Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/15695
DOI URL: http://dx.doi.org/10.21474/IJAR01/15695

RESEARCH ARTICLE

THE COLOBOMAEYE SYNDROME - A RARE CASEREPORT

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Manuscript Info

Manuscript History
Received: 15 September 2022
Final Accepted: 19 October 2022
Published: November 2022

Key words:-
Treacher-Collins, Coloboma, Hypoplasia, TCS- Treacher Collins Syndrome

Abstract

The COLOMBOMA EYE which means a lash less eye becomes one of the striking features of a rare disorder called TREACHER COLLINS SYNDROME. It may be a condition that affects the development of facial bonesand other tissues of the face. This condition features a wide range of signs and symptoms,from hardly perceptible to severe. Treacher Collins syndrome also called as Franceschettisyndrome is an autosomal dominant disorder of craniofacial development with variableexpressivity. Its named after E Treacher Collins who described the essential components ofthe condition in 1900. It is caused by the mutation of particular gene of which 81-90% of cause will be due to the mutation of TCOF1 gene. Incidence of this syndrome is approximately one in fifty thousandlive births and it affects both genders equally. It affects structures which are derivatives of theprimary and second brachial arches. The foremost common manifestations of TCS are theantimongloid slanting of the palpebral fissures, colobomas of the lower eyelid, hypoplasia ofzygoma and mandible; and a spread of ear abnormalities. People with Treacher Collinssyndrome usually have normal intelligence.This article describes clinical and radiographicfeatures of TCS in a 29 yr old male who had reported to the department of Oral Medicineand Radiology with the complaint of forwardly placed upper and lower front teeth since birth.Alsopathogenesis, diagnostic procedure, diagnosis based onscore, management andpreventive aspects are discussed.

Introduction:-

Treacher Collins syndrome (TCS), also called Treacher Collins-Franceschetti syndrome or mandibulofacial dysostosis, is an autosomal dominant disorder affecting the development of structures derived from the first and second brachial arches during early embryonic development.

TCS is characterized by deafness, hypoplasia of facial bones (mandible, maxilla and cheek bone), antimongoloid slant of palpebral fissures, coloboma of the lower lid and bilateral anomalies of auricle. It is a condition in which the cheek bones and jawbones are underdeveloped.

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Thomson was the first to refer to this syndrome in 1846. In 1900, Dr E Treacher Collins, a British ophthalmologist, described two children who had very small cheek bones and notches in their lower eyelids. Therefore, the condition gets its name from him. For unaffected parents with one child with TCS, the chance of giving birth to a second child with the condition is negligible. Adults with TCS have a 50% chance of passing the condition to the offspring. When a parent with TCS passes on the genes, the children may be affected in varying degrees. The degree may be the same as the parent, milder or more severe. There are two possible ways that TCS develops. First, TCS can develop as a new mutation. This means that both parents pass on normal genes to their child. The second way that TCS develops is by inheriting it from one of the parents. The only gene currently known to be associated with TCS is TCOF1 which is mapped to chromosome 5 q31.3-q33.3, encoding a serine/alanine- rich protein, called 'treacle'. There is no preference among genders or races and it consists of autosomal dominant trait of variable expressiveness. Its phenotypical expression probably results from bilateral congenital malformation involving the first and second brachial arches.

Case report

A 26-year-old male patient reported to the Department of Oral Medicine & Radiology, Karpaga Vinayaga Institute of Dental sciences, with a chief complaint of the forwardly placed upper and lower front teeth since birth. He also complained of asymmetry of his face and deafness since birth. Past medical history reveals no history of diabetes mellitus, hypertension, tuberculosis, ischaemic heart disease, bronchial asthma, and bleeding disorders. No relevant drug history. No adverse habit history. No relevant dental history. Family history reveals,patient is unmarried and his elder brother has a similar deformity and all other family members are apparently normal. His parents had a first-generation consanguineous marriage. On General physical examination, the patient was poorly built with short stature. He had mild hearing loss and slurring of speech. He is conscious, cooperative, and well oriented to time, place, and person. On examining, extra orally malformation of external ears, lower eyelid abnormality (sparse eyelashes), anti-mongoloid slant of the palpebral fissure, hypoplasia of malar bone, parrot beak nose appearance.

