Itchy and Scratchy

A 14-Month Old Boy with Failure to Thrive and Cholestasis

Stephens, John R, MD
Hospital Medicine Program, Department of General Pediatrics and Adolescent Medicine
University of North Carolina School of Medicine

Objectives:

- Review the differential diagnosis for cholestatic liver disease in infants
- Learn the cardinal features of **Alagille** syndrome
- Understand the basics of diagnosis, treatment and prognosis for **Alagille** syndrome

Case Presentation:

• A 14-month old boy was admitted with failure to thrive and pruritis. He had 10 to 14 stools daily, occurring within 15 minutes of eating. There were no recent fevers or vomiting. There was no history of jaundice, icterus or meconium ileus.

• Past medical history included solitary L kidney with mild hydronephrosis and poor weight gain.

• Weight, length and head circumference were all <3rd %ile.

Scleral icterus was present. He had a III/VI systolic murmur, loudest at left upper sternal border with radiation to back and axillae. Abdomen was soft, with firm liver edge palpable 1 cm below right costal margin. Skin had pearly, white to yellow papules on fingers and hands and diffuse excoriations were present on trunk. Ophthalmologic exam was normal.

Lab testing:

AST 139, ALT 113, GGT 1079, Alk Phos 1498, Tbili 2.9, Dbili 2.5. PT 9.2. Cholesterol 1625, lipase 35.

Fecal fat was moderate.

Abdominal ultrasound was without organomegaly or bile duct dilatation

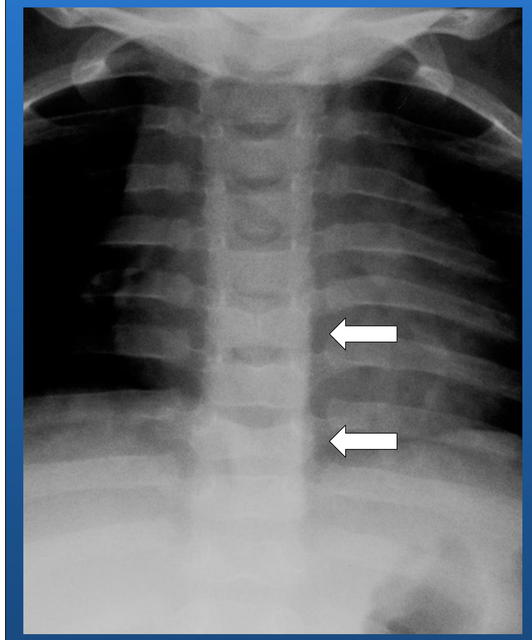
CXR demonstrated multiple butterfly vertebral anomalies.

Sweat chloride testing was negative

Echocardiogram revealed mild-moderate bilateral branch pulmonary artery stenosis

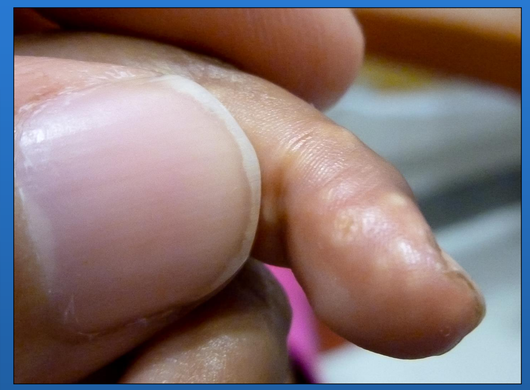
Skin biopsy of papule was consistent with xanthoma

Genetic testing showed *Jagged-1* gene mutation, confirming the diagnosis of Alagille syndrome.

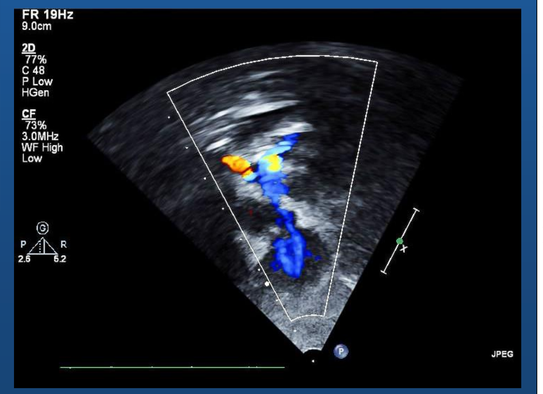


Butterfly Vertebrae

Acknowledgments:
Thanks to Ajay Gulati, MD, UNC Pediatric Gastroenterology, Dean Morrell, MD, UNC Pediatric Dermatology and John Cotton, MD, UNC Pediatric Cardiology



Xanthomas



Bilateral Branch Pulmonary Stenosis

Discussion:

• Infant cholestasis is a diagnostic challenge for general pediatricians as it can arise from a number of causes:

	Most Common	Age of onset	Associated symptoms
Obstructive	Biliary atresia	Neonate to 2 mos	Progressive jaundice
Infectious	Sepsis, UTI, adeno, EBV, parvo	Variable	Fever
Toxic	TPN	Variable	Jaundice, asymptomatic
Genetic/ metabolic	CF, α-1 AT def, Alagille	Variable	Failure to thrive

• Our patient had almost all cardinal features of Alagille syndrome, an autosomal dominant genetic disorder associated with paucity of bile ducts and cholestatic jaundice. A mutation of the gene *Jagged-1* is identified in the majority of patients. Typical presentation is cholestatic jaundice in infancy. Pruritis is a common symptom. Frequent associations include cardiac anomalies, particularly pulmonary artery stenosis, skeletal anomalies, especially butterfly vertebrae, renal anomalies, xanthomas, and posterior embryotoxin deposition (Schwalbe's line) in the eye. In patients with a typical presentation and confirmatory gene testing, liver biopsy is unnecessary.

• Treatment is supportive and typically involves ursodiol, rifampin and/or cholestyramine to manage the jaundice and pruritis. Patients often have fat malabsorption and diarrhea, and may require ADEK supplements. 20% of patients progress to end stage liver disease. The liver disease is amenable to transplantation, though this does not impact extra-hepatic manifestations of the disease.