LETTER TO EDITOR

CODEN: AAJMBG

Alagille syndrome- A rare autosomal dominant disorder

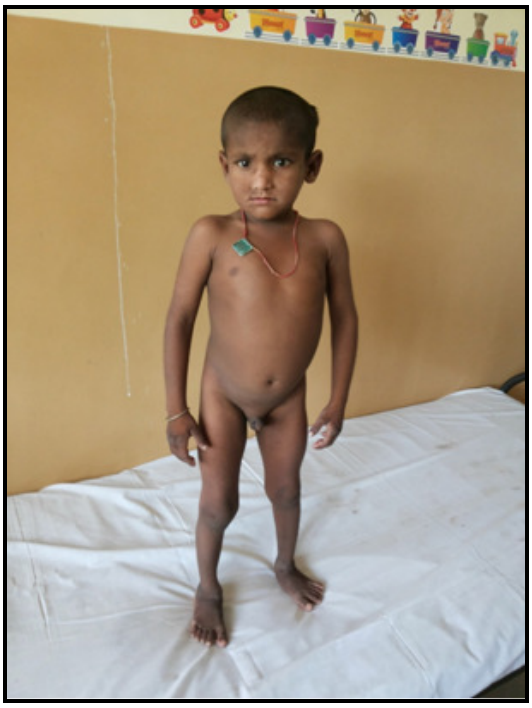
Dear Editor:

Alagille syndrome is a rare autosomal dominant disorder characterized by abnormal development of liver, heart, skeleton, eye, face and, less frequently, kidney [1-2]. In the fully expressed syndrome, affected subjects have intrahepatic bile duct paucity and cholestasis, in conjunction with cardiac malformations, most frequently peripheral pulmonary stenosis, ophthalmological abnormalities typically of the anterior chamber with posterior embryotoxon being the most common, skeletal anomalies (most commonly butterfly vertebrae), and characteristic facial appearance. Jag1 mutations have been identified in 60–70% of ags patients studied, and these include total gene deletions (-6%), protein-truncating mutations (insertions, deletions and nonsense mutations) (82%) and missense mutations (12%) [3-7].

It is named for daniel alagille. in 1973, watson and miller reported 9 cases of neonatal liver disease with familial pulmonary valvular stenosis. Then in 1975, alagille et al described several patients with hypoplasia of the hepatic ducts with associated features [8-10]. The estimated prevalence of alagille syndrome is 1 in every 100,000 live births. The severity of the disorder can vary within the same family, with symptoms ranging from so mild as to go unnoticed to severe heart and/or liver disease requiring transplantation [11-12]. Approximately 30 to 50 percent of cases, an affected person inherits the mutation or deletion from one affected parent. People with alagille syndrome may have distinctive facial features including a broad, prominent forehead, deep-set eyes, and a small, pointed chin [13-14]. The authors regard this case worthy of publication because this is a rare autosomal dominant disorder.

A 3yr old male child born out third degree counsanguineous marriage presented with yellowish discoloration of both eyes & urine since birth along with itching all over body & gradual abdominal distension since 1 yr. There was a h/o failure to thrive .There was no h/o pain abdomen, disturbances in mental status, oedema. Child was hospitalised at 4 months of age with progressive pallor & received blood transfusion .Birth history was uneventful, child received basic immunization upto 9 months of age, he was exclusively breastfed upto 1st of life & gradual weaning was started with home based foods. Developmental milestones were appropriate for age, no such history was noted from any of family members.

Fig-1: Facial features - Broadened forehead, elongated nose with bulbous tip,everted umbilicus.



O/E- BP 108/78 mm of hg, PR 108 bpm ,RR 26 cpm , pallor +, icterus +, grade 3 clubbing with b/l inguinal hernia.