On intraoral examination,spacing was seen in upper & lower anterior tooth region, Molar class III relation was seen on the right and left side, Grade III mobility in relation to 31, 41, Recession in relation to 31, 32, 41, 42.

Differential Diagnosis

1. Nager syndrome (also called acrofacial dysostosis)
2. Miller syndrome
3. Goldenhar syndrome (also called hemifacial macrosomia, oculoauriculovertebral spectrum)
4. Branchial arch syndrome
5. Bauru syndrome
6. Pierre Robin sequence

Investigations

OPG

Orthopantomogram reveals Prominent antegonial notch, Reduced ramus height and width, generalized bone loss, Impacted 18, Reduced body width on the right side, Protraction of the lower border of the mandible on the right side.

Lateral CEPH

Class III skeletal base with the retrognathic maxilla, Prognathic mandible, Downward and backward rotation of the mandible, Vertical growth pattern, Maxilla tip forwards, Increased lower anterior facial height, Proclined upper and lower incisors, Acute nasolabial angle, Incompetent lips.

CT

Bilateral Zygomatic hypoplasia, Retrognathia of mandible
Hypoplastic left middle ear cavity with aplasia of ear ossicles
Hypoplasia of condyle
Narrowed frontal bone with conchae hypertrophy

Final diagnosis:

1. Angle's class III malocclusion
2. Franceschetti syndrome

3. Chronic generalized gingivitis with localized periodontitis in relation to 31, 32, 41, 42

Treatment plan:
1. Genetic counselling has to be given
2. Multidisciplinary approach is necessary to coordinate oral, ocular, dental, and craniofacial care
3. Extraction of 31, 32, 41, and 42 are advised
4. Orthodontic treatment for malocclusion is planned
5. Complete scaling is advised
6. Advice prothesis for the replacement of edentulous space

Treatment done
1. Complete scaling done
2. Extraction of 31,32,41,42
3. Replacement of edentulous space with fixed partial denture

Discussion:-

Treacher Collins syndrome (TCS), otherwise known as mandibulofacial dysostosis, Berry's syndrome and Franceschetti-Zwahlen-Klein syndrome. It is a congenital disorder of craniofacial development that occurs with Incidence of 1 in 50,000 live births. The two theories which is said to be associated with the syndrome are failure of the facial and mandibular facial processes to fuse and Manifestation of a combined Tessier 6, 7, 8 facial clefts.

The main etiologic factors of Treacher – collins syndrome are
• Autosomal dominant inheritance in 40%
• Sporadic inheritance in 60%
• Variable penetrance
• Linked to TCOF1, PLORIC, POLR1D

Franceschetti syndrome is a genetic disorder resulting in congenital craniofacial malformation. It is also referred to as Treacher Collins syndrome, Klein syndrome, or mandibulofacial dysostosis. It is a rare genetic disorder of facial dysmorphism that affects structures of the first and second pharyngeal arches. Patients have normal intelligence, but often face social challenges throughout life because of their physical appearance.

Pathogenesis
Neural crest cells migrate over extensive distances to the periphery of the face giving rise to most of the cartilage, bone, connective and peripheral tissues in the head. Most disorders of craniofacial development are thought to be caused by defects in the formation, proliferation, migration and/or differentiation of cranial neural crest cells and TCS is no exception. Hence, abnormal neural crest migration, ectopic cell death and inappropriate differentiation have all been hypothesized as underlying causes of TCS. It is genetically heterogeneous. The clinical features are a result of a loss of function, mutation of the TCOF1 gene on chromosome 5.

Type I: Pathogenic variants of the TCOF1 gene, autosomal dominant (86%)
Type II: Pathogenic variants in the POLR1D gene, autosomal dominant & recessive (6%)
Type III: Pathogenic variants in the POLR1C gene, autosomal recessive (1.2%)
Type IV: Pathogenic variants in the POLR1B gene, autosomal dominant (1.3%)

Clinical Features
Diagnostic Clinical Features
These are the diagnostic features of TCS:
I. Eyes
a. Antimongoloid slant of the palpebral fissures
b. Coloboma and hypoplasia of the lower lids and lateral canthi
c. Partial absence of eyelid cilia
d. Hypertelorism.
II. Ears
a. External ear anomalies
b. External auditory canal abnormalities

c. Middle ear cavity ossicular deformities
d. Conductive hearing loss results from variable degrees of hypoplasia of theexternal auditory canals and ossicles of the middle ears.

