Joubert Plus Syndrome with Self-Mutilation: A Case report

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Background: *Joubert syndrome is a very rare condition with dismal prognosis. It is characterized by several abnormalities including molar tooth sign on MRI. When coupled with mega cisterna magna- a feature of the Dandy Walker syndrome- it is categorized as Joubert plus syndrome.* ***Case report:*** *A 16 month old male child with Joubert syndrome was referred to the Pediatric Dentistry Department Clinic, Faculty of Dentistry Alexandria University, complaining of severe tongue and lower lip injury due to self-mutilation. He required multiple teeth extractions under general anesthesia to prevent further tongue and lip mutilation.* ***Conclusion:*** *Joubert plus syndrome is a very rare occurring condition. Because self-mutilation is sometimes fatal, a treatment plan tailored to each patient's need is mandatory. A multidisciplinary approach is recommended.*

Key words: *Joubert syndrome, Molar tooth sign, MRI, Self-mutilation*

INTRODUCTION

Joubert syndrome (JS) is a rare autosomal or x-linked recessive disorder affecting cerebellar vermis and brain stem that was first identified in 1969 [1,2].This entity is underreported with a prevalence of less than 1 in 100,000. [3,4] Only about 200 cases have been reported worldwide.[5] Its main radiographic feature is a brain abnormality called "molar tooth sign" which could be diagnosed on MRI.[6,7] (Fig 1)

It is characterized by hypotonia, ataxia, and episodic tachypnea alternating with apnea during early infancy, ocular abnormalities, delayed development and cognitive impairment. Associated findings may include retinal dystrophy, renal cystic disease and polydactyly. [8] Self-mutilation is an uncommon finding in JS.

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Case report

A 16 month old male child, product of a healthy consanguineous marriage presented to the Pediatric Dentistry Department Clinic, Faculty of Dentistry Alexandria University, complaining of severe tongue and lower lip injury due to self-mutilation.

The child was delivered at term by Cesarean Section because of fetal distress. There was history of seizures, abnormal breathing pattern, difficulty in feeding and swallowing. He was intubated for 7 days in order to facilitate feeding.

At 1 month, he was hospitalized because of reduction in nursing abilities, anemia and urinary tract infection. He received blood transfusion twice.

Intraoral examination revealed severe lower lip injury with heavy candida albicans infection on the dorsum of the abnormally eroded tongue which was diagnosed by typical raised furry white patches (Fig 2), which were easily, removed leaving raw, bleeding surface. The primary maxillary and mandibular incisors and canines were erupted, in addition to partial eruption of primary first molars. The teeth were normal in size and shape and eruption followed the normal chronology. Moreover they were free of any carious lesion. The patient has been on intermittent antibiotic therapy, following repeated fever episodes.

The patient was referred to the Human Genetics Department, Institute of Medical Research, Alexandria University. Medical examination revealed tachypnea, hypotonea with lack of neck support, brachycephaly with bitemporal narrowing, frontal bossing, flat supraorbital ridges, prominent glabella, squint, nystagmus, epicanthic folds, ocular hypertelorism, slanting up of palpebral fissures, scanty arched eyebrows,

prominent nose, triangular large mouth, thin tented upper lip, long oval asymmetric face, bilateral post axial polydactyly of hands (fig 3), hyperextensible fingers and kyphosis.

Laboratory investigations revealed normal: karyotype, liver and kidney functions, thyroid functions, and unremarkable echocardiogram.

Full term for MRI findings included: Mildly hypoplastic remnant, suspected vermian cleft and prominent superior cerebellar peduncles giving "Molar tooth appearance", large mega cisterna magna, multiple nodular gray matter along the sub-ependymal surface of both lateral ventricles and nodular heterotopia.

According to the previous findings the case was diagnosed as Joubert plus syndrome.

Management

Written consent was obtained from the parent after explaining the full details of the treatment procedure.

The patient presented with antibiotic intake that was prescribed elsewhere, this was discontinued upon examination. Mycostatin at a dose of 2 ml 200,000 units 4 times daily was prescribed to control candidal infection. When infection improved, upper and lower alginate impressions were obtained. An appliance that would hinder the patient from tongue and/or lower lip biting was designed. This comprised upper and lower soft rubber bite blocks attached posteriorly, where a window was kept open anteriorly to allow breathing [9] For added retention straps were fitted to be tied around the ears. (Fig 4)

The appliance was positively tolerated for two days, with starting healing of the lower lip, after which the parents reported that the child started to displace the appliance by continuous tongue movements. They presented a few days later with a detached section of the tongue and stated that he inserted the tongue below the lower border of the appliance with continuous biting which caused profuse bleeding. The detached segment was submitted to histopathologic examination, that revealed capillary hemangioma with polypoid formation.

