Case Report

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A case report on Alagille syndrome and its clinical features

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Abstract

Alagille syndrome is a rare, chromosome dominant inherited complex disorder affecting varying organs like the liver, heart, kidneys, skeleton, and brain. It invariably happens because of Notch signaling pathway defects, primarily as a result of JAG1 mutation (ALGS type 1), but it conjointly occurs seldom because of neurogenic locus notch homolog protein (NOTCH2) mutation (ALGS type 2). The symptoms and severity of Alagille syndrome can vary widely, often in the same family, from person to person. Some people may have mild forms, while others may have more severe forms. Blocking of bile flow from the liver (cholestasis), yellowish discoloration of the skin and mucosal membranes (jaundice), low body weight, and extreme itching (pruritis) are the common symptoms, which often occur within the first three months of life. In this current study, we tend to report a case of 14 years old female child who was hospitalized with characteristic facial features like a broad forehead, yellowish discoloration of sclera and skin, posterior embryotoxon, intense itching, dry, coarse skin, mild splenomegaly, mild hepatomegaly. She conjointly had a history of progressive neonatal jaundice with prominent skin lesions and edema. Therefore our study emphasizes and focuses mainly on understanding and identification of distinct features associated with this syndrome to aid better management in all cases.

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INTRODUCTION

Alagille syndrome is additionally named as Alagille-Watson Syndrome or arteriohepatic dysplasia, which might classically involve the liver, eye, skeleton, kidneys, and heart. Mutations were found on the genetic material of chromosome 20 that includes a copy of the JAG I gene (Chitayat *et al.*, 2016) in most of the individuals with Alagille syndrome. A very few people have mutations in an exceedingly completely different gene, stated as NOTCH2. AGS has traditionally been diagnosed supported the presence of intrahepatic bile duct paucity on liver biopsy in association with a minimum of 3 of the foremost vital clinical features (Kamath *et al.*, 2010): distinguished facial features with a broad forehead, triangular small pointed chin, yellowish discoloration of the skin(jaundice), deep-set eyes(icterus), irritable itching (pruritis), fat deposition below the skin (xanthomatosis), characteristic feces, prior growth, heart murmurs, hepatosplenomegaly, posterior ernbryotoxon, butterfly vertebrae, renal dysplasia. Symptoms vary from mild to severe and might vary greatly from one person to a distinct, even within

the identical individuals among the same family who share identical mutation (Dědič *et al.*, 2015). This case is reportable for the rarity of this entity, notably within the Indian literature and to highlight the facts for the early diagnosis of this disorder.

A Case Report

A 14-years-old female offspring born of non-consanguinous parents presented with complaints of neonatal onset of jaundice from 3 months of age, associated with episodes of clay colored stools and high colored urine, pedal edema, abdominal distention. She had mild pallor, icterus, and clubbing. On examination, the child presented with peculiar facial features in the form of the broad forehead, yellowish discoloration of sclera, and skin presented in Figure 1.

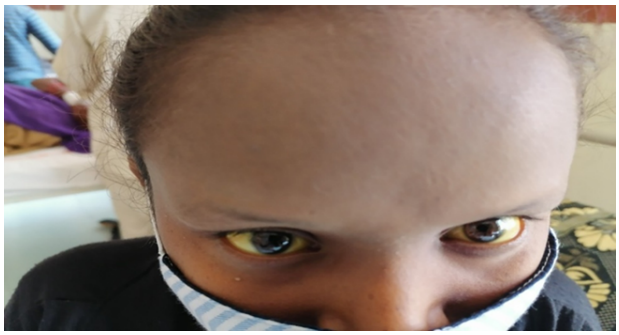

Figure 1: Broad forehead with discoloration of the sclera and posterior embryotoxon

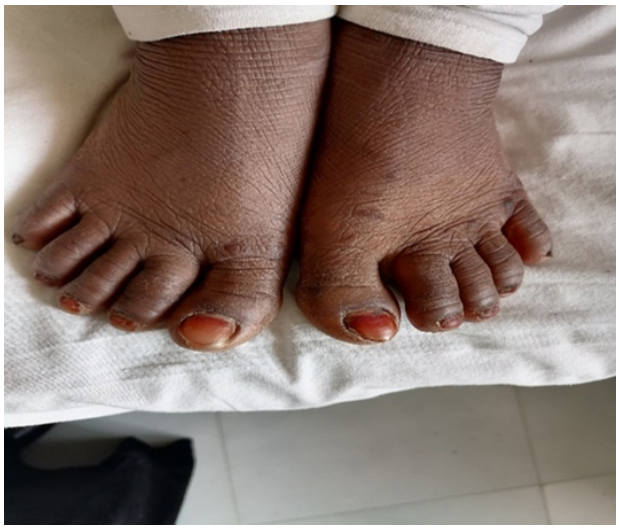

Figure 2: Edematous foot with dry, scaly skin

On evaluation, her ultrasound Scan shows an enlargement of the liver (around 14.2cms) and spleen (around 13cms). An eye examination demonstrated posterior embryotoxon. Dermatological examination shows dry, coarse skin, edematous fingertips with generalized pruritus over hands and legs, pigmented spots over hands as shown in Figure 2 and Figure 3. On systemic examination, a cardiac murmur splits at the pulmonary area. The biochemical parameters of the patient, along with corresponding reference ranges for the laboratory, are represented in Table 1. She tested negative for hepatitis- B surface antigen and HCV antibody.

