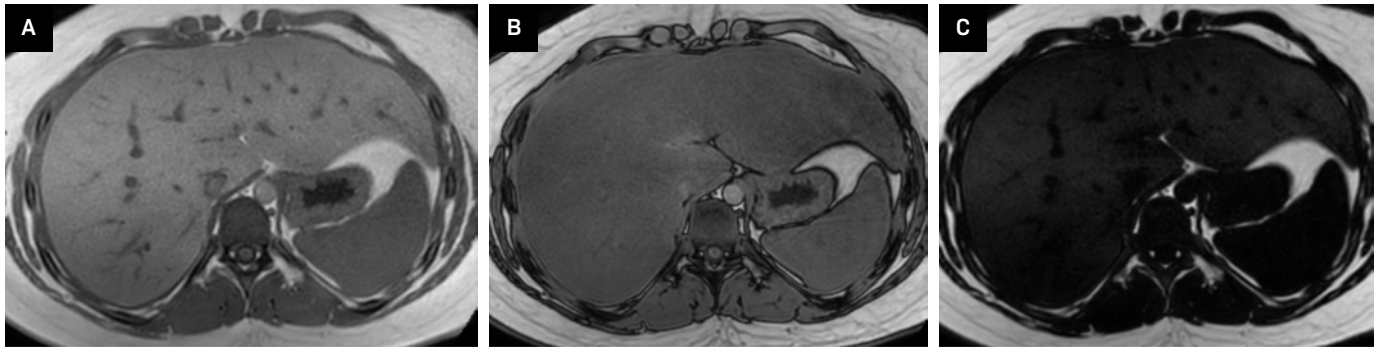


Figure 2. Axial CT image of the liver demonstrates diffusely decreased attenuation of the liver relative to the spleen. Average Hounsfield unit measurements were 66 for the liver and 119 for the spleen.



Figure 3. Longitudinal US image of the right kidney showing increased echogenicity of the liver relative to the renal cortex, consistent with hepatic steatosis.



enriched in alcohol-producing bacteria.⁵ Lifestyle factors, such as poor diet and physical inactivity, further contribute to disease risk.

Several noninvasive imaging modalities are available to quantify liver fat and monitor the progression of steatohepatitis.⁶⁻⁸ Conventional US is widely used for screening due to its accessibility, though it offers only moderate accuracy. In steatosis, the liver demonstrates increased echogenicity relative to the adjacent right kidney. As hepatic fat accumulates, there is progressive loss of visualization of the portal triads, and eventually, the right hemidiaphragm becomes less distinct. US shear-wave elastography provides a quantitative assessment of liver stiffness, with elevated shear-wave velocities indicating increased tissue stiffness that may correlate with fibrosis progression.⁹

MRI-derived proton density fat fraction (MRI-PDFF) quantifies the proportion of liver parenchyma composed of fat.⁹ A value greater than 5% is considered indicative of hepatic steatosis. It is important to note that MRI-PDFF measures the percentage of fat within the parenchyma, whereas histopathologic assessment quantifies the percentage of hepatocytes containing lipid droplets. MR elastography is also used to assess liver stiffness and evaluate for fibrosis. Prior studies have suggested a threshold of 2.71 kPa to predict significant hepatic fibrosis.¹⁰ However, the complex interplay between fat and fibrosis can variably affect liver stiffness measurements.¹¹

Liver biopsy remains the gold standard for diagnosing MASLD and MASH, as it provides direct assessment of hepatic

inflammation and fibrosis. However, it is invasive and carries limitations, including sampling variability and interobserver differences in interpretation. Given these limitations, noninvasive tools such as elastography and MRI-PDFF are increasingly used to support diagnosis and monitor disease progression.

Management of MASLD and MASH primarily relies on dietary and lifestyle modifications. Unfortunately, the success of these interventions is often hindered by low rates of adherence. Pediatric health care providers should routinely monitor body mass index z-scores and engage families in weight management strategies. A multidisciplinary approach involving dietitians, social workers, and exercise physiologists can improve adherence and outcomes. Additionally, attention to modifiable perinatal risk factors, such as preventing gestational diabetes and avoiding excessive maternal weight gain, may help reduce future risk.⁵

The degree of hepatic fibrosis is the strongest predictor of disease progression, hepatic decompensation, and mortality. Early identification and monitoring of fibrosis are essential for risk stratification and guiding treatment decisions.

