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CASE REPORT

Percutaneous dual intervention in a child with Alagille syndrome – A case report.

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ABSTRACT

Alagille syndrome (ALGS) is a rare autosomal dominant (AD) genetic disorder. It is a multisystemic disease which involves liver, heart, skeleton, eyes, kidneys and skeletal abnormalities. The disease may involve a particular system like facial dysmorphism, cardiac or musculoskeletal system. Some individual may not have hepatic involvement. Here we report unusual case of 9-year-old boy with large ostium secundum atrial septal defect (16 mm) and branch pulmonary artery stenosis (Left). The boy had facial dysmorphism (broad forehead, frontal bossing, triangular facies, hypertelorism, prominent ear and pointed chin, straight nose with bulbous tip). His psychological assessment revealed borderline IQ. He also had butterfly vertebrae in thoracic and lumber region which was found incidentally. He underwent device closure for atrial septal defect and balloon pulmonary valvuloplasty for left pulmonary artery stenosis. Both the procedure was performed simultaneously without complications. As there is no curative management for the disorder so symptomatic management is the only treatment option. We suggest screening of suspected individual, so that early intervention can safe patient from devastating complications of involved organ system.

Keywords: Alagille syndrome, autosomal dominant genetic disorder, facial abnormalities, Ballon pulmonary valvuloplasty, facial dysmorphism, cardiac defect.

Introduction

Alagille syndrome was first described in 1969 by Daniel Alagille[1]. Its mode of inheritance is AD[2]. It is a complex multisystem disorder with variable phenotypic expression[3]. It is associated with JAG1(90%) and NOTCH 2 mutation[2,4]. The disease prevalence is very low due to lack of genetic testing[5]. The traditional clinical criteria have been changed due to emerging molecular screening[6]. Diagnosis of Alagille syndrome (ALGS) can be made if three out of five major criteria presents. The major criteria are hepatic cholestasis, cardiac defect, facial dysmorphism, skeletal abnormality (butterfly vertebra) and ocular manifestation[2,4]. Here we got a boy with 3 criteria (facial dysmorphism, butterfly vertebra and cardiac defect). Our case is unique because the main clinical manifestation of ALGS is infantile cholestasis[7]. Most common cardiac defects are peripheral pulmonic stenosis, Tetralogy of Fallot, Ventricular septal defect and Atrial septal defect[8]. Cardiac disease is associated with decreased life expectancy[7,9].

Here we report a rare case of AGS in a 9-year-old boy presenting with large ostium secundum defect and left pulmonary artery stenosis who had a different clinical presentation from the usual presentation of the ALGS.

Case Presentation

A nine -year-old boy residing in rural area of Bangladesh presented with cough , breathing difficulty and easy fatiguability for last 3 year. He also had dyspnoea on exertion. These was episodic in nature. For these he visited to several doctor but his disease was not diagnosed. As his symptoms was not improving he came to Dhaka and visited to our University hospital. Then after thorough evaluation he was diagnosed to have large ostium secundum atrial septal defect(ASD) and left pulmonary artery (LPA) stenosis. He also had facial dysmorphism like frontal bossing, triangular facies, hypertelorism, broad forehead, deep-set eyes, prominent ears, saddle like straight nose with bulbous tip and pointed chin. His psychological assessment was done by WISE -R scoring and revealed borderline IQ associated with poor speech and cognition. His motor development was normal. Ocular examination revealed normal findings. Chest X-ray showed abnormal segmentation in the vertebrae (butterfly presentation) (Figures: 2). He had no history of neonatal cholestasis. These clinical features are suggestive of ALGS.

Colour doppler echocardiography revealed large ostium secundum ASD (size 8.5 x12 mm) with L-R shunt, deficient posterior rim with all other adequate rim, mild pulmonary hypertension (PASP 43 mm Hg), moderate LPA stenosis with GDT 42 mmHg and dilated RA &RV with good biventricular function.

X-Ray spine both A-P and lateral view showed butterfly vertebra involving different vertebrae(small midline cleft)

CT angiogram revealed large ostium secundum type ASD (12mm) and left pulmonary artery stenosis. (Figure 4).

