DOI: 10.7860/JCDR/2023/58913.17383

Case Report

Dentistry Section

Full Mouth Rehabilitation of a Child with Aicardia-Goutières: A Rare Syndrome

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ABSTRACT

Aicardi-Goutières Syndrome (AGS) is a rare genetic disorder with autosomal recessive inheritance. AGS is characterised by an early-onset encephalopathy that usually, but not always, results in severe intellectual and physical disability. Involuntary muscular spasms between the ages of four months and four years are the typical starting point for Aicardi syndrome. Hepatosplenomegaly, increased liver enzymes, thrombocytopenia, and abnormal neurologic signs in a subgroup of AGS children at birth strongly imply congenital infection. Agenesis of the corpus callosum, chorioretinal lacunae, and seizures are all symptoms of Aicardi syndrome. They frequently exhibit the subacute onset of a severe encephalopathy that is characterised by intense irritability, sporadic sterile pyrexias, loss of abilities, and slowed head growth. In 40% of cases, skin lesions like chilblains can appear on the fingers, toes, and ears. This disease can be diagnosed with Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) scans with the appearance of calcification of the basal ganglia. The associated behavioural challenges with syndromic patients demand pharmacological management of oral rehabilitation. The literature is scarce regarding the oral manifestations of this syndrome. Hence, authors present the successful full-mouth rehabilitation of severe Early Childhood Caries (ECC) in a 3-year-old child with AGS under General Anaesthesia (GA).

Keywords: Behaviour management, Congenital viral infection, Early childhood caries, Mimic of congenital infection, Oral manifestations

CASE REPORT

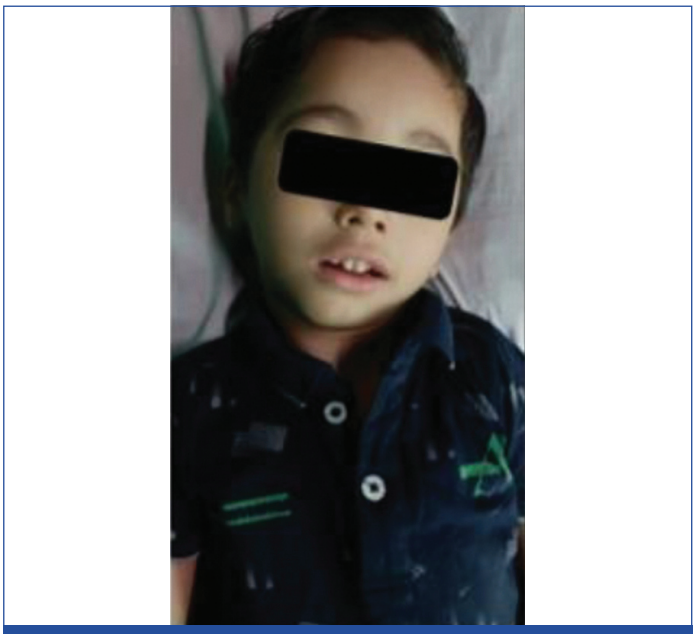
A known case of a 3-year-old male patient with Aicardi-Goutières Syndrome-Type 3 reported with a chief complaint of multiple ulcers who had a history of fever since 15 days. History revealed painful recurrent oral ulcers with a frequency of appearance of two months, for which he was advised multivitamins by his paediatrician.

The prenatal history was non contributing to any genetic disorder. The parent's marriage was third-degree consanguineous marriage. There was no fever or infection, and no drugs were taken by the mother during pregnancy. He has no siblings. Natal history revealed the presence of neonatal jaundice. Postnatal history of febrile seizures at six months of age and was hospitalised for two days for the same. Physical examination revealed dystonia and a squint. The child does not hold his neck and sits with support [Table/Fig-1]. Milestone regression was seen since six months of age. Peripheral spasticity, dystonic posture (especially of the upper limbs), truncal hypotonia, and poor head control are common in those who are affected. Upto 50% of afflicted children report having seizures, however, they are typically manageable [1]. It was the same in the present case characterised by severe neurological symptoms with a high-risk of seizures. The child was on medication (Levipil, Lorazepam, And Pacitane) with regular follow-ups.

The MRI brain, CT brain, and molecular genetics were advised as investigation procedures. MRI Brain showed-diffuse cerebral atrophy for age with cerebral myelination for age, calcific foci in the deep white matter of the left frontal lobe. CT brain showed-multiple calcific areas in bilateral frontoparietal, occipital lobes, and basal ganglia, which appear metabolic generalised cerebral atrophy [1].