Conclusion

Steatohepatitis in children most commonly arises in the setting of MASLD but can also occur in association with other conditions, including Wilson disease, Reye syndrome, cystic fibrosis, viral hepatitis,

and inherited metabolic disorders. While liver biopsy remains the diagnostic gold standard, noninvasive imaging techniques such as US and MRI-PDFF play an important role in screening and monitoring disease progression. Lifestyle modification remains the cornerstone of therapy for MASLD, although adherence challenges persist. Early recognition and management are essential to prevent potential progression to advanced fibrosis, cirrhosis, and hepatocellular carcinoma.

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Hepatic Cirrhosis

Tatiana Mikhailova, BA; Richard B. Towbin, MD; Carrie M. Schaefer, MD; Alexander J. Towbin, MD

Abstract

Hepatic cirrhosis is a progressive disease that results from chronic liver injury and leads to fibrosis, architectural distortion, and ultimately liver failure. In children, biliary atresia is the leading cause, while metabolic and infectious etiologies are less common. Imaging plays a central role in diagnosis and follow-up. Key features include surface nodularity, heterogeneous parenchymal echotexture, altered hepatic volume distribution, and secondary signs of portal hypertension. Elastography provides a noninvasive method for assessing liver stiffness, with MR elastography offering the highest accuracy for detecting and staging fibrosis.

Keywords: gastrointestinal, liver, chronic injury, abdomen, metabolic

Case Summary

A child with a history of biliary atresia and prior Kasai procedure received surveillance imaging after blood tests revealed elevated alpha-fetoprotein levels.

Imaging Findings

US (Figure 1) and MRI (Figure 2) showed the liver to be small, with a nodular contour and lobular band of apparent fibrosis. There were findings of portal hypertension with an enlarged main portal vein and splenomegaly.

Diagnosis

Hepatic cirrhosis caused by biliary atresia

Discussion

Hepatic cirrhosis is a progressive liver disease caused by chronic hepatocellular

injury that leads to the replacement of normal parenchyma with collagenous scar tissue. The prevalence and causes of pediatric cirrhosis vary worldwide. In the United States, biliary atresia is the leading cause and the most common indication for pediatric liver transplantation. Less common causes include genetic metabolic disorders such as alpha-1 antitrypsin deficiency and Wilson disease. Chronic viral hepatitis, now rare in the United States due to routine vaccination, remains a leading cause of pediatric cirrhosis in Africa and Southeast Asia, where the prevalence of hepatitis B seropositivity among young children can reach 4.7%.^{1,2}

Patients with early, compensated cirrhosis may be asymptomatic or present with nonspecific symptoms such as loss of appetite, nausea, or vomiting. Symptoms typically develop as liver fibrosis increases and blood flow through the cirrhotic tissue becomes impaired. In the later, decompensated stage, patients may show extrahepatic manifestations of liver dysfunction, including jaundice,

Figure 1. Transverse US of the liver showing the liver to have a heterogeneous parenchyma with a nodular contour. Fine hyperechoic bands of fibrosis intersperse the nodules.



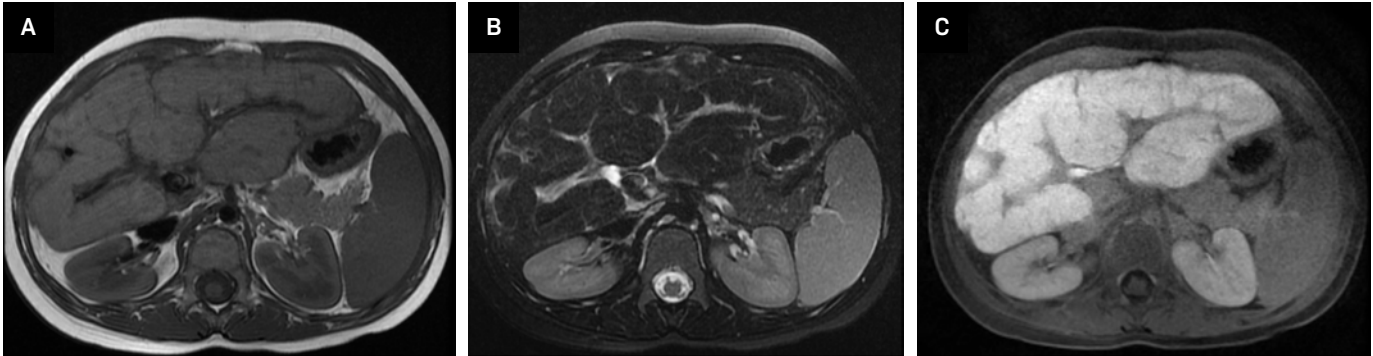
ascites, hepatosplenomegaly, and variceal bleeding secondary to portal hypertension.² Although biopsy remains the gold standard for diagnosis and staging, cirrhosis can also be identified through a combination of liver function testing and US imaging, with reported diagnostic accuracy of approximately 86%.³ Imaging findings such as surface nodularity, hepatic atrophy, altered parenchymal elasticity, and signs of portal hypertension are similar in both children and adults.⁴

