p.Arg142Ter Variant Causing IFT52 Gene Mutation Resulting in Asphyxiating Thoracic Dystrophy-Juene Syndrome-A Rare Case Report

A C Mammen[a], Binukuttan PV[a], Reni G Varghese[a], Salini Sasidharan[a]

a. Department of Paediatrics and Neonatology, Sanjivani Multispeciality Hospital, Alacode P.O, Kollakadavu, Chenganur, Kerala*

ABSTRACT

Published on 26th March 2021

Asphyxiating thoracic dystrophy or Juene syndrome is a rare condition of congenital dwarfism. Incidence is 1 per 100000-130000 live births1.A term neonate born in our hospital had respiratory distress soon after birth. On examination, the baby had polydactyly on all four limbs and small bell-shaped thorax. Xray revealed small metacarpals, short ribs, short iliac bones acetabular spurs. Mutation analysis revealed mutation in the gene coding IFT52 in Exon 6 with pArg142Ter as variant.Since this variant is reported less in literature,we report this case.

Keywords: Juene Syndrome, pArg142Ter, Asphyxiating Thoraccic Dystrophy, Skeletal Anomalies

*See End Note for complete author details

INTRODUCTION

Juene syndrome, asphyxiating thoracic dystrophy is an uncommon autosomal recessive condition with a frequency of 1 in every 100000 - 130000 live births.[1] It has got variable seriousness and different musculoskeletal indications. It is an uncommon short rib skeletal dysplasia described by short limbed dwarfism, small narrow bell-shaped thorax, varying degrees of rhizomelic brachymelia, micromelia, polydactyly of hands and feet, pelvic peculiarities, renal abnormalities with an extensive neonatal mortality because of respiratory distress.[2] Renal, hepatic, pancreatic and visual complications may happen in later life. Radiological confirmation is needed. Prognosis of the disease depends on the seriousness of the chest deformities and the greater part of the patients are lost in the principal year in view of respiratory issues.[3] We present a newborn, born in our NICU with milder form of Juene syndrome (IFT52 gene mutation, exon6, pArg142Ter variant) and report this case because of its rarity.

CASE REPORT

A first order full term male baby born by LSCS to a primigravida nonconsanguineous married couple, developed respiratory distress soon after birth. The baby had skeletal abnormalities. Weight of the baby was 2.6 kg, length being 43cm, head circumference being 36 cm with chest circumference of 33cm. The neonate had typical bell-shaped thorax, bilateral short upper limb and polydactyly **(Figure 1)**. Xray revealed typical finding of horizontal short ribs, enlarged costochondral junction, small and horizontal clavicles **(Figure 2).** The newborn required CPAP support for 5 days due to respiratory distress.

After 5 days ,when the respiratory distress came down patient was shifted to headbox. Septic screen was negative. Feeds were gradually increased as per tolerance and keeping a check on the respiratory rate. Once full feeds were achieved patient was shifted to mother side. Baby was not able to feed directly from the breast because of respiratory distress, so baby was fed by paladay feeds. Blood was collected and sent for gene analysis.

USG revealed mild hepatic fibrosis with normal liver function test. Eye examination revealed mild retinal degenerative changes. Patient was discharged and was asked to follow-up in the Neonatology OPD with gene analysis report.

Cite this article as: Mammen AC, Binukuttan PV, Varghese RG, Sasidharan S. p.Arg142Ter Variant Causing IFT52 Gene Mutation Resulting in Asphyxiating Thoracic Dystrophy-Juene Syndrome-A Rare Case Report. IMA Kerala Medical Journal. 2021 Mar 26;14(1):11–3.

Corresponding Author:
Dr. A C Mammen, Consultant in Pediatrics and Neonatology, Sanjivani Multispeciality Hospital,Kollakadavu P.O, Chengannur. Mobile: 9496323897 E-mail: arunmammen16@gmail.com