With physical examination, clinical examination, and investigations the differential diagnosis was made as follows-

- TORCH [Toxoplasmosis, Others (syphilis, hepatitis B), Rubella, Cytomegalovirus (CMV), and Herpes simplex] congenital infections, Microcephaly-Intracranial Calcification Syndrome (MICS)-mainly the heterogeneous group of diseases.
- Band-like Calcification Polymicrogyria (BLC-PMG; pseudo-TORCH syndrome)-it has observation of polymicrogyria that differentiate from AGS that has never been reported with it.



[Table/Fig-1]: Physical or extraoral photograph.

- Hoyeraal Hreidarsson syndrome (a severe form of dyskeratosis) is associated with pancytopenia while some individual with AGS shows thrombocytopenia that usually resolves in the first few weeks of life.
- Neonatal lupus erythematosus, Cerebroretinal microangiopathy with calcifications and cysts.

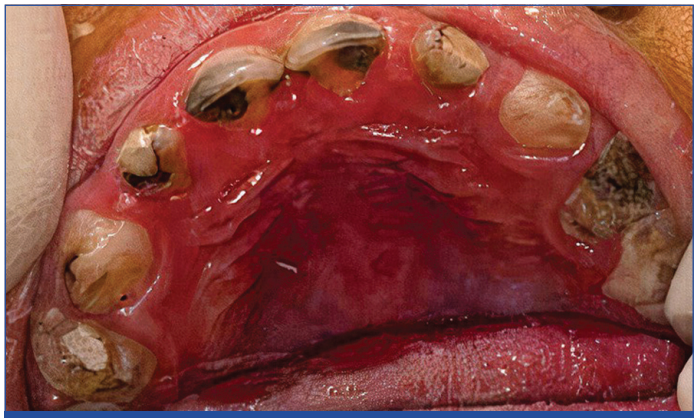
Genetic analysis showed homozygous autosomal recessive chromosome 11 Aicardi-Goutières Syndrome Type 3 [Table/Fig-2]. The final diagnosis was made as generalised cerebral atrophy with AGS-Type 3 with global developmental delay.

On intraoral examination, small multiple ulcers were seen on the lower lip and buccal mucosa, which were diagnosed as multiple aphthous ulcers. Teeth showed debris, plaque accumulation, multiple carious teeth, gingivitis, and overall oral hygiene was poorly maintained.

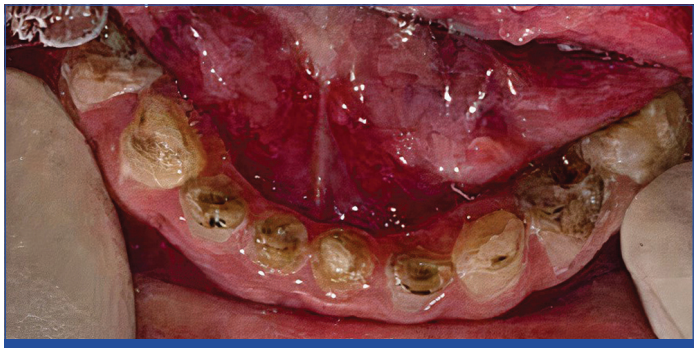
Location	Phenotype	Phenotype MIM number	Inheritance	Phenotype mapping key	Gene/locus	Gene/locus MIM number
11q13.1	Aicardi-Goutières syndrome- type 3	610329	Autosomal Recessive	3	RNASEH2C	610330

[Table/Fig-2]: Phenotype-gene Relationships.

