Question 4 – August 22

A 3 year old girl is found to have jaundice and pruritus. She had a remarkable physical exam with a triangular face, broad forehead and pointed chin. Imaging revealed biliary hypoplasia.

What gene defect is the girl most likely to have?

A. PKHD1
B. SLCO1B1
C. ABCC2
D. JAG1
E. SBDS

Answer: D

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. Dubin Johnson syndrome has genetic mutations associated with ABCC2 gene. SLCO1B1 and SLCO1B3 mutations are associated with Rotor syndrome.

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.