CASE REPORT

Joubert Syndrome with a Rare Finding of Pathological Mandibular Angle Fracture

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Abstract:

Joubert Syndrome (JS) is a rare congenital condition first reported by French Neurologist Marie Joubert in 1969 which shows multi-organ manifestations including developmental, neurological, renal, hepatic, ocular and orofacial abnormalities. This condition also shows a unique neuro-radiological imaging feature "Molar Tooth Sign" (MTS) in MRI. We report a case of a young boy of consanguineous parents who presented to the dental department with some unique orofacial features along with a discussion on the various general, orofacial, and imaging features and management of this condition.

Keywords: Tongue hamartomas, Joubert syndrome, Pathologic fracture, Ciliopathies, Polydactyly, Syndactyly, Nasal Bridge, Hypertelorism

Introduction:

Joubert Syndrome (JS) is a rare congenital condition first reported by a French Neurologist Marie Joubert in 1969 [1]. It has multi-organ manifestations, developmental, neurological, renal, hepatic, ocular, and orofacial abnormalities [2]. The true prevalence is 1 per 1, 00,000 live births while an estimated prevalence is around 1 per 2, 58,000 livebirths [3]. It is predominantly an autosomal recessive condition and strongly linked to consanguineous marriage [3]. A unique type of cerebellar and brainstem malformation affecting the brain exhibiting the "Molar Tooth Sign" (MTS) upon imaging is pathognomonic of this condition [1, 4]. This disorder affects mainly the normal functioning of cilium. The primary cilium has been identified as a crucial regulator of a variety of cell biological processes, from development to homeostasis to cancer progression [2]. This condition has a variable phenotypic presentation which makes it relatively challenging to diagnose. The current average age of diagnosis is therefore around 33 months [1]. So far, about 200 cases have been reported in the medical literature but very few in the dental literature. We report a case of a young boy of consanguineous parents who presented to the Dental Department with some unique orofacial features along with a discussion on the various general, orofacial, and imaging features and management of this condition.

Case Report:

A 12-year-old boy visited the Department of Oral Medicine and Radiology of Manipal College of Dental Sciences with a complaint of multiple nodules present on his tongue which made his chewing difficult (Fig. 1). He had a positive family history of parents with consanguineous marriage. There was no prenatal, perinatal and postnatal significant history except for mild breathing difficulty and delay in milestones. He was not thoroughly assessed for his IQ and was not attending any schools. On general examination, he had short stature with a height of 144 cm and 45 kg weight and walked with a waddling gait. His

general features revealed his short stubby hands with characteristic polydactyly with polydactyly and syndactyly in the toes (Figs. 2 and 3). Facial feature showed a noticeable depressed nasal bridge, thick eyebrows, and thick lower lips (Fig. 4).

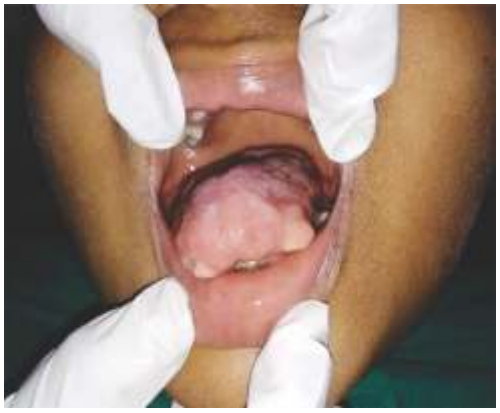
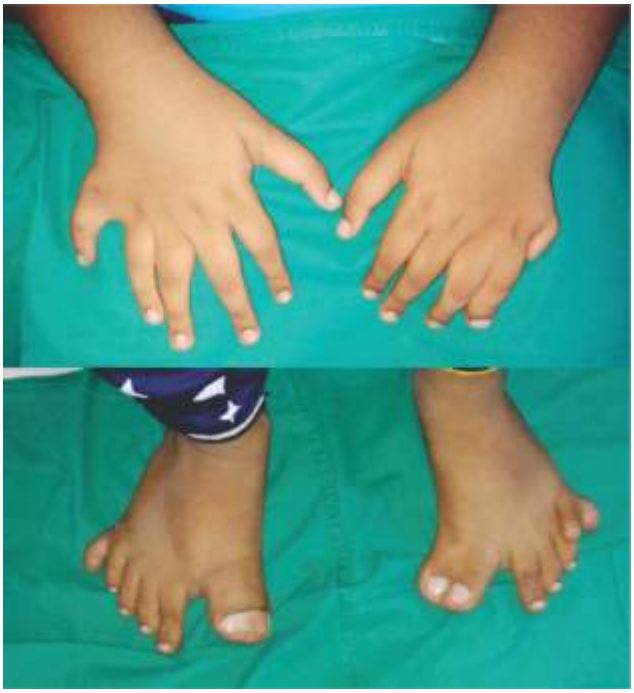