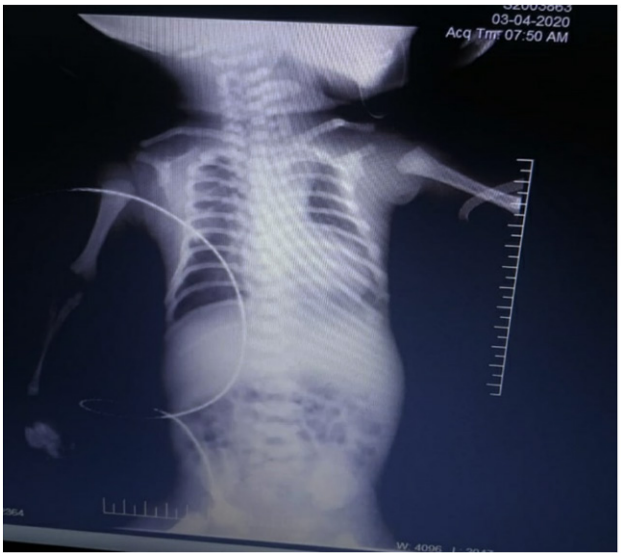

Figure 1. **Small and horizontal clavicles**

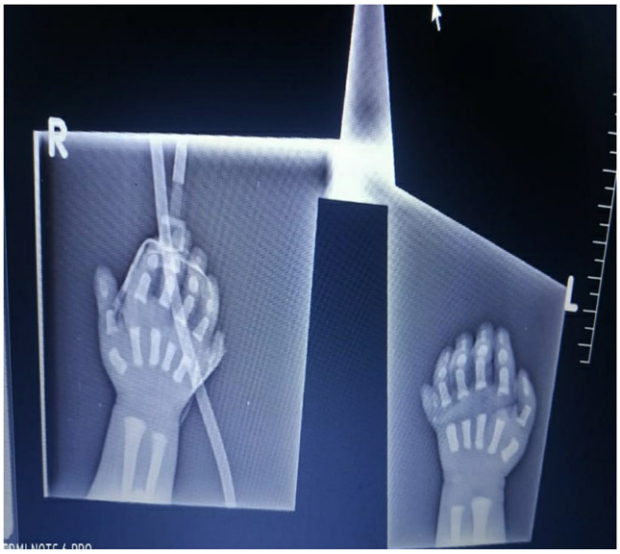

Figure 2. **Bilateral upper limb and polydactyly**

DISCUSSION

Juene syndrome otherwise called asphyxiating thoracic dystrophy is an uncommon autosomal disorder. Different studies have demonstrated that the locus on12p,15q13 chromosome is responsible for this syndrome.[4] The molecular basis of this condition has been elucidated showing inclusion of the IFT80(3q25.33), DYNC2H1(11q22.3), WDR19(4p14) and TTC21B(2q24.3) genes each encoding an intra-flagellar transport protein which affirms that Juene disorder has a place with ciliopathies group.[5] Mutations in different genes may also be implicated in the disorder and still remains unidentified. Exome sequencing recognizes DYNC2H1 transformations as a typical reason for asphyxiating thoracic dystrophy (Juene Syndrome) without major polydactyly, renal or retinal involvement.[6] It is because of the dysfunction of inter flagellar transport or primary ciliary dysfunction. It is named one of the 6 short rib polydactyly condition (SRPS) disorders.[7] The principle clinical features are dwarfism with short ribs, short appendages, polydactyly of hands and feet and classical radiographic changes in the ribs (small bell-shaped thorax) and pelvis (short iliac bones with acetabular spurs)[1] with retinal degeneration. Lung hypoplasia probably because of limited thoracic cage causes alveolar hypoventilation and around 60-70% of the patients of Juene condition die from respiratory failure in early life.[8] Chronic renal failure can happen in survivors. Other skeletal dysplasia which are close differentials are achondrogenesis, achondroplasia, osteogenesis imperfecta, thanatrophic dwarfism, hypophosphatasia.[9] Pre-birth ultrasonography can help in conclusion.

CONCLUSION

Juene syndrome although a rarity should be kept in mind on seeing a baby with polydactyly, narrow chest wall, mesomelia etc.

Novel Insights: We report this case because the gene analysis revealed

- IFT52 gene mutation at Exon 6
- pArg142Ter as variant.

Established Facts:

- Juene syndrome locus on12p,15q13 chromosome
- IFT80(3q25.33),DYNC2H1(11q22.3),WDR19(4p14) and TTC21B(2q24.3) genes has been elucidated.

END NOTE

Author Information

1. Dr A.C.Mammen, MD(Paediatrics), DAA(CMC Vellore), Fellowship in Neonatology (London, UK), Consultant. Department of Paediatrics and Neonatology, Sanjivani Multispeciality Hospital, Alacode P.O, Kollakadavu, Chenganur, Kerala.
2. Dr Binukuttan P.V, MD(Paediatrics), Consultant, Department of Paediatrics and Neonatology, Sanjivani Multispeciality Hospital, Alacode P.O, Kollakadavu, Chenganur, Kerala.
3. Dr Reni G Varghese, DCH, Consultant, Department of Paediatrics and Neonatology, Sanjivani Multispeciality Hospital, Alacode P.O, Kollakadavu, Chenganur, Kerala.

4. Dr Salini Sasidharan, MD, Fellowship in Neonatology(IAP)), Consultant, Department of Paediatrics and Neonatology, Sanjivani Multispeciality Hospital, Alacode P.O, Kollakadavu, Chenganur, Kerala.

Conflict of Interest: None declared

Acknowledgement: This case was born in our hospital. Dr.Salini Sasidharan helped in the clinical management of the baby, Dr.Reni Gee Varghese collected similar case reports from different journals and articles.

Dr.Binukuttan P.V did the proof read and helped in compiling the case report.

Dr.Arun Mammen is the principal investigator and the corresponding author.

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