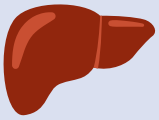
ALAGILLE SYNDROME

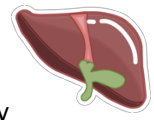


An **autosomal dominant** multisystem disorder and the **most common** form of **familial intrahepatic cholestasis**, occurring in approximately 1 in 30,000 births. It is primarily associated with mutations in the JAG1 gene (95% of cases) and the NOTCH2 gene (5% of cases).

AD
Autosomal dominant

CLINICAL FEATURES

Hepatic:
- **Cholestatic jaundice**
- Jaundice may improve with age
- **Paucity of bile ducts**

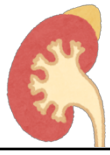


Facial:
- **Triangular facies**
- Broad forehead
- Small, pointy chin

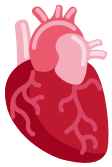
Ocular:
- **Posterior embryotoxon**

Skeletal:
- **Butterfly vertebra**

Renal:
- Renal disease



Cardiac:
- **Peripheral pulmonic stenosis**
- Tetralogy of Fallot



Additional Common Findings:
- Short stature
- **Hearing loss**
- Pancreatic insufficiency

DIAGNOSIS

- **Confirmatory genetic test:**
  - **JAG1** sequencing (~95 %)
  - **NOTCH2** sequencing (~5%)
- Alternative:
  - **Chromosomal microarray**

INVESTIGATIONS

Laboratory workup:
- **GGT extremely elevated** (20x upper limits of normal)
- **Elevated ALT** and **serum bile acids**

Liver biopsy:
- **Paucity of bile ducts**
  - *May be normal until 6 months of age*

Evaluate for associated abnormalities (eg: ECHO, ECG, ophthalmology, audiology, etc)

MANAGEMENT

Management focuses on **symptom relief** and **monitoring**:

Hepatic:
- **Liver function monitoring**: to assess liver health.
- **Medications**: **ursodeoxycholic acid** for bile flow and itching relief.
- **Nutritional support**: **high-calorie diet** and **fat-soluble vitamin supplementation**.
- **Liver transplantation**: considered for severe liver disease.

Other:
- **Cardiology evaluation**: assessments for heart defects and surgical repair as required.
- **Ophthalmological care**: management of eye abnormalities.
- **Developmental** and **psychosocial supports**

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