Fig. 1: Multiple Hamartomas on the Tongue



Figs. 2 and 3: Poly and Syndactyly of the Fingers of the Hand and Poly and Syndactyly of the Fingers of the Feet

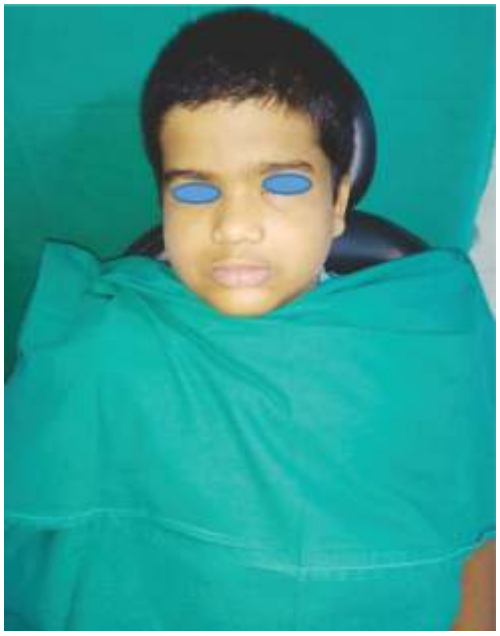


Fig. 4: Facial Profile Picture of the Patient with Flat Nasal Bridge

On intraoral examination, he presented with multiple fibrous nodules on the tip and lateral border of the tongue, which on palpation were non tender and soft in consistency. He had poor oral hygiene and marginal gingivitis. The dental findings revealed the absence of left and right maxillary canines, although remaining full complement of permanent teeth was present as per his chronological age. Gross carious destruction of left maxillary central incisor and right mandibular canine and left mandibular first molar was noted (Fig. 5). A panoramic radiograph taken to see the position of the impacted canines revealed a unique radiographic appearance (Fig. 6). His mandible exhibited a sparse trabecular pattern with generalized rarefaction and loss of cortical thickening resulting in a ground glass and osteoporotic appearance. Additional unexpected finding was the presence of a well-defined oblique linear radiolucency seen in the posterior body of

the mandible close to angle of the right mandible suggestive of a pathological fracture. Almost all his teeth had open apex. Yet the patient was completely unaware and also presented with no clinical signs and symptoms of a fracture or difficulty in opening the mouth. On further questioning about his general health status, although parents denied any systemic health problem, they furnished MRI images which showed a characteristic molar tooth sign (Fig. 7). Hence, considering the clinical picture and the neuroradiological findings a diagnosis of tongue hamartomas secondary to underlying Joubert syndrome was derived. The patient was referred to a pedodontist for further management, eventually the patient was lost to follow up.