Fig-2: Growth retardation, pubertal delay, Protrubrent abdomen

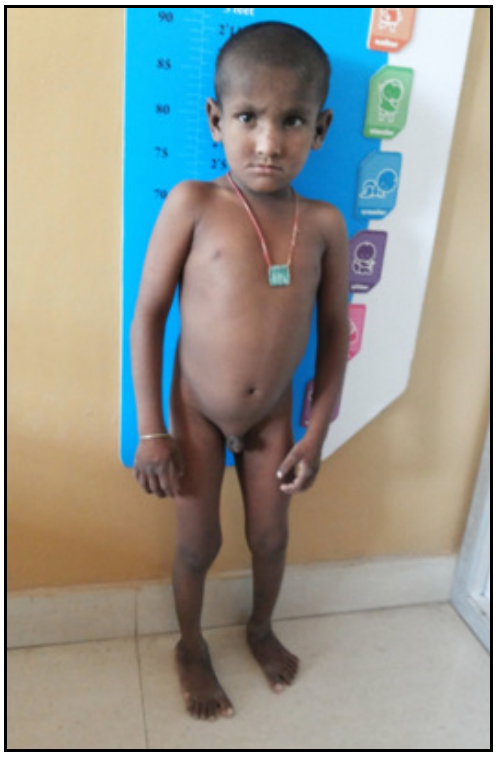
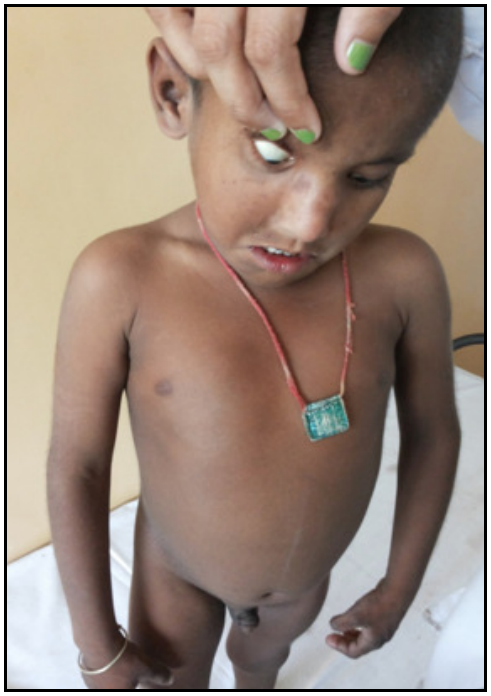


Fig-3: Yellowish discoloration of both eyes



Multiple dark coloured popular pinhead size lesions all over body with severe itching, corneal xerosis +, b/l bowed legs, wrist widening, normal genitals.

P/A- abdominal distension with everted umbilicus, no hepatomegaly with liver span of 6 cm, spleen enlarged 5 cm below costal margin. CVS-S1, S2 heard, with non radiating grade 3 systolic murmur over mitral area,

- RS – clear.
- CNS – NAD, fundus examination normal.
- IQ /DQ–average intelligence.

CBC revealed wbc count of 16,000 /mm3, hb 9.4 gm %, hct 29.8, platelets 1.83 lacs, total bilirubin 8 mg/dl, u bilirubin 4.1 mg/dl, bun 10, sr creat 0.4, Na 139, k 4.1, SGPT 42, SGOT 75 alk phos 429, ca/phos 9.3/11.6, ph 7.353, po2 49.5, pco2 36, hco3 19.5, total protein 7.3. sr albumin 3.6 , pt 12 sec. sr cholesterol 110 ,sr triglycerides 195 osmatic fragility increased s/o spherocytes. Blood culture NAD, urine culture NAD, urine for reducing substances absent.

Alpha 1 antitrypsin - 286 mg/dl (88-174), Afp - 0.82iu / ml (0.83-12.4), Anti lkm - 4.55 u/ml - negative, anti smooth muscle absent.

X ray spine - spinal bifida noted at L1, L2 with absent coccyx, soft tissue swelling suggestive of menigocele.

Abdomonal usg & Doppler ab-mod spleenomealy. Upper GI Endoscopy - NAD, MRCP – mild hepatospleenomegaly, 2d Echo-cong. acyanotic heart disease with peripheral pulmonary stenosis Cardiac MRI - diffuse hypoplasia of rt pulmonary artery - 4.2 in proximal portion, 2.8mm in mid region, 3.6 mm at distal portion.

Liver biopsy – paucity of intrahepatic bile ducts, periportal fibrosis, intrahepatic cholestasis, Flow cytometry normal, Skin biopsy -phyneroderma

Mutations in either jagged-1 (jag1) or notch-2 (notch2) have been reported in patients with alagille syndrome. The syndrome has been mapped to the 20p12-jagged-1 locus, jag1, which encodes a ligand critical to the notch gene–signaling cascade that is important in fetal development. notch signaling has been found to regulate formation of 3-dimensional intrahepatic biliary architecture in murine models [15-17] presentation of alagille

syndrome (as) varies. Some patients are diagnosed after prolonged neonatal jaundice or when liver biopsy findings reveal paucity of intrahepatic bile ducts. Others may be diagnosed during evaluation for right-sided heart disease [18]. Some individuals are diagnosed by careful examination after an index case is identified in the family.

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Cite this article as: Rizwan UZ, Jeergal NJ, Malagi NAN, Naganoor RG and Uzra Kaleem SY. Alagille syndrome- A rare autosomal dominant disorder. *Al Ameen J Med Sci* 2018; 11(1):76-78.

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