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JOUBERT SYNDROME AND RELATED DISORDERS - RENAL MANIFESTATIONS , NEUROLOGICAL AND SKELETAL CHANGES : A CASE REPORT

Radiodiagnosis

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ABSTRACT

Joubert syndrome [JS] is an autosomal recessive neurodevelopmental disorder involving the cerebellar vermis and brainstem. Isolated Joubert syndrome is seldom noted as compared to Joubert syndrome and related disorders [JSRD]. We report a rare case of renal rickets as a complication of Joubert syndrome and related disorders [occulo renal phenotype]. Jouberts syndrome with occulo renal defects and oro facial digital defects were diagnosed and confirmed by radiological investigations [MRI,USG,X-RAY]

KEYWORDS

Joubert syndrome [JS] , joubert syndrome and related disorders [JSRD], Molar tooth sign [MTS], Rickets , Nephronophthisis.

INTRODUCTION

Joubert syndrome [JS] is an autosomal recessive disorder that presents clinically with developmental delay and hypotonia[1]. Other conditions may also be associated with JS and referred to as joubert syndrome and related disorders [JSRD] [2,3]. It is often difficult to diagnose this entity clinically due to its variable phenotypes. The diagnosis is seldom made for several years after birth. It is diagnosed on MRI with its characteristic molar tooth sign, midbrain-hindbrain malformation[4]. It is often associated with multi organ involvement, predominantly retinal dystrophy and other ocular pathologies, polydactyly, renal diseases and hepatic fibrosis. Jouberts related renal rickets is one of the still rarer entity complicating the presentation, thus should be sought out for with necessary investigations in order to provide treatment.

CASE REPORT

Twelve year old male child ,born of second degree consanguineous marriage, came with complaints of inability to walk for 2 months and one episode of general tonic clonic seizure lasting 5 mins. Patient was born at term after an uneventful pregnancy and post natal events were insignificant. However he experiences global developmental delay [head control at the age of 3, standing and walking at the age of four. Fine motor skills till date includes writing numbers. Language skills-disyllable].

On examination, he was alert. Presence of widened wrists, polydactyly, knock knees and flat foot was noted . The child was severely malnourished with body mass index of 11.3. His height [115cm] and weight [15kg] were retarded [<3rd percentile]. Central nervous system examination revealed non paralytic convergent squint and intermittent nystagmus. Cranial nerves were normal. The tone of both lower limbs were increased. Power of bilateral lower limbs was 4/5. Left lower limb reflexes were sluggish. However rest of the central nervous system examination was unremarkable. His vitals were normal and rest of the systemic examination were unremarkable.

Laboratory investigations showed serum creatinine of 3.7, Calcium-6.7, Phosphate 5.7, Alkaline phosphatase- 408. Ultrasound abdomen [Figure-1] revealed bilateral increased renal cortical echoes, with poor cortico-medullary differentiation, consistent with chronic kidney disease of nephronophthisis. X-ray of the wrist showed diffuse bone rarefaction with polydactyly and irregular ulnar and radial metaphysis and delayed ossification [Figure 2]

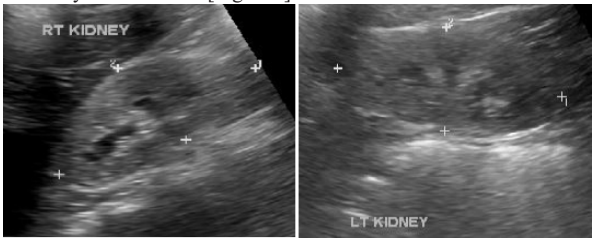

Figure 1- USG B mode of right kidney and left kidney respectively, shows increased renal cortical echoes, with poor cortico-medullary differentiation, consistent with chronic kidney disease of nephronophthisis.

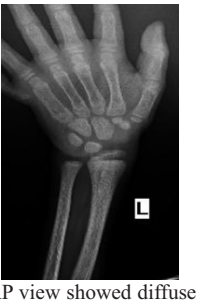

Figure 2- X-ray wrist AP view showed diffuse bone rarefaction with polydactyly and irregular ulnar and radial metaphysis and delayed ossification

MRI brain in a 1.5 tesla GE machine with multiplanar T1, T2, FLAIR and diffusion sequences were performed. The findings revealed thick superior cerebellar peduncle, elongated and abnormally oriented perpendicular to the dorsum of the pons. [Figure 3]The above finding in concordance with the deep interpedencular cistern, elongation and thinning of the isthmus gives rise to the 'molar tooth ' appearance. Moderate dilatation of the 4th ventricle with a bat wing configuration is also noted. The cerebellar vermis was aplastic. Rest of the cerebellum and ventricular system appears normal.

