Question 8 – October 19

A 3 year old boy was referred to a pediatric gastroenterologist for evaluation of jaundice and pruritus. The physical exam was remarkable for a triangular face with broad forehead and pointed chin. Investigations revealed biliary hypoplasia and a defect in JAG1 gene on chromosome 20. What is the diagnosis?

A. Caroli's syndrome
B. Alagille syndrome
C. Schwachman-Diamond syndrome
D. Williams syndrome
E. Rotor syndrome

Answer: B

Biliary hypoplasia in a child with characteristic triangular facies and JAG1 gene defect are diagnostic of Alagille syndrome. Originally described in 1976 by a French hepatologist, this autosomal dominant syndrome affects multiple organs including vertebrae, heart, eyes, kidneys and probably pancreas. Most children have liver disease by the age of 3. Cholestasis can progress to require liver transplantation in some children. Caroli's syndrome is an autosomal recessive disorder from mutations in PKHD1 gene (adult recessive polycystic kidney disease) characterized by segmental cystic dilatation of intrahepatic bile ducts associated with congenital hepatic fibrosis. Schwachman-Diamond syndrome is an autosomal recessive disorder from mutations in SBDS gene that causes bone marrow failure, pancreatic insufficiency and short stature. Williams syndrome is an autosomal dominant disorder with mutations in multiple genes associated with supravalvular aortic stenosis, hypercalcemia and characteristic facial appearance of small upturned nose, small chin and wide mouth. Rotor syndrome is an autosomal recessive disorder with increased conjugated bilirubin but the liver and bile ducts are normal.

Reference:

Hartley JL, Gissen P and Kelly DA. Alagille syndrome and other hereditary causes of cholestasis. Clin Liver Dis. 2013 May;17(2):279-300.