

Late Onset Joubert Syndrome: Case Report**Dr. Rita Hajela¹, Dr. Arshdeep Singh², Dr. Santosh Bhalke³, Dr. Seema Rai⁴**^{1,4}Assistant Professor, ²Associate professor, ³Professor, Department of Pediatrics and Department of Radiology, Maharishi Markandeshwar Medical College and Hospital, Kumarhatti, Solan, PIN code 173229, Himachal Pradesh, India***Corresponding author**

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Abstract: Joubert Syndrome (JS) is a rare congenital autosomal recessive disorder. Obligatory finding and Hallmark feature is Molar tooth sign, a complex midbrain hindbrain malformation visible on MRI brain. Cardinal clinical feature is hypotonia evolving into ataxia usually presenting in infancy as hypotonia or early childhood as ataxia. When syndrome is associated with other system involvement it is called Joubert syndrome and related disorders (JSRD). We report a 13 year old boy who presented with progressive ataxia and hypotonia of one year duration and was diagnosed as having Joubert Syndrome on the basis of MRI Scan and other primary criteria. Management was limited to Physiotherapy, genetic counseling and advice for a regular follow up for early recognition of any other system involvement and complications.**Keywords:** Joubert Syndrome, Molar tooth sign, Cerebellar peduncles, Hypoplasia Vermis, Cerebellar Ataxia, Hypotonia.

INTRODUCTION:

Diagnosis of Classic or pure Joubert syndrome, also known as Joubert –Boltshauer syndrome, cerebelloparenchymal disorder IV CPD4, is based on presence of three primary criteria

- The molar tooth sign comprising prominent straight and thickened superior cerebellar peduncles, Hypoplasia of cerebellar vermis and an abnormally deep interpeduncular fossa seen in MRI of Brain [1, 2]
- Hypotonia and later development of ataxia.
- Developmental delay /intellectual disability.

The signs and symptoms not only vary among individuals but also between affected individuals of the same family. Prevalence of JSRD including JS is between 1:80,000 and 1:100,000.[4] Classification system of JSRD is still evolving, many eponyms were used in past but now OJRD (orphanet journal of rare diseases) classifies it into six phenotypes: Pure JS(JS), JS with ocular defect(JS-O), JS with renal defect (JS-R), JS with oculorenal defect (JS-OR), JS with hepatic defect(JS-H), JS with oro, facio, digital defects (JS – OFD)[5]. We report a case of pure JS with father also retrospectively diagnosed as a case of JS after 18 years of illness.

CASE REPORT:

A 13 year old male child born to parents with a nonconsanguineous marriage was brought to us by mother in an outreach community health camp for

gradually increasing difficulty in holding objects, tremors in hands, sudden falls while walking from last one year. On examination he had cerebellar ataxia, generalized hypotonia, weak reflexes, and weak muscles with muscle power varying from grade 3 to 4 in different group of muscles. (Figure3) He was able to walk with an awkward gait. Speech was slow but otherwise normal, he took longer in finishing his meals but otherwise difficulty in swallowing was not noted. Ocular movements and fundus examination was normal. There was no H/o developmental delay but his IQ was subnormal with a very poor handwriting.

MRI brain showed typical molar tooth sign with elongated superior cerebellar peduncles, hypoplastic vermis, both cerebellar hemispheres were also hypoplastic with prominent fourth ventricle and cisterna magna.[Figure1] His EEG, ECG, X ray chest and USG abdomen all were within normal limits. His ESR, Renal function tests, Liver function tests, thyroid profile, Urine examination all were within normal limits. However CBC showed mild anemia with Hb 9.8 and MCV 60.9 mm³. His ocular examination was within normal limits. Pulmonary function tests showed FVC only 10-15 ml which was either due to noncoordination, weakness and hypotonia of muscles or due to poor understanding of procedure due to subnormal IQ, or both. He has an elder sister aged 15, apparently normal, however mother had one abortion at 4 months of gestation,

He was advised physiotherapy, treatment of anemia, general support and help in education, periodic reevaluation and genetic counselling.

Family history revealed, Father Aged 38 was presently confined to bed with a progressive illness starting at about age of 18. Mother got worried when

child started showing similar symptoms of illness as his father had in the beginning of his illness. Father had slowly deteriorated, remained undiagnosed and is now confined to bed. Father's MRI Brain also showed Molar tooth sign and similar features suggestive of a diagnosis of JS in him. [Figure2]