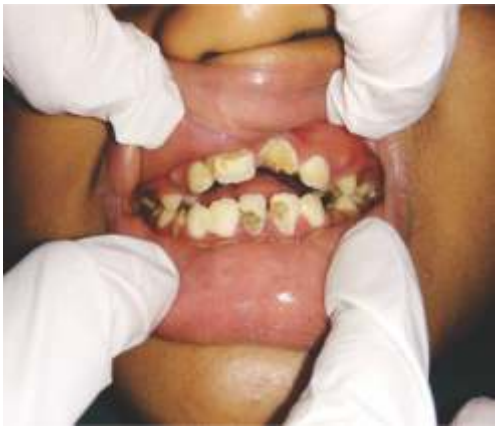


Fig. 5: Intraoral Examination showing Multiple Carious Teeth

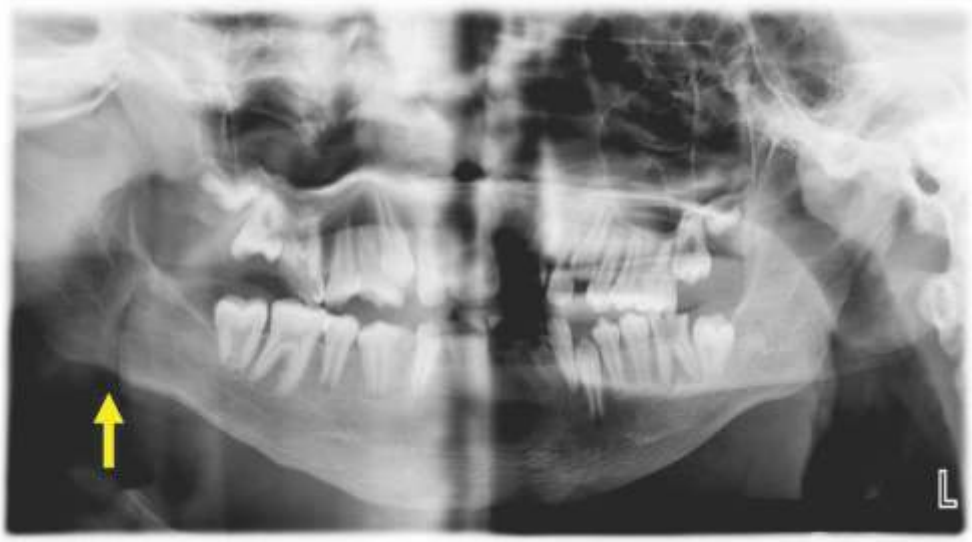


Fig. 6: Panoramic Image with Osteoporotic Appearance with Pathological Fracture

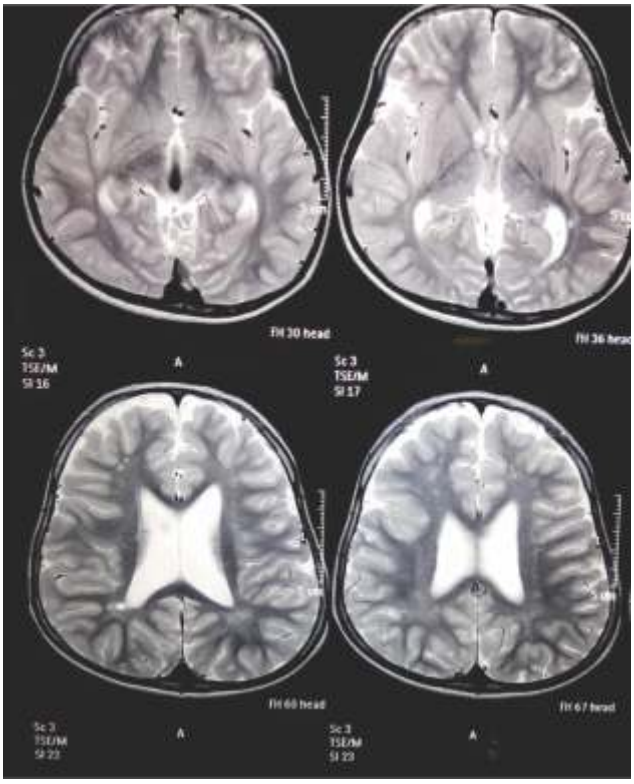


Fig. 7: MRI Sections showing Molar Tooth Sign

Discussion:

Joubert syndrome also known as Joubert-Boltshauser syndrome [OMIM#213300], was first described in 1969 in four siblings with hypotonia, ataxia, mental retardation, oculomotorapraxia, and neonatal breathing dysregulation [6, 2]. The syndrome is seen more prevalent in Ashkenazi Jews and Hutterites. Altogether 21 causative genes have been identified. These genes code for mutant proteins resulting in the defective structure of cilia, resulting in the various congenital manifestations, hence this condition is also termed as ciliopathies. The pathognomonic neuroradiological imaging feature of MTS is also shared by other conditions and they are called Joubert syndrome-related disorders [7]. Joubert syndrome - related disorders are phenotypically classified as Pure JS; JS with ocular defects; JS with renal defects; JS with oculo-renal defects; JS with hepatic defects; JS with orofacial-digital defects [5].