III. Nose/mouth

a. Respiratory compromise in severely affected patients as a result of the following two factors:
I. Presence of maxillary hypoplasia, which tends to constrict the nasal passages and results in a degree of choanal stenosis or atresia.
II. Presence of mandibular micrognathia and a retro-positioned tongue obstructing the oropharyngeal and hypopharyngeal spaces.
b. Nasal deformity
c.Microstomia
d.Cleft palate with or without cleft lip
e. High-arched palate
f. Malocclusion
g. Open bite.

IV)Facial bone malformation—the most characteristic findings are as follows:
a. Hypoplasia of the malar bones
i. Often with clefting through the arches.
ii. Limited formation of the residual zygomatic complex.
b. Orbits
i. Hypoplastic lateral aspects of the orbits
ii. Dysplastic inferior lateral orbit.
c. Maxilla and mandible
i) Characteristically hypoplastic
ii) Variable effects on the temporomandibular joints
iii) Anterior open bite
iv) A steep occlusal plane.
d.Sleep apnea and sudden infant death syndrome.

Very frequent
Downward-slanting palpebral fissures
Malar hypoplasia/hypoplasia of zygomatic complex
Conductive hearing loss
Mandibular hypoplasia / micrognathia

Frequent
Atresia of the external ear canal
Microtia
Coloboma (notching) of the lower lid
Delayed speech development
Asymmetry
Preauricular hair displacement

Rare
Nasogastric tube or gastrostomy in neonates
Cleft palate
Intubation or tracheostomy in neonates
Choanal stenosis/atresia
Cardiac malformation

Very rare
Rachis malformation
Renal malformation
Microcephaly
Intellectual disability / delayed motor development
Limb anomaly

Scoring Systems to Rate Severity of Clinical Findings

Features	Points Assigned	
	Taber et al (2004)	Vincent et al (2016)
Downward-slanting palpebral fissures	2	1
Malar hypoplasia/ hypoplasia of zygomatic complex	2	1
Conductive hearing loss	1	2
Mandibular hypoplasia / micrognathia	2	1
Asteria of external ear canal	1	1
Microtia	2	1
Coloboma	2	1
Delayed speech development	Not assigned	Not assigned
Asymmetry	Not assigned	1
Preauricular hair displacement	1	1
Nasogastric tube or gastrostomy in neonates	Not assigned	2
Cleft palate	1	1
Intubation or tracheostomy	1	2
Choanal stenosis	1	2
Cardiac malformation	Not assigned	Not assigned
Rachis malformation	Not assigned	Not assigned
Renal malformation	Not assigned	Atypical
Microcephaly	Not assigned	Atypical
Intellectual Disability/ motor dysfunction	1	Atypical

According to the scoring systems to rate the severity of clinical findings,
• Maximum score is 17 for both systems.
• Scores ≤8 = mildly affected
• Scores ≥9 = severely affected

Differential Diagnosis

1. Nager syndrome (also called acrofacial dysostosis)

Similar features:
• Anti-mongoloid slant of the palpebral fissure
• Absence of eyelashes
• Deformed ears
• Hearing deformity

Distinguishing feature:

• Limb deformities, preaxial abnormalities (e.g., small or absent thumbs, triphalangeal thumbs, radial hypoplasia or aplasia, radioulnar synostosis)

2. Miller syndrome
Similar features:
• Deformity of face
Distinguishing feature:
• Limb deformities, postaxial abnormalities (e.g., small or absent 5th digit including 5^{th} metacarpal, ulnar hypoplasia, absent 5th toe)

3. Goldenhar syndrome (also called hemifacial macrosomia, oculoauriculovertebral spectrum)
Similar features:
• Deformity of face
• Hypoplastic zygomatic arch
• Downward slanting of the palpebral fissure
Distinguishing feature:
• Ocular epibulbar dermoid cyst

4. Branchial arch syndrome
High-arched palate

5. Bauru syndrome
Up slanting palpebral fissures & hypoplastic tragus & ear lobes

6. Pierre Robin sequence
Micrognathia, glossoptosis& airway obstruction with cleft palate deformity

Treatment Modalities
In the acute setting, airway and nutrition are the primary goals. Airway compromise and poor feeding are issues relating to maxillary hypoplasia, mandibular hypoplasia, and narrow pharyngeal diameter.
• Prone positioning or nasopharyngeal airway
• Tube feeding if failure to thrive