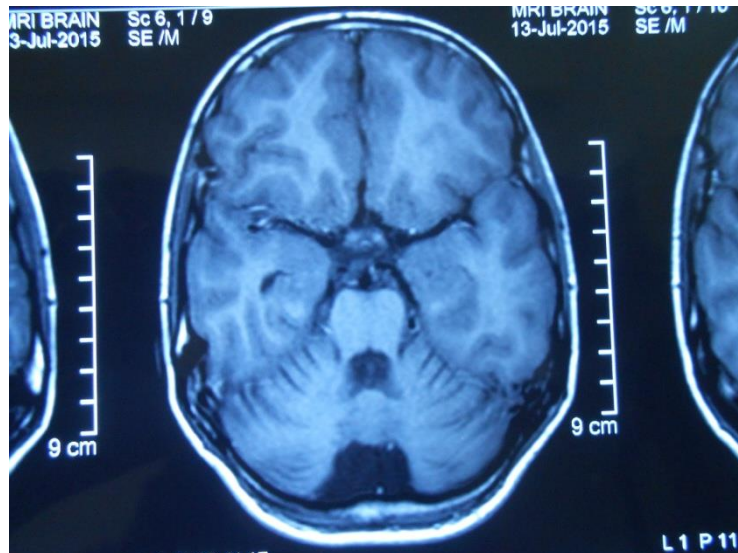


Figure 1 - Son – T2 W axial MRI of brain showing elongated superior cerebellar peduncles (Molar Tooth sign) with vermin hypoplasia

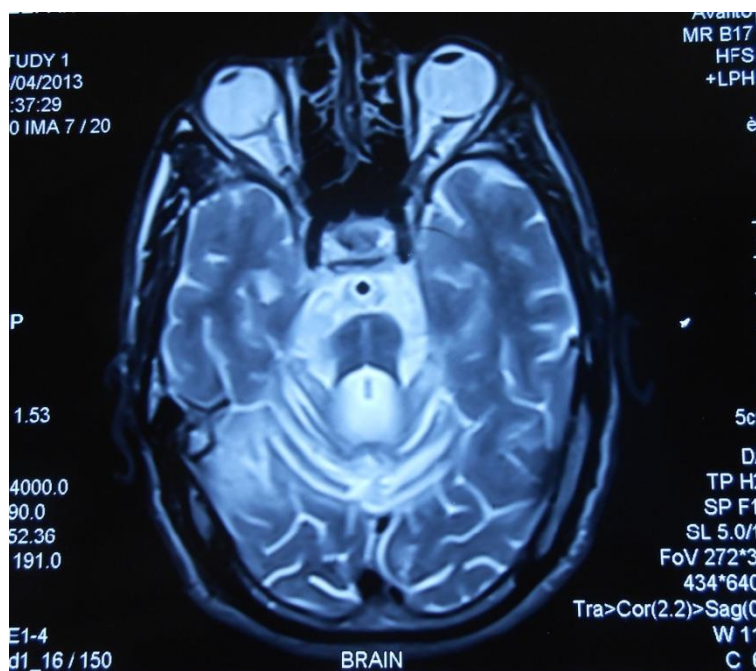


Fig-2 -Father – showing similar findings



Fig-3



Fig-4

DISCUSSION:

Joubert syndrome was earliest reported by Joubert *et al.*; in 1969 [6], however the name was suggested by Boltshauser in 1978 citing his earlier article hence it is also known as Joubert-Boltshauser syndrome [7]. When syndrome is associated with other system involvement it is called Joubert syndrome and related disorders (JSRD).

Signs and symptoms vary among individuals, and also between affected members of the same family. Clinically and genetically it is a heterogeneous group of disorder characterized by hypoplasia of cerebellar vermis with a typical Molar tooth sign visible in

neuroimaging (magnetic resonance Imaging) along with neurological symptoms forming the criteria for diagnosis. Marie *et al.*; reviewed clinical features and suggested distinctive facial features also as broad forehead, arched eyebrows, droopy eyelids, widely spaced eyes, low set ears and triangle shaped mouth [8]. Our case also showed somewhat similar appearance but not clearly. (Figure 4)

Joubert syndrome has a variable presentation and full spectrum of symptoms and signs have not been fully described yet. It may present in neonatal period with breathing dysregulation and episodes of fast or slow breathing. 10 genes have been associated with this

disorder AH1, ARL13B, CC2D2A, CEP 290 ,INPP5E ,NPHP1, OFD1, RPGR1L,TMEM216,TMEM 67 but in 50% of cases genes have not been identified.OMIM classifies them from JBTS1 to JBTS 22 along with different gene mutations. We could not do gene study as it was neither available at our place nor affordable by parents. Our case had typical features of classical pure Joubert syndrome. Father also has similar features and was diagnosed as a case of pure Joubert syndrome after son was diagnosed. Since available treatment for JS till now is only symptomatic and supportive, the interventions made were in form of physiotherapy, genetic counselling, breathing exercises, antioxidants, multivitamins and treatment of anemia.

CONCLUSION:

Early recognition of disease and genetic counselling is needed for preventing recurrence in family. Symptoms were noticed as late as 12 years, which is rather unusual but goes in favor of wide variability in presentation. As father remained undiagnosed, all cases of hypotonia and ataxia should undergo MRI and radiologists should specially look for Molar Tooth sign in such cases .The disorder might be underreported so far where as for better understanding of the disease and future hope case reports are necessary [9].

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