

TEACHING FILES (GRAND ROUNDS)

JAUNDICE WITH TRIANGULAR FACIES AND PULMONARY STENOSIS

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Case Report

A 2½ years old girl born of third degree consanguineous marriage presented with progressive abdominal distension for one and a half months along with jaundice at onset. There was no bleeding manifestation or altered sensorium. She was born at full term and there were no perinatal problems. She has an eight month old sister who is asymptomatic. She is immunized for age and has normal milestones. On examination, she had pinched nose with triangular facies. Vital parameters were normal. On systemic examination she had hepatosplenomegaly. Other systems were normal. Ultrasound abdomen showed hepatosplenomegaly. Serum bilirubin was 11.5 mg/dl (direct bilirubin = 5.8 mg/dl), SGOT was 118 IU/L, SGPT = 120 IU/L, total proteins = 5.9 gm/dl, albumin = 3.4 gm/dl, alkaline phosphatase = 553 IU/L. Her hemoglobin was 11.6 gm%, white cell count of 5,900/cumm and platelet count of 2,01,000/cumm. Echocardiography showed left ventricular hypertrophy with mild pulmonary stenosis and liver biopsy showed bile duct paucity. X-Ray spine and ophthalmological examination was normal.

What is the diagnosis?

Discussion

Alagille syndrome is an autosomal dominant disorder that is caused by defects in genes involved in the Notch signaling pathway, most frequently due to a mutation in the JAG1 gene, but occasionally NOTCH2 or others. (1) The prevalence is 1:70,000. (2) Like most genetic disorders, the phenotype is variable, but often includes five aspects (i.e. the 'classic criteria'): a paucity of bile ducts and resulting cholestasis, congenital heart disease, dysmorphic facies, skeletal abnormalities, and eye pathology. Other features of Alagille syndrome include intracranial hemorrhage, vascular anomalies, dysplastic kidneys, renal tubular acidosis, failure to thrive, pancreatic insufficiency, and mental retardation. (3, 4) Most patients of Alagille syndrome present before six months of age with jaundice and failure to thrive or cardiovascular symptoms. (5) Besides jaundice, cholestasis can result in pruritus, xanthoma, and abnormal liver function tests. Due to cholestasis, the concentration of bile acids in the intestine decreases, and malabsorption of dietary lipids and fat soluble vitamins results in malnutrition and severe growth retardation particularly in the first years of life. (6) Some

patients may present with ocular manifestations which include posterior embryotoxon, iris abnormalities, optic disc anomalies, fundus changes (irregular pigmentation at the level of the retinal pigment epithelium, diffuse hypopigmentation, punched out chorioretinal atrophy), and choroidal folds. (7) Other cardiovascular anomalies which may be seen in such patients involve defects in pulmonary valve, artery, and branches with peripheral pulmonary stenosis. Tetralogy of Fallot is the most-reported complex cardiac malformation in subjects with Alagille syndrome. Other cardiac disorders include ventricular septal defect, atrial septal defect, aortic stenosis, coarctation of the aorta, pulmonary atresia, and hypoplastic left heart syndrome. (8) The most common skeletal anomaly in Alagille syndrome is 'butterfly' hemivertebrae, mainly in the thoracic spine. This consists of a sagittal cleft in 1 or more vertebrae. Other skeletal abnormalities include narrowing of interpeduncular spaces in the lumbar spine, pointed anterior process of the first cervical vertebra, spina bifida occulta, hemivertebrae, fusion of adjacent vertebrae, absence of the 12th rib, bony connections between ribs, short fingers, radio-ulnar synostosis, and lower limb long bones. (8)

Treatment of cholestasis, severe itching and xanthomas include ursodeoxycholic acid and other medications such as cholestyramine, rifampicin, naltrexone. In certain cases, partial external biliary diversion has been effective. (9) Liver transplantation is indicated in children with cirrhosis and liver failure. (10)

Compliance with Ethical Standards

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Conflict of Interest: None

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