Timeline for surgical modalities
• Orbital Reconstruction:7 years after bone development
• Mandible: during early teenage years
• Middle ear: after external ear reconstruction
• Reconstructive surgeries
• The reconstructive strategy should be individualised to the patient. The goal is to restore function, treat deficits or excesses and improve cosmesis.
• Bone graft: orbital floor, zygomatic hypoplasia
• Costochondral graft: TMJ reconstruction, mandibular deformities
• Mandible: advancements, distraction, Le Fort I osteotomy
• Oculoplastics: Lateral Canthopexy
• Soft Tissue Flaps: ear reconstruction,
• Rhinoplasty: dorsum hump and loss of nasal tip projection

Genetic Counselling
Genetic counseling is the process of providing individuals and families with information on the nature, mode(s) of inheritance, and implications of genetic disorders to help them make informed medical and personal decisions.It deals with genetic risk assessment and the use of family history and genetic testing to clarify the genetic status of family members.It is not meant to address all personal, cultural, or ethical issues that may arise or to substitute for consultation with a genetics professional.

Conclusion:-

Treacher Collins syndrome patients typically undergo, over several years, multiple major reconstructive surgeries that are rarely fully corrective. Prenatal diagnosis and genetic counseling are mandatory to help parents to make decisions regarding pregnancy. These patients require care from birth through adulthood. Proper treatment planning, counseling, and surgical management are essential for optimizing patient outcomes.

Figures:-

Figure 1:- Malformation of external ears.

Figure 2:- Obliterated nasofrontal angle.

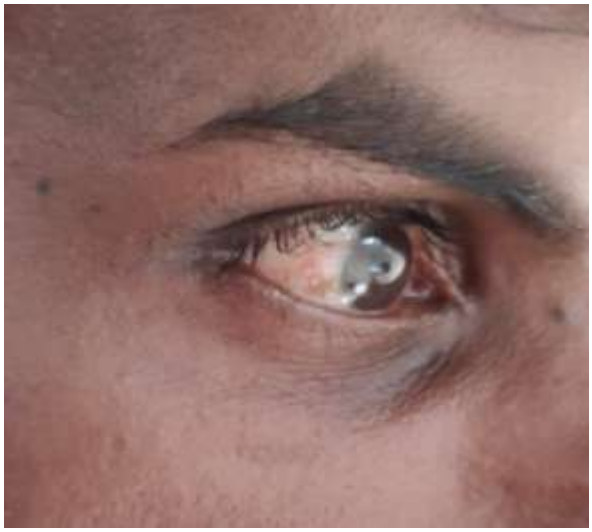

Figure 3:- Lower eyelid abnormality (sparse eyelashes).

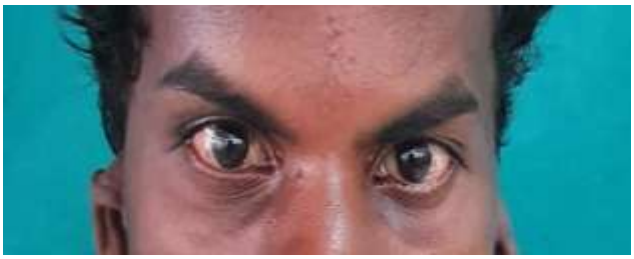

Figure 4:- Anti-mongoloid slant of the palpebral fissure.

Figure 5:- Hypoplasia of malar bone and Parrot beak nose appearance.

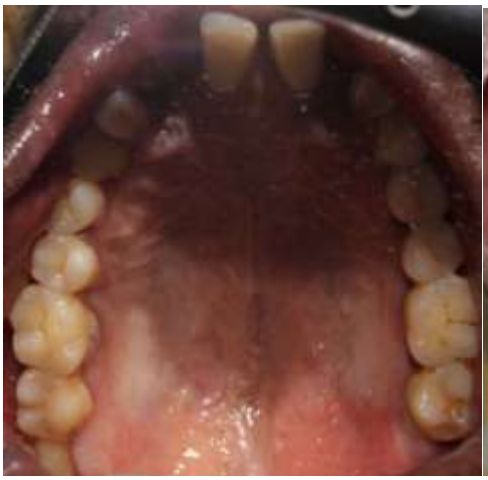

Figure 6:- Intra-oral maxilla