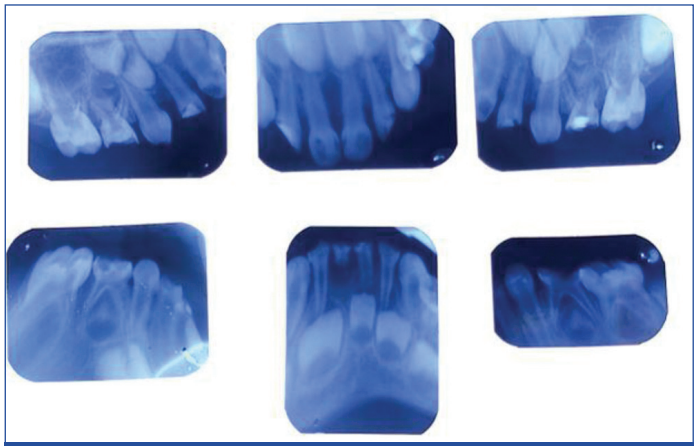
Dental treatment was deferred till the resolution of oral ulcers. Till that time patient was on an antibiotic course, multivitamins, and local application of the topical anaesthetic gel. The child was not responsive to verbal commands and falls in the definitively negative category of Frankel's behaviour rating scale. The preoperative intraoral examination was done by restraining the child. Intraoral examination revealed pulp involvement of 51,52,54,61,62,64,71, 72,74,75,81,82,84 teeth. Dental caries with 55,53,63,65,85. Grade II mobility with 71 [Table/Fig-3,4]. The Intraoral Periapical Radiographs (IOPA) were taken and the final diagnosis of severe ECC was confirmed [Table/Fig-5]. Complete rehabilitation was planned treatment and parental informed consent was obtained for the same.



[Table/Fig-3]: Preoperative intraoral photographs of the upper arch.



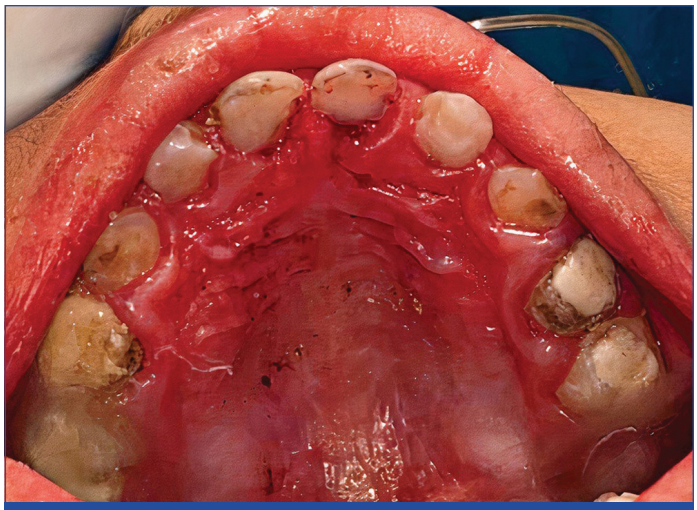
[Table/Fig-4]: Preoperative intraoral photographs of the lower arch.



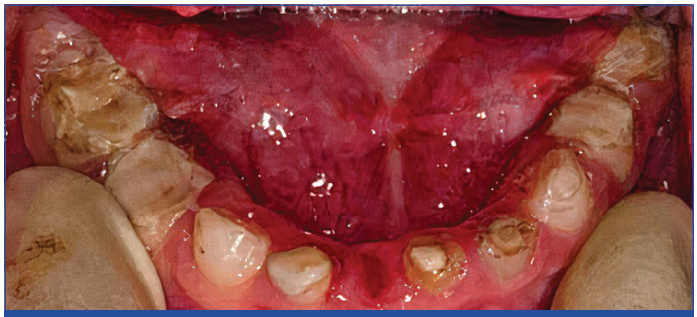
[Table/Fig-5]: Preoperative radiographs.

A Preanaesthetic Check-up (PAC) was performed and categorised in American Society of Anaesthesiologist (ASA) III. The anesthesiologist categorised him under high-risk for general anaesthesia as the child suffers from febrile seizures and severe neurological disorders. Initially, parents were counselled and dietary instructions were given.

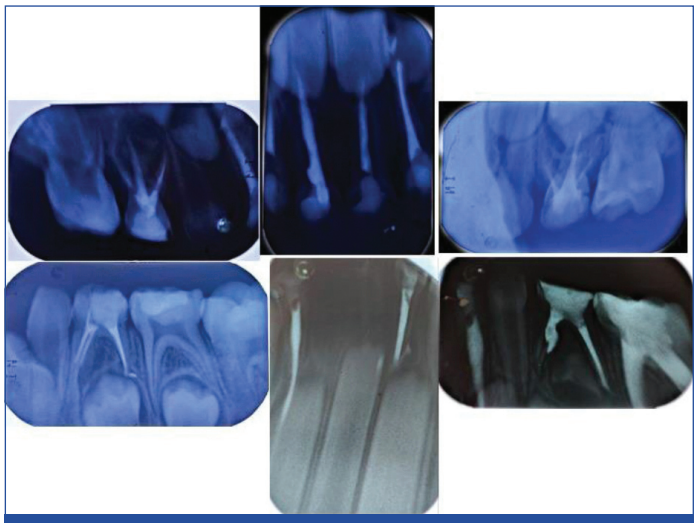
After the due appointment, the patient was admitted to the Bharati Hospital Pune and taken up for full mouth rehabilitation under GA with nasal intubation. In the corrective phase, the treatment of endodontically involved teeth and restoration of teeth were done. Pulpectomies were done with 51,52,54,61,62,64,72,74,75,81, 82,84 teeth followed by composite restoration. The surgical phase consisted of the extraction of unrestorable teeth, 71. Glass ionomer cement (GIC) restorations was done with 55,53,63,65,85 [Table/Fig-6-8]. The child was extubated and shifted to Postanaesthesia Care Unit (PACU) and later shifted to the paediatric ward. After a day, the patient was discharged from the hospital with no swelling, pain, or fever symptoms. Regular follow-up after eight days for the postoperative evaluation was done. Further, a follow-up every three months will be done to evaluate for oral health.