A patient with pure Joubert syndrome displays the pathognomonic MTS along with hypotonia/ataxia, developmental delay with intellectual disability, irregular breathing, and abnormal eye movements as the cardinal clinical manifestations. Although respiratory abnormalities are considered a classic hallmark of JS, they are reported in only up to 71% of patients and, thus, are not a consistent finding [7]. JSRD are clinically heterogeneous and exhibit neurological signs combined with variable multi-organ involvement like retina, renal, and liver involvement [2]. The retina is one of the most commonly involved organs in JSRD, where the patient may present with retinal dystrophy, associated with progressive degeneration of photoreceptor cells, colobomas affecting the unilateral or bilateral posterior segment of the eye, nystagmus, strabismus, ptosis, and ocular motor apraxia [3]. About 25% of patients with JSRD are also reported to be affected by renal disorders. Skeletal features like polydactyly are reported in about 8-16% of patients with JSRD. The most common form is postaxial polydactyly, variably affecting hands and feet [5]. Our patient also presented with short, stubby hands with polydactyly of fingers and poly plus syndactyly in the toes. The association of JS with polydactyly and oral defects defines a condition known as orofaciodigital type VI or Varadi-Papp syndrome. Congenital heart defects are not typically associated with JSRD but have been reported occasionally [8].

Table 1: Orofacial Manifestations of Joubert Syndrome

Soft tissue changes	Hard tissue changes
Bifid tongue Lobulated tongue / tongue with fibromas / hamartomas Cleft lip Additional frenula Notched upper lip Flat/broad nasal bridge	Micrognathia High arched palate Cleft Palate High risk for dental caries Hypertelorism Frontal bossing

In our case the child presented with short stature of 144 cm (<50th percentile) and a weight of 59.5 (>95th percentile) for his age. An abnormal gait is a regular but non-specific finding and the child in our case walked with a waddling gait. Orofacial features like cleft lip and palate are also associated with JS [9]. A flattened nasal bridge and prominent supraorbital ridge were seen which are common features reported in this syndrome. Table 1 enlists the various orofacial manifestations reported in the literature [9, 2, 8].

Along with anterior open bite and malocclusion, our patient also presented with multiple nodules on the tongue, which was firm, non-tender on palpation. Similar findings have been reported earlier in the literature [8, 5].

The uniqueness of the case was the presence of the pathologic fracture of the angle of the mandible and a ground glass osteoporotic mandible which has not been reported till date in the literature. Apart from the conventional radiographic imaging, the brain imaging in patients with Joubert syndrome reveals a pathognomonic neuro-radiological imaging characteristic "Molar Tooth Sign" which refers to the shape formed by a midbrain-hindbrain malformation [1]. It is formed due to hypo-dysplasia of the cerebellar vermis, abnormally deep interpeduncular fossa at the level of the isthmus and upper pons, and horizontal, thickened, and elongated superior cerebellar peduncles [1]. A similar radiographic feature was noted in our patient.

Recognizing Joubert syndrome at an early stage is crucial as it decides the outcome of the condition. A fetal MRI in the 5th month of intrauterine life has shown to be an antenatal diagnostic method [9-10]. Dental considerations in these patients include initiating early preventive methods, with periodic oral hygiene counselling to the patient as well as the patient's parents or caregivers, behaviour management during or before dental treatment, regular oral prophylaxis as lack of dexterity for efficient brushing might be present in patients and thorough airway assessment before any invasive dental treatment under anaesthesia [9, 11].

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How to cite this article:

Patil V, Acharya S, Proothi C, Tripathi P, Tamrakar A, Vineetha R. Joubert Syndrome with a Rare Finding of Pathological Mandibular Angle Fracture. *J Krishna Inst Med Sci Univ* 2021; 10(3): 88-93.

Submitted: *10-Feb-2021* ***Accepted:*** *01-Jun-2021* ***Published:*** *01-Jul-2021*