The decision was to extract all the teeth to prevent further tongue and lip mutilation. After consultation with the anesthesiology team the child was admitted to hospital where general anesthesia was used to perform extractions. Induction was performed with propofol 3mg/kg followed by trachium .3mg/kg for intubation. Anesthesia was maintained using sevoflurane, with ventilation controlled to achieve an endtidal CO_2 partial pressure of 40 mm Hg. Analgesia was achieved with local injection of 2ml Mepicane 2% with adrenaline 1:100,000. All erupted teeth were extracted and the gingiva sutured. The surgical procedure lasted 15 minutes after which atropine .02mg/kg and neostigmine .05mg/kg were administered. Extubation was performed after adequate spontaneous ventilation, and recovery was uneventful. The patient was transferred to the intensive care unit for observation for twelve hours and was dismissed at the same day.

Fig 1: molar tooth sign in MRI

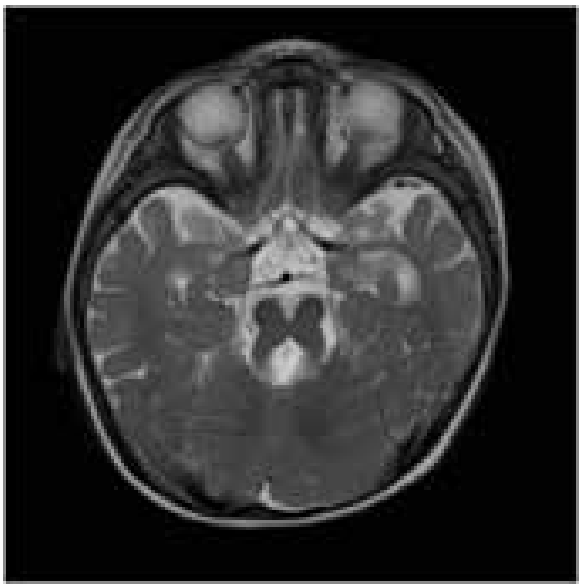


Fig 2: lower lip injury with heavy candida infection of the oral cavity

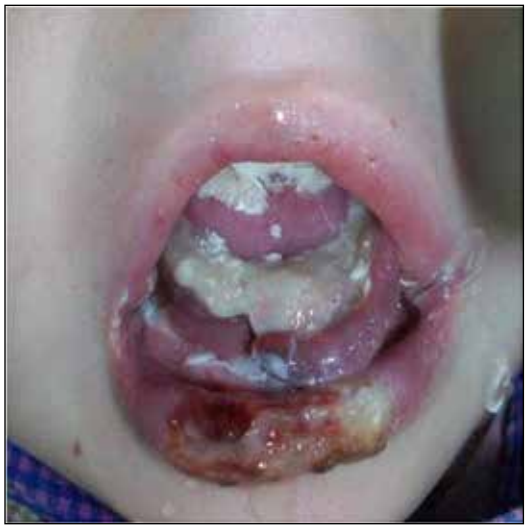


Fig 3: Polydactyly of both hands

DISCUSSION

Joubert syndrome is a rare autosomal recessive disorder with an onset early in the neonatal period and a very poor prognosis. [10)] The clinical features are usually hypotonia, ataxia, severe mental retardation and abnormal ocular movements. Autistic features have also been reported in JS. [11,12] It is characterized by pathologic findings of cerebellar vermian hypoplasia with a midline cleft. The underlying abnormality in this syndrome may be an inability of the posterior fossa fiber tracts to cross the midline, although the cause for this is not known.[5] Vermian hypoplasia and abnormalities of the pontomesencephalic junction are the distinguishing features that lead to the diagnosis of JS. [13,14]. Reported prevalence of some of the associated findings such as coloboma of retina and retinal dystrophy was 50%, renal cystic disease 30% and polydactyly 15%. The molar tooth sign was identified in 85% of patients with JS and has been reported to be pathognomonic of this disorder.[15] Kendall *et al* [2] reviewed the features of 16 children with JS and found them developmentally delayed, many had neonatal breathing abnormalities, congenital retinal dystrophy and supranuclear ocular motor abnormalities. Romano *et al* [16] described 13 patients with JS and emphasized the molar tooth sign. Quisling *el al* [17] classified patients with large mega cisterna magna in addition to the molar tooth sign as Joubert Plus syndrome.