[Table/Fig-6]: Postoperative intraoral photographs of the upper arch.



[Table/Fig-7]: Postoperative intraoral photographs of the lower arch.



[Table/Fig-8]: Postoperative radiographs.

DISCUSSION

Aicardi-Goutières syndrome, a rare syndrome is a disorder that mainly affects the brain, the immune system, and the skin. Most newborns with this syndrome do not show any signs or symptoms of the disorder. However, about 20% are born with a combination of features that include hepatosplenomegaly, elevated blood levels of liver enzymes, thrombocytopenia, and neurological abnormalities. It is sometimes called a "mimic of congenital infection." as it shows similar signs and symptoms to Congenital viral infection [2]. This autosomal recessive disorder is characterised by the onset of encephalopathy in the first year of life following normal early development. Extreme irritability, intermittent unexplained fever, chilblains, progressive microcephaly, stiffness, dystonia, and severe psychomotor retardation are all symptoms of the suffering kid. Similarly, in the present case child is unable to stand, has irritable behaviour, and does not hold the body straight. According to laboratory tests, the cerebral fluid has lymphocytosis and elevated levels of alpha-interferon [3]. The review of the literature shows that it is extremely rare and the exact prevalence of this disorder is unknown. This syndrome can be categorised into type 1 to type 7 [4]. It has been estimated about 300 and 500 cases of Aicardi syndrome reported worldwide inclusive of all types [5] .

The AGS shows two forms: an early-onset and a later-onset. The diagnosis of AGS is established with typical clinical findings and characteristic abnormalities in cranial CT (calcification of the basal ganglia and white matter) and MRI (leukodystrophic changes); AND/OR by identification of one of the following: Biallelic pathogenic variants in ADAR, RNASEH2A, RNASEH2B, RNASEH2C, SAMHD1, or TREX1 [6,7]. AGS3 is caused by a mutation in the RNASEH2C gene which was evident after genetic testing of the child. Wu D et al., reported that the AGS case of a 6-month-old Chinese girl with the novel TREX1 variants lead AGS for the first time [7]. However, as per our literature search, this is the first case report relating to the dental manifestations and management of a child patient with AGS Type 3.

Due to poor oral hygiene, a soft diet, difficulty in chewing and swallowing, and greater usage of sugary oral medications, children with this disorder are more likely to develop oral symptoms such as ECC. Behavioural challenges associated due to mental retardation demands pharmacological management of oral rehabilitation [8].

General anaesthesia was the choice for treating unmanageable children. The great challenge in planning such a patient under GA is the child's fitness and the associated risk. Therefore, assessing medical readiness in such cases is crucial and implementing an appropriate treatment strategy.

CONCLUSION(S)

In Paediatric Dentistry, we often encounter children with special healthcare needs or who suffer from syndromes, which usually seem detached and non communicative. In the present case, there was an urgent need for dental management to improve the child's general health. Hence, pharmacological behaviour management (General Anaesthesia) improved quality, as well as complete oral healthcare in a single visit. Here, a multidisciplinary strategy aids in the child's complete oral rehabilitation as well as long-term success in therapeutic and preventive care.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Jul 07, 2022
- Manual Googling: Aug 09, 2022
- iThenticate Software: Oct 28, 2022 (14%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Jul 06, 2022**
Date of Peer Review: **Aug 10, 2022**
Date of Acceptance: **Oct 29, 2022**
Date of Publishing: **Jan 01, 2023**