Ultrasonography of hepatobiliary system and KUB reveals normal finding.

Figure 1: 9 year child diagnosed to be a case of Alagille Syndrome

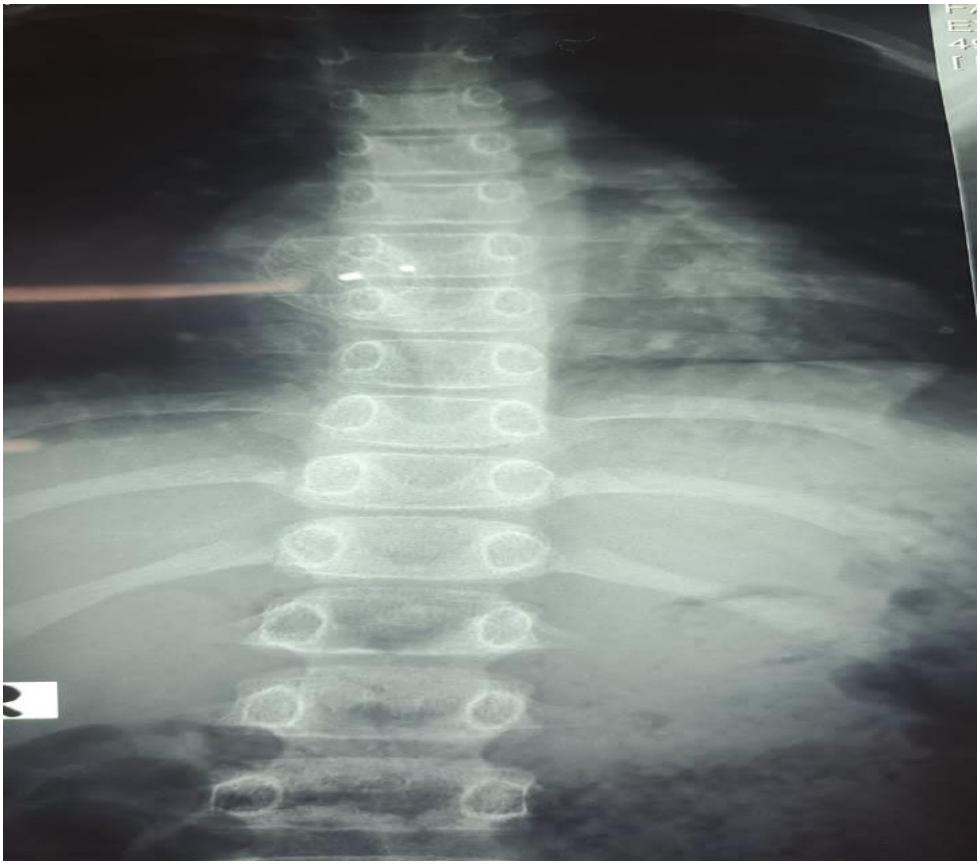

Figure 2: X-ray spine showing Butterfly vertebra

The patient was planned for device closure of ASD and balloon pulmonary valvuloplasty for LPA stenosis. All the preoperative investigations CBC, PT, APTT, urine for R/M/E, viral markers and covid test was done. All the preoperative parameters were within normal limit and covid test was negative.

