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CASE REPORT

# Alagille Syndrome: A Case Report

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## Introduction

Alagille syndrome is an autosomal recessive disorder which occur because of notch signaling pathway defects, primarily as a result of JAG1 mutation (ALG type 1), but it conjointly occurs seldom because of neurogenic locus notch homolog protein (NOTCH2) mutation (ALG type 2).[1,2] The syndrome and severity of Alagille can vary widely, often in the same family, from person to person. Some people may have mild form, while others may have more severe form. It is characterized by abnormalities in the liver, heart, eyes, face and skeleton. The main clinical manifestation of Alagille syndrome is cholestasis resulting from paucity of intrahepatic bile ducts and it is commonly associated with other clinical signs: heart disease, skeletal abnormalities, ocular abnormalities and facial dysmorphism.[3]

Typical facial alterations include sunken eyes, wide forehead, prominent chin, bulbous nose and small or malformed ears. Laboratory findings are increased blood levels of bile acids and direct bilirubin; increased transaminase, alkaline phosphatase, and gamma-glutamyltransferase activities and hypercholesterolemia. Histological findings are the presence of bile pigments in the cytoplasm of hepatocytes and in the lumen of bile canaliculi, ductules and ducts often associated with secondary cell injury.[4,5]

Several diseases can present cholestasis as a symptom; therefore, differential diagnosis continues to pose a challenge for pediatrician. In this case report, we present a patient in whom diagnosis of Alagille syndrome was done. It is important to be familiar with Alagille syndrome, so that its diagnosis can be suspected when a patient presents specific physical and morphological features, in addition to jaundice.

## Case report

A 7 months old female infant born of non-consanguineous parents presented with a history of jaundice since birth with progressive worsening along with episodes of acholic stool, intense itching and abdominal distension. There was no family history of sib death or family history of similar types of illness. She had mild pallor, icterus along with peculiar facial features in the form of broad forehead, deep seated eyes and prominent chin. Anthropometrically the child was severely under-weight, severely wasted and moderately stunted. Skin survey revealed multiple scratch mark due to excessive itching. On abdominal examination liver was enlarged 5cm from right costal margin, firm in consistency and on cardiovascular examination cardiac murmur splits at pulmonary area.

**Fig.-1:** *Triangular face with broad forehead, and saddle nose, deep set eyes and pointed chin*

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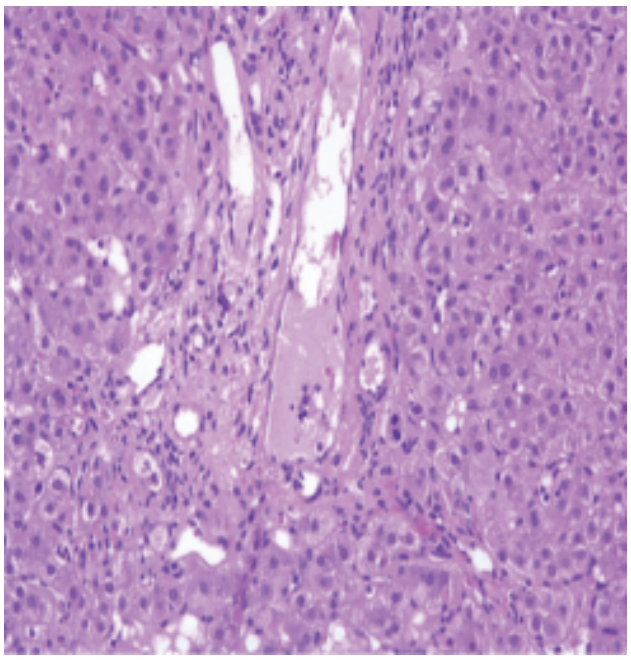

**Fig.-2** *Liver biopsy shows portal tract without any bile duct*

Investigations showed normal blood counts. Serum total bilirubin was 19.9 mg/dl (conjugated bilirubin 11.69 mg/dl), alanine transaminase 173 U/L, alkaline phosphatase 266 U/L, γGT 660 U/L, INR 1.09. A blood test for cytomegalovirus IgM was negative. Ultrasonography of whole abdomen hepatomegaly with raised parenchymal echotexture. X-ray spine showed butterfly vertebra. Echocardiography showed pulmonary stenosis. Hepatic histopathological examination revealed paucity of interlobular bile ducts. The child was diagnosed as a case of Alagille syndrome and started on ursodeoxycholic acid, cholestyramine and fat soluble vitamins. Jaundice and pruritus was improved partially with these treatments.

**Discussion**

Allagille syndrome is a multisystem autosomal dominant disorder, additionally referred to as arteriohepatic dysplasia, Alagille-Watson syndrome, Watson-Miller syndrome or syndromic common bile duct paucity which is characterized by variable clinical manifestations,[6] even among the similar family and usually include hepatic cholestasis, characterized by bile duct paucity in conjunction with liver (liver biopsy), cardiac abnormalities primarily involving the pulmonary arteries, skeletal (butterfly-like vertebrae and arch defects), ophthalmological finding (posterior embryotoxon) and facial findings. Additional features are intracranial bleeding and dysplastic kidneys.[7]

A diagnosis of Alagille syndrome is created mostly based upon identification of characteristic symptoms, a detailed patient history, a thorough clinical analysis and associated with a variety of tests including abdominal ultrasound, liver biopsy, echocardiography, vertebral radiography, slit lamp examination of the eyes, renal ultrasound with dropler, brain MRI and molecular genetic testing to rule out the symptoms.[8] In a study of 92 cases of Alagille syndrome, Emerick et al[9] described interlobular bile ductular paucity in 85%, cholestatic jaundice in 96%, cardiac abnormalities in 97%, characteristic triangular facies in 96% cases. Vertebral defects (butterfly vertebra) found in 51% and posterior embryotoxon in the eyes in 78% cases. Though we could not do mutation analysis due to lack of facilities in our country but our case had four of five features of Alagille syndrome and these were characteristic triangular facies, pulmonary artery stenosis, butterfly vertebra and bile ductular paucity. Pruritus was the major symptom and some of the cases respond to bile acid binding agents like cholestyramine. Our patient also showed response to cholestyramine.

The presence of heart murmur is the most common manifestation of Alagille syndrome. The majority of these murmur is caused by pulmonary stenosis. Intracardiac lesions such as Tetralogy of fallot and extra cardiac vascular lesions such as coarctation of aorta, patent ductus arteriosus may be present.[10] Our patient had pulmonary stenosis.

The most common radiological finding is butterfly shaped thoracic vertebrae, secondary to clefting abnormalities of the vertebral bodies. The reported frequency of butterfly vertebra ranges from 33% to 93%.[11] In the present case, vertebral radiography showed butterfly vertebrae.

Treatment for patients with Allagille syndrome aimed towards optimizing nutrition and managing complications associated with cholestasis and pruritus. Specific treatment is additionally indicated for individuals with the medications ursodeoxycholic acid, antihistamine, rifampin and cholestyramine.[1] In our case we treated our patient with ursodeoxycholic acid, cholestyramine powder and fat soluble vitamins.

## Conclusion

Cholestatic jaundice in infancy is one of the biggest diagnostic challenges faced by paediatricians. Paediatrician who first see the patient must be familiar with the several diseases involved to facilitate an early diagnosis. Alagille must be a part of the differential diagnosis in patients who in addition to jaundice present with physical and morphological characteristics of this syndrome.

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