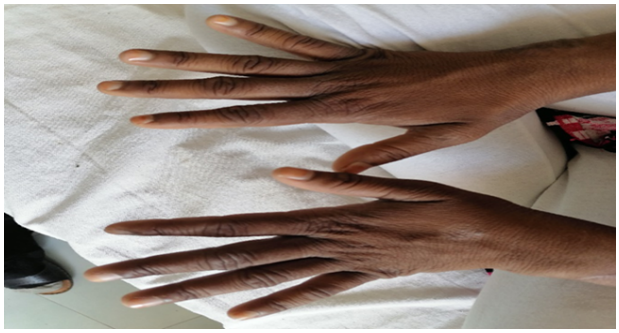

Figure 3: Hyperpigmented spots over hands

Our patient had no previous history of altered sensoriurn, hematemesis, or passage of black stools. Findings from respiratory and neurological examinations were normal. She was born preterm at 32 weeks of gestation with a low birth weight (2.0kg). But the child revealed with a family history that her elder sibling had presented with similar episodes of neonatal jaundice till 2 years and find recovered upon treatment.

All these symptoms may exacerbate in the child only during the onset of jaundice, which usually occurred once a year from birth, lasted for 10- 12 days, and gets improved upon treatment. Hence the patient was finally diagnosed as having Alagille Watson syndrome and was treated with ursodeoxycholic acid, L-Ornithine and L-Aspartame tablets, cholecalciferol syrup, and vitamin supplements. Her parents were suggested to attend follow-up appointments.

Furthermore, the patient confined that having multiple physician visits every year contributed to her symptoms of jaundice and severe pruritis. By meeting other adolescents with similar facial features and life circumstances, we have a tendency to hope the patient within the current study can improve her health.

DISCUSSION

Alagille syndrome (ALGS) may be 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 (Huang *et al.*, 2017), even among the similar family, and usually include hepatic (cholestasis, characterized by bile

Table 1: Laboratory profile of the patient along with reference range

Parameters	Analytical Values	Reference Range	Inference
Haemoglobin	12g/dl	12-15g/dl	Normal
Total WBC	12000 cells/mm^3	4-11000 cells/mm^3	Increased
Total platelets	1 lakh/mm^3	1.5-4 lakh/mm^3	Decreased
Serum urea	12 mg/dl	5-20 mg/dl	Normal
Serum creatinine	0.5 mg/dl	0.6-1.4mg/dl	Decreased
Total bilirubin	17.1 mg/dl	0.3-1.2mg/dl	Increased
Total proteins	5.2 g/dl	6.0-8.3g/dl	Decreased
Serum albumin	2.5 g/dl	3.5-5 g/dl	Decreased
Serum globulin	2.7 g/dl	1.8-3.6 g/dl	Increased
SGOT	68 IU/L	8-40 IU/L	Increased
SGPT	57 IU/L	5-35 IU/L	Increased
ALP	228 IU/L	12-115 IU/L	Increased

duct paucity in conjunction with liver (liver biopsy), cardiac (primarily involving the pulmonary arteries), renal (renal dysplasia), skeletal (butterfly-like vertebrae and arch defects), ophthalrnologic (posterior embryotoxon), and facial findings. (Chitayat *et al.*, 2016; Kamath *et al.*, 2010) Additional features are intracranial bleeding and dysplastic kidneys (Elkhoury *et al.*, 2019).

This disease was just about associated with the mutations within the JAG I gene on chromosome 20 (97%) (Kamath *et al.*, 2010), and a small proportion (1 -2%) are caused by mutations within the NOTCH2 gene (Singh and Pati, 2018). ALGS might even be mentioned as type 1 (JAG1-associated) or type 2 (NOTCH2-associated) (Ma and Song, 2014). The typical facial features are almost universally present in ALGS because of JAGl mutations and not seems to be as prevailing in people with ALGS carrying a NOTCH2 mutation (Chitayat *et al.*, 2016).

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 specialized tests include an abdominal ultrasound scan, liver biopsy, echocardiography, vertebral radiography, slit-lamp examination of the eyes, and renal ultrasonography with Doppler (Ayoub and Kamath, 2020), Brain MRI, molecular genetic testings to rule out the symptoms. As a result of the symptoms of Alagille syndrome are extraordinarily variable, obtaining a diagnosis is often typical.

Treatment for patients with ALGS is accessory and aimed towards optimizing nutrition and managing complications associated with cholestasis and pruritus. Specific treatment is additionally indicated for individuals with the medications ursodeoxycholic acid, antihistamines, rifampin, cholestyramine, and naltrexone (Turnpenny and Ellard, 2012).

Keeping the skin properly hydrous with moisturizers is additionally suggested. Preliminary studies show that IBAT inhibitors like Maralixibat and Odevixibat hold promise as a future treatment strategy for pruritus, which may probably also prove to be hepatoprotective.

Regular investigations are warranted to explore their therapeutic impact on the natural history of the cholestatic disease in ALGS (Ayoub and Kamath, 2020).

Abbreviations

SGOT-Serum glutamic oxaloacetic transaminase , SGPT- Serum glutamic pyruvic transaminase

ALP- Alkaline phosphatase, IBAT- Ileal bile acid transporter.

CONCLUSION

Alagille syndrome is a genetic condition that causes narrowing, deformation, or reduced numbers of the bile ducts, making it difficult for the body to transport bile as needed. Children and adults also share physical characteristics, including a broad forehead, deep-set eyes, and a narrow chin. These characteristics are not abnormal to children; they actually are typical to children with Alagille syndrome. In general, management is recommended to minimize complications, increase bile flow from the liver, maintain normal growth and development, and reduce blood cholesterol levels.

Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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