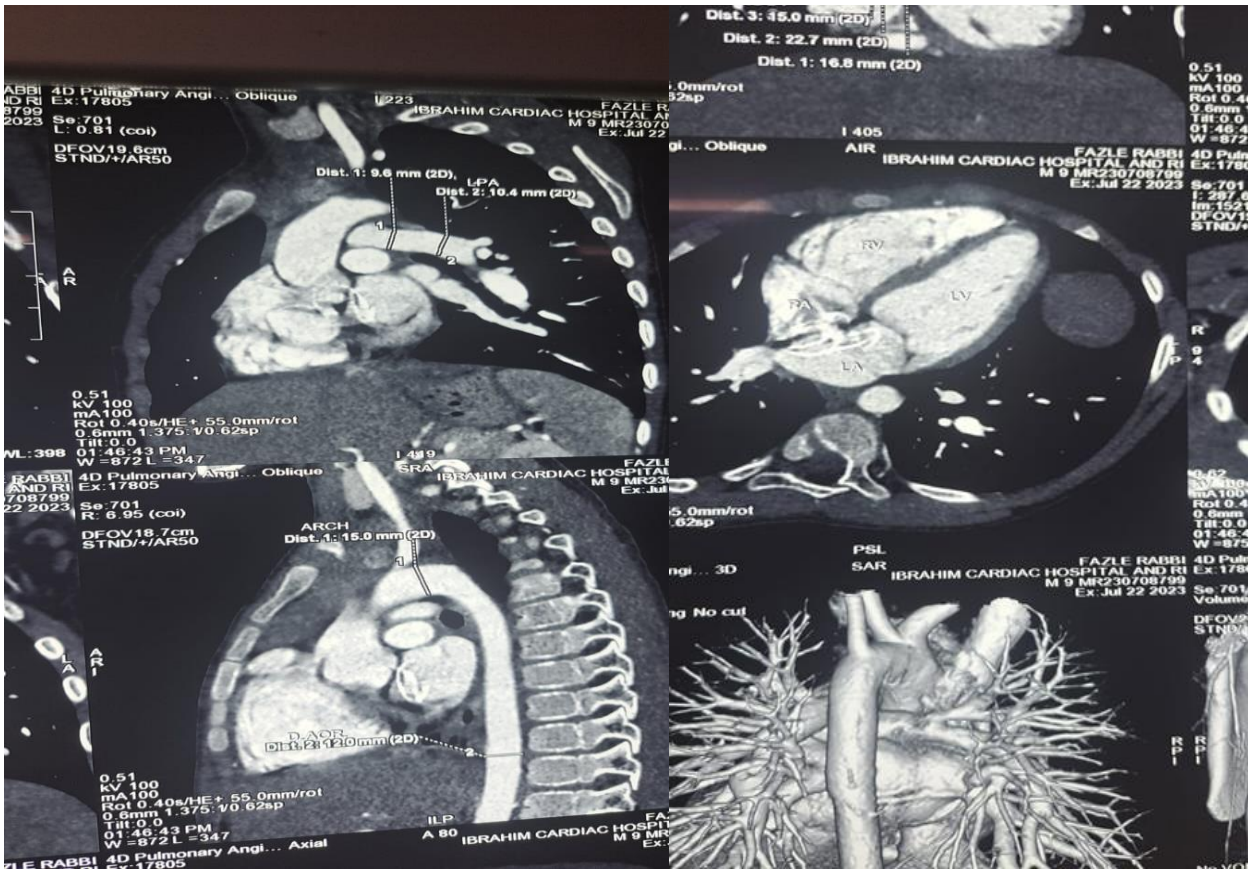

Figure 3: Cardiac CT angiogram showing LPA stenosis

The boy underwent percutaneous interventions. His RV angiogram AP and lateral view revealed moderate LPA stenosis. The diameter of LPA in pre stenotic, stenotic and post stenotic segment was 9.5 mm,6.5 mm and 12 mm respectively. Pre procedure PPG was 33/13/20 mm Hg. Balloon dilatation of LPA was done with Tyshak II balloon sized 8mmx4 cm. balloon pulmonary valvuloplasty (BPV) was done successfully. Post balloon LPA PPG was 20/11/14 mmHg. After BPV, ASD was closed by Amplatzer septal occluder size -16 mm at the same time. There were no procedure related complications.

The next morning after performing BPV and ASD device closure an colour doppler echocardiography was performed. Post procedure echocardiogram showed ASD device in situ with no residual flow, mild pulmonary hypertension

(35 mm Hg)mild LPA stenosis with GDT 25 mm Hg , good flow through SVC and IVC, good biventricular function.

He was discharged after 5 days of intervention and scheduled for a follow-up after 1 months. He was advised to continue tab aspirin for 6 months.