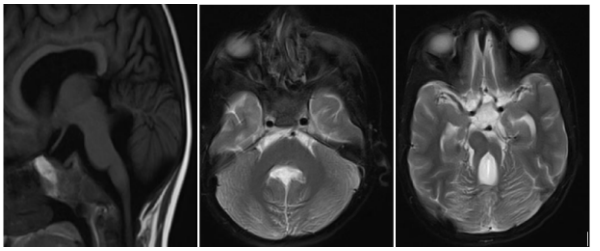

Figure 3- A, T1-weighted sagittal MRI depicting thick superior cerebellar peduncle oriented perpendicular to the posterior aspect of the brain stem. Dilated fourth ventricle with concavity of the roof .

B, Section of axial T2-weighted MRI depicting the classical bat-wing /umbrella sign.

C, Section of axial T2-weighted MRI showing molar tooth sign.

DISCUSSION :

Jouberts syndrome is an autosomal recessive disorder characterized by hypotonia progressing into ataxia and developmental delay, altered respiratory pattern, abnormal ocular movements and intellectual

disability [5]. Due to the absence of biochemical or genetic marker for Joubert syndrome and the fact that the phenotypes are variable, one cannot diagnose the exact type of Joubert syndrome related disorder [6, 7,8]. In addition to the molar tooth configuration, Joubert syndrome is further classified as pure Joubert syndrome, Joubert syndrome with ocular defect [JS-O], Joubert syndrome with renal disease [JS-R], Joubert syndrome with occulo-renal defects [JS-OR], Joubert syndrome with hepatic defects [JS-H], Joubert syndrome with oro-fascio- digital defects [JS-OFD] [9].

A diagnosis of JSRD should be suspected in all infants with the above mentioned clinical features and MRI brain is mandatory for the basis of detection of "molar tooth sign" [deep posterior interpedencular fossa, prominent and thickened superior cerebellar peduncle and vermian hypoplasia/dysplasia. Other neuroimaging features of JS include - deep interpedencular cistern, narrow ponto-mesenchephalic junction [isthmus], lack of decussation of superior cerebellar peduncles, dilated and rostrally deviated fourth ventricle giving a "bat wing " appearance[10], dysplastic vermis, thick vertical superior cerebellar peduncles, wide foramen of magendie. The brainstem and upper cervical spinal cord tends to be small. Once the diagnosis of JSRD has been made, a diagnostic protocol to assess the possible multi organ involvement must be speculated.

A noteworthy variant of Jouberts syndrome is one as observed in our case with overlap of the clinical subtypes of the Jouberts syndrome. Our patient presented with a spectra of JS-OR and JS-OFD [Renal defects associated with oro-facial digital defects]. [11-14]

Renal disease affects approximately 25% of the patients with JSRD, presenting as Nephronophthisis (NPHP) that constitutes to the most common genetic cause for end-stage kidney disease (ESKD) in the first 2 decades of life, requiring dialysis or kidney transplantation. Initial symptoms are relatively mild consisting of anemia, polydipsia, polyuria and secondary enuresis [15]. An elevated serum creatinine is noted at an average in the first decade, before ESKD invariably develops within a few years. Ultrasound reveals increased echogenicity. In the second decade, cysts appear at the cortico medullary junction within kidneys of normal or slightly reduced size.

Chronic kidney disease results in hypocalcemia due to the inability of the damaged kidney to convert vitamin D3 to calcitrol (the active form)and phosphate retention (hyperphosphatemia) giving rise to renal rickets as noted in our case, thus complicating the preexisting pure Joubert syndrome features.

CONCLUSION :

Although a rare cause of developmental delay and hypotonia in children, Jouberts syndrome must be suspected and necessary investigations should be timely taken. Once the diagnosis of Joubert syndrome has been made, a diagnostic protocol to assess the possible multi organ involvement must be speculated in order to estimate the course of systemic manifestations and provide adequate treatment for the same.

CONFLICT OF INTEREST : None

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