

A previously healthy 5-year-old girl is brought to the emergency department with lethargy and altered mental status. She was in her usual state of health until 5 days ago when she developed a low-grade fever, malaise, headache, cough, coryza, and a sore throat. The fever has resolved with over-the-counter aspirin. The patient developed nausea, vomiting, and lethargy this morning. She has no chronic medical problems and takes no other medications. The girl did not receive the seasonal influenza vaccine but her other vaccinations are up to date. The patient's weight and stature are average. Examination shows a febrile sleepy girl with hepatomegaly. There is no jaundice or splenomegaly. She is not oriented to person, place, or time. Nasal antigen testing is positive for influenza B. Laboratory results are as follows:

Complete blood count

Hemoglobin	14.2 g/L
Platelets	180,000/ μ L
Leukocytes	8,300/ μ L

Chemistry panel

Sodium	140 mEq/L
Potassium	3.8 mEq/L
Chloride	102 mEq/L
Bicarbonate	24 mEq/L
Blood urea nitrogen	16 mg/dL
Creatinine	0.6 mg/dL
Glucose	72 mg/dL

Liver studies

Total bilirubin	0.9 mg/dL
Direct bilirubin	0.3 mg/dL
Alkaline phosphatase	120 U/L
Aspartate	258 U/L

Chloride	102 mEq/L
Bicarbonate	24 mEq/L
Blood urea nitrogen	16 mg/dL
Creatinine	0.6 mg/dL
Glucose	72 mg/dL

Liver studies

Total bilirubin	0.9 mg/dL
Direct bilirubin	0.3 mg/dL
Alkaline phosphatase	120 U/L
Aspartate aminotransferase	358 U/L
Alanine aminotransferase	410 U/L
Ammonia	94 mcg/dL (normal <45 mcg/dL)

Coagulation studies

Prothrombin time	18 sec
Partial thromboplastin time	44 sec

Percutaneous liver biopsy would most likely show which of the following?

- ☐ A. Bile plugs in the bile ducts, portal tract edema, and hepatic fibrosis
- ☐ B. Cirrhosis and periportal eosinophilic inclusion bodies
- ☐ C. Macrovesicular fatty infiltration
- ☐ D. Microvesicular fatty infiltration
- ☐ E. Sinusoidal congestion and hemorrhagic necrosis

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Percutaneous liver biopsy would most likely show which of the following?

- ☐ A. Bile plugs in the bile ducts, portal tract edema, and hepatic fibrosis [4%]
- ☐ B. Cirrhosis and periportal eosinophilic inclusion bodies [10%]
- ☐ C. Macrovesicular fatty infiltration [9%]
- ☒ D. Microvesicular fatty infiltration [49%]
- ☐ E. Sinusoidal congestion and hemorrhagic necrosis [27%]

Proceed to Next Item

Explanation:

User Id: [redacted]

Explanation:

User Id: [REDACTED]

Reye syndrome	
Pathophysiology	Microvesicular fatty infiltration & hepatic mitochondrial dysfunction
Etiology	Pediatric aspirin use in the setting of influenza or varicella infection
Clinical features	<ul style="list-style-type: none"> • Acute liver failure • Encephalopathy
Laboratory findings	<ul style="list-style-type: none"> • ↑ Transaminases • ↑ PT, INR, PTT • ↑ Ammonia

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Reye syndrome is characterized by **encephalopathy** and **acute liver failure** after a viral infection. The incidence has declined significantly after the 1980s due to widespread education about salicylate (eg, aspirin) avoidance in children and adolescents, especially during viral infections. Most cases occur with **aspirin** use in the setting of **influenza B** (most common), influenza A, or **varicella zoster** infection. Aspirin is a mitochondrial toxin that can cause acute hepatic dysfunction in young individuals.

Clinical features of hepatic dysfunction include nausea, vomiting, and hepatomegaly. Laboratory derangements include **elevated transaminases**, **coagulopathy** (prolonged prothrombin time [PT], international normalized ratio [INR], and partial thrombin time [PTT]), and **hyperammonemia**. Excess ammonia is neurotoxic and causes cerebral edema and encephalopathy.

Reye syndrome diagnosis is rare but potentially life-threatening (~30% mortality). The presence of **microvesicular steatosis** on liver biopsy in the context of acute hepatic encephalopathy is consistent with Reye syndrome. Parents should be reminded that aspirin is generally contraindicated in children, except in the treatment of Kawasaki disease and rheumatologic diseases (eg, juvenile idiopathic arthritis).

(Choice A) Biliary atresia presents in infancy with direct hyperbilirubinemia, jaundice,

Clinical features of hepatic dysfunction include nausea, vomiting, and hepatomegaly. Laboratory derangements include **elevated transaminases**, **coagulopathy** (prolonged prothrombin time [PT], international normalized ratio [INR], and partial thrombin time [PTT]), and **hyperammonemia**. Excess ammonia is neurotoxic and causes cerebral edema and encephalopathy.

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(Choice A) Biliary atresia presents in infancy with direct hyperbilirubinemia, jaundice, and hepatomegaly. Biopsy shows bile plugs in the bile and canalicular ducts, portal tract edema, and fibrosis. This patient's age and normal bilirubin levels make this diagnosis unlikely.

(Choice B) Alpha 1-antitrypsin is characterized by chronic liver dysfunction in infancy and childhood followed by emphysema later in life. Cirrhosis and periportal eosinophilic inclusion bodies are typically seen on liver biopsy.

(Choice C) Macrovesicular fatty changes are seen in alcoholic hepatitis and in obese patients with nonalcoholic fatty liver disease. In contrast to Reye syndrome, most patients with alcoholic or nonalcoholic fatty liver disease are asymptomatic.

(Choice E) Congestive heart failure can lead to congestive hepatopathy. Examination shows fluid overload and palpable hepatomegaly. Histologic findings include sinusoidal congestion and hemorrhagic necrosis.

Educational objective:

Reye syndrome is a dangerous complication in children who received aspirin for virus-induced fever. Hyperammonemia, transaminitis, coagulopathy, vomiting, and mental status changes are typical manifestations of fulminant hepatic failure and encephalopathy.

References:

1. [Reye syndrome and reye-like syndrome.](#)
2. [FPIN's Clinical Inquiries. Aspirin use in children for fever or viral syndromes.](#)