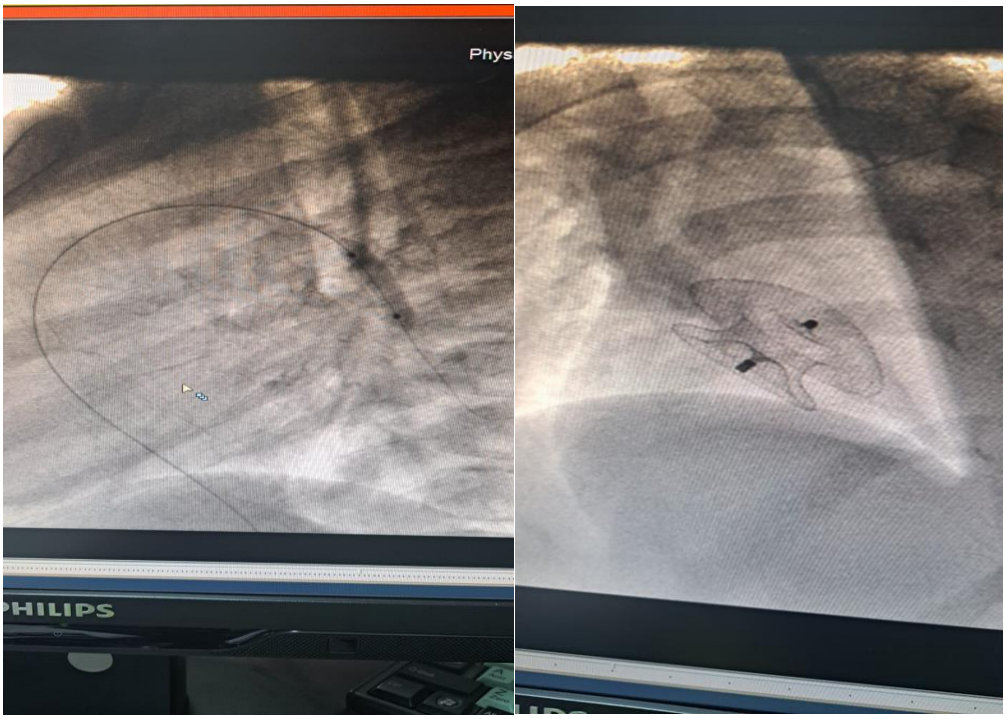

Figure 4: BPV of LPA and ASD device closure

Discussion:

Alagille syndrome is an autosomal dominant disorder caused by the mutation of JAG1(97%) and NOTCH 2 genes[10,11]. It is also known as arteriohepatic dysplasia/cardio-vertebral syndrome[12]. It is a multisystem involving disorder, can affect the hepatobiliary, facial dysmorphism, eye , cardiovascular, renal and musculoskeletal system[13]. The prevalence of AGS is1:70,000 to 1:100000[14].

Cardiac involvement occurs 75-94% patients. Most common cardiac defects are peripheral pulmonic stenosis, Tetralogy of Fallot (TOF), Ventricular septal defect (VSD) and ASD[8]. The cardiac defect may require interventions or surgery[15].

Our patient presented with large ostium secundum ASD and moderate LPA stenosis without history of neonatal cholestasis. This was consistent with the study reported by Vishal and Hardil[1]

The hepatobiliary system may be affected from-89-100%. The patient may present with the features of jaundice, intense pruritus, cutaneous xanthomas, coagulopathy[16]. On USG there may be hepatic dysfunction, portal hypertension, fibrosis or biliary atresia may be present[17,11]. The hepatic manifestation may require liver transplantation[11]. These findings were absent in our patient which was atypical.

ALGS can affect the renal system. There may be renal tubular acidosis, vesicoureteral reflux, renal dysplasia. Renal involvement was also absent in our patient[18].

The most common musculoskeletal abnormality in ALGS is butterfly abnormality of vertebral column[19]. It occurs in 33-87% patient formed by the incomplete fusion of anterior arch[20]. The name is based on the pattern that the two

hemivertebrae appear on x-rays as butterfly wings from the central gap .it may be associated with low back pain and fracture[21]. Butterfly vertebra was present in our patient.