Fig 4: Protective appliance

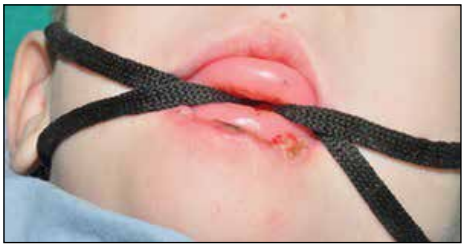
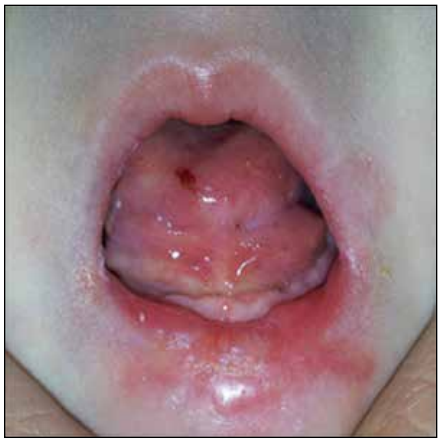


Fig 5: Healing after extraction



Treatment is usually symptomatic and supportive, including physiotherapy, and occupational and speech therapy. The prognosis of these patients is poor, with a survival rate of only 50%.

The episodic tachypnea/apnea presents problems during and after anesthesia.[3] The respiratory abnormalities are likely due to hypoplasia of the cerebellar vermis and brainstem. [19] Although the medical aspects of nearly one hundred patients with JS have been reviewed,[6] the management of anesthesia in these patients has been described in only a few reports. [10, 20] The apparent high sensitivity of children with JS to the respiratory depressant effects of anesthetic agents, including nitrous oxide and opioids, may be explained by the abnormal function of the respiratory control centers in the hypoplastic cerebellum or adjacent brainstem. For this reason, the use of regional anesthesia to avoid using opioids would be much favored. In the present case, the use of general anesthesia to perform multiple tooth extraction was deemed necessary in order to prevent severe effects of mutilation in view of the ineffectiveness of the guard appliance that was custom fabricated and the repeated candida infection. Following extraction, the lip and tongue showed healing, with scar tissue formation along the whole length of the lower lip and the tongue. (Fig 5)

It has been stated that as the child grows older, the pattern of breathing may improve.[10] In the present case, the patient's breathing improved when he was around 6 months according to the parents' report. General anesthesia was well tolerated and recovery occurred with no complications neither during the postoperative observation period nor later on.

Self-mutilation is not a common feature of JS, with scarce information in the literature. Nevertheless, Srour [21] reported a case of a French Canadian who was diagnosed JS and had significant aggressive and self-mutilating behavior consisting of head banging and biting that required treatment with antipsychotic agents, mouth guard and protective helmet.

In the present case, the patient inflicted serious injury to his lower lip and tongue despite the antipsychotic drugs that were used to relieve the condition. Appropriate management is difficult, especially when the mutilation is particularly severe. The anterior part of the tongue to the level of the lingual frenum was totally detached in spite of the construction of a protective appliance. Serious injury of that severity could not be understood beyond the context of impaired sensation. Impaired sensation with self-mutilating behavior has been reported in other syndromes as congenital insensitivity to pain with anhidrosis (CIPA) and Lesch–Nyhan Syndrome. [22- 24] Neves *et al* [23] reported treating a two years old patient with CIPA by extraction of all erupted teeth to prevent further self-induced injuries.

The fact that the parents are first cousins supports the autosomal recessive inheritance mode. They were offered the proper counseling since the recurrence rate is 25 %. [5]

Prenatal diagnosis of at risk pregnancies is now possible using serial ultrasounds combined with fetal MRI at 20-24weeks of gestation.[18] Since there is no definitive

treatment for these cases, the only prevention would be through awareness, proper genetic counseling and intra-uterine diagnosis.

CONCLUSION

Joubert plus syndrome is a very rare occurring condition. Because self-mutilation is sometimes fatal, a treatment plan tailored to each patient's need is mandatory. A multidisciplinary approach is recommended.

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