Abdominal US is the preferred initial noninvasive imaging method for assessing cirrhosis in children and adolescents. Findings may include surface nodularity and heterogeneous parenchymal echotexture.² In cases of neonatal hepatitis, US is used to evaluate for

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Figure 2. (A) Axial T1-weighted, (B) T2-weighted, and (C) T1-weighted obtained during the hepatobiliary phase of contrast administration showing the liver to be small and have a nodular contour. Bands of fibrosis intersperse the nodular contour.



biliary atresia. Potential findings include a hyperechoic band of tissue anterior to the portal vein (the triangular cord sign) and an atretic gallbladder.⁴ As hepatic cirrhosis progresses, portal hypertension may develop, leading to secondary findings such as splenomegaly, ascites, varices, and portosystemic shunts.⁴ MRI and CT are typically used as second-line modalities to further characterize parenchymal changes and hepatic nodules, and to evaluate abdominal vasculature.⁵ Early cirrhotic changes may include altered hepatic volume distribution, with decreased right lobe volume and compensatory hypertrophy of the left and caudate lobes.⁴ In advanced disease, parenchymal atrophy results in overall reduction in liver size, widening of the hepatic fissures, and enlargement of the gallbladder fossa.

Metabolic dysfunction-associated fatty liver disease is the most common cause of liver disease in children. In this condition, excess fat accumulates within hepatocytes, resulting in hepatic steatosis. In some patients, inflammation and fibrosis develop, leading to metabolic dysfunction-associated steatohepatitis (MASH). A small subset of patients with MASH will progress to cirrhosis. US shear-wave elastography and MR elastography (MRE) measure liver stiffness and serve as noninvasive surrogate markers for fibrosis. These techniques are increasingly used instead of liver biopsy for diagnosis, staging, and monitoring of pediatric liver disease. While US offers the advantages of portability and

ease of use, current evidence suggests that MRE provides greater accuracy for assessing fibrotic changes.^{6,7} In children, MRE stiffness thresholds generally align with adult criteria, with values above 2.8 kPa considered abnormal and values above 4.0 kPa typically associated with advanced fibrosis.⁸⁻¹⁰

Management of pediatric cirrhosis focuses on treating the underlying cause to prevent further liver damage, minimizing complications, and managing symptoms.² Prognosis varies depending on etiology, disease severity, associated complications, and comorbid conditions. Patients who develop complications such as variceal hemorrhage or ascites generally have a poorer prognosis. Ascites are managed with sodium restriction and diuretics, with paracentesis or shunting reserved for refractory cases. Regular endoscopic surveillance and prophylactic band ligation are recommended for varices, particularly when high-risk features are present.² In children with decompensated chronic liver disease or severe complications unresponsive to medical therapy, liver transplantation is the treatment of choice.²

Conclusion

Hepatic cirrhosis is a progressive disease that results from chronic liver injury and leads to fibrosis, architectural distortion, and ultimately liver failure. In children, biliary atresia is the leading

cause, while metabolic and infectious etiologies are less common. Imaging plays a central role in diagnosis and follow-up. Key features include surface nodularity, heterogeneous parenchymal echotexture, altered hepatic volume distribution, and secondary signs of portal hypertension. Elastography provides a noninvasive method for assessing liver stiffness, with MRE offering the highest accuracy for detecting and staging fibrosis.

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