Facial dysmorphism is one of the most important clinical findings characterized by frontal bossing, triangular facies, hypertelorism, broad forhead, deep-set eyes, prominent ears, saddle like straight nose with bulbous tip and pointed chin. Our patient had facial dysmorphism[22].

ALGS may presented with ocular involvement like posterior embryotoxon, macular atrophy and irregular pigmentation of retina[23]. Posterior embryotoxon present in 8.3%of patient[16]. Our pt's eye examination revealed normal findings.

Other abnormalities are growth failure, delayed puberty and splenomegaly[10].

Vascular abnormalities are common presentation of ALGS patients. the most common finding is pulmonary artery stenosis[23]. The intracranial vessels , aorta ,coeliac , sup mesenteric and subclavian arteries may involve[8]. Patients may present with intracranial bleeding[24]. There was no history of intracranial bleeding in our patient. But he had moderate LPA stenosis.

There may be mild intellectual disability and motor delay which was present in our patient[10].

ALGS is associated with impaired T cell function which can be manifested by recurrent RTI[1]. Recurrent RTI was present in our patient.

Treatment of ALGS depends on the systemic involvement and severity of disease[11]. Hepatobiliary system may require liver transplantation .it is necessary to reduce pulmonary artery pressures before liver transplantation[18]. Cardiac lesions may be treated by percutaneous or surgical intervention[24].

Conclusions

Clinical suspicion is the key to diagnose a rare disorder. The classic criteria should be focused. The disease can be diagnosed by evaluation according to clinical protocol. Genetic test can confirm the diagnosis, but it is less available. Family assessment is necessary for diagnosis of ALGS. The patient may present with hepatic or cardiac abnormalities. there is no curative treatment for the disease. Though current therapeutic approaches are supportive, timely intervention can safe patient from devastating complications. Prevention of the mutation need to be developed. Genetic engineering and pharmacologic agents can help to augment the notch signalling pathway for prevention.

Conflict of Interest:

Author declared no conflict of interest.

Authors` contributions:

1. Case report theme, data collection and write up – Dr Tahmina karim
2. Cath data and reference paper collection – Dr Sumona Shafinaz Khan
3. Reference article collection – Nuzhat Tabbassum Kanti
4. Reviewed by – Professor Dr. Md Tariqul Islam

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References:

1. Bhende VV, Majmudar HP, Sharma TS, Pathan SR, Mehta DV, Pathan S. Nonhepatic Alagille syndrome associated with predominant cardioskeletal anomalies: a rare case. Cureus. 2021 Aug 25;13(8).

2. Saleh M, Kamath BM, Chitayat D. Alagille syndrome: clinical perspectives. The Application of Clinical Genetics. 2016 ;30:75-82.

3. Kim J, Yang B, Paik N, Choe YH, Paik YH. A case of Alagille syndrome presenting with chronic cholestasis in an adult. Clinical and Molecular Hepatology. 2017 Sep;23(3):260.

4. Sanderson E, Newman V, Haigh SF, Baker A, Sidhu PS. Vertebral anomalies in children with Alagille syndrome: an analysis of 50 consecutive patients. Pediatric radiology. 2002 Feb; 32:114-9.

5. Ayoub MD, Kamath BM. Alagille Syndrome. Diagnostic Challenges and Advances in Management. Diagnostics (Basel). 2020 Nov 6;10(11):907.

6. Li J, Wu H, Chen S, Pang J, Wang H, Li X, Gan W. Clinical and Genetic Characteristics of Alagille Syndrome in Adults. J Clin Transl Hepatol. 2023 Feb 28;11(1):156-162

7. Amimoto S, Ishii M, Tanaka K, Araki S, Kuwamura M, Suga S, Kondo E, Shibata E, Kusuhara K, Yoshino K. Alagille-like syndrome with surprising karyotype: a case report. J Med Case Rep. 2023 Apr 26;17(1):186.

8. Tretter JT, McElhinney DB. Cardiac, aortic, and pulmonary vascular involvement in Alagille syndrome. Alagille syndrome: pathogenesis and clinical management. 2018:77-90.

9. Yuan SM. Pulmonary artery pathologies in Alagille syndrome: a meta-analysis. Advances in Interventional Cardiology/Postępy w Kardiologii Interwencyjnej. 2022 Jun 1;18(2):111-7.

10. Harada T, Fukae K, Matsuo O, AndoY. Peripheral Pulmonary Artery Growth in Alagille Syndrome after Central Pulmonary Artery Enlargement: A CaseReport. Ann Clin Case Rep. 2024; 9:2555.

11. Spinner NB, Gilbert MA, Loomes KM, Krantz ID. Alagille Syndrome Synonyms: Arteriohepatic Dysplasia, Syndromic Bile Duct Paucity. Gene;1:2.

12. Andrew GM, Brian T, Fowler MD, Stephen C, Dryden MD, Grace S et al.Alagille syndrome. american academy of ophthalmology. 2023 Jan 26

13. .Martin E, Mainwaring RD, Collins RT 2nd, MacMillen KL, Hanley FL. Surgical Repair of Peripheral Pulmonary Artery Stenosis in Patients Without Williams or Alagille Syndromes. Semin Thorac Cardiovasc Surg. 2020 Winter;32(4):973-979

14. BaykanA, Argun M, Özyurt A, Pamukçu O, Sezer S, Üzüm K, Nari N. Cutting balloon angioplasty and stent implantation for left pulmonary artery stenosis in a case with Alagille syndrome. Turk Gogus Kalp Dama 2014; 22:642-644

15. Herceg S, Dilber D, Šarić D, et al192 Alagille syndrome in infant with fallot tetralogy. Archives of Disease in Childhood 2021;106:A81-A82

16. Semenova N, Kamenets E, Annenkova E, Marakhonov A, Gusarova E, Demina N, Guseva D, Anisimova I, Degtyareva A, Taran

N, Strokova T, Zakharova E. Clinical Characterization of Alagille Syndrome in Patients with Cholestatic Liver Disease. Int J Mol Sci. 2023 Jul 21;24(14):11758

17. Katsuura Y, Kim HJ. Butterfly Vertebrae: A Systematic Review of the Literature and Analysis. Global Spine J. 2019 Sep;9(6):666-679.

18. Huang H, Wang LF. Radiological changes of spine and liver in a case of Alagille syndrome. Quant Imaging Med Surg 2018;8(3):368-371.

19. Rao A, Gaikwad S, Taksande A, Wanjari MB. An Incidental Finding of Butterfly Vertebrae in a Case of Vertebral Defects, Anal Atresia, Cardiac Defects, Tracheo-Esophageal Fistula, Renal Anomalies, and Limb Abnormalities (VACTERL). Cureus. 2023 Jan 5;15(1):e3340

20. Joshi A, shah I.Jaundice with triangular facies and pulmonary stenosis.paediatric on call journal 2018;15:87-88.

21. Yoon HL, Youg JH, Seon HL, Sang YL,Jung MK,Il-soo HA, Hee GK. A patient with multiple arterial stenosis diagnosed with Alagille syndrome: A case report. Journal of Genetic Medicine *2021;142-146*

22. Akagi K, Tanaka T, Baba S. Successful living donor liver transplantation after stent implantation in a patient with Alagille syndrome and severe bilateral pulmonary artery stenosis. Cardiology in the Young. 2018 Dec;28(12):1465-7.

23. Rodriguez RM, Feinstein JA, Chan FP. CT-defined phenotype of pulmonary artery stenoses in Alagille syndrome. Pediatric radiology. 2016 Jul;46:1120-7.

24. Luong R, Feinstein JA, Ma M, Ebel NH, Wise-Faberowski L, Zhang Y, Peng LF, Yarlagadda VV, Shek J, Hanley FL, McElhinney DB. Outcomes in patients with Alagille syndrome and complex pulmonary artery disease. The Journal of Pediatrics. 2021 Feb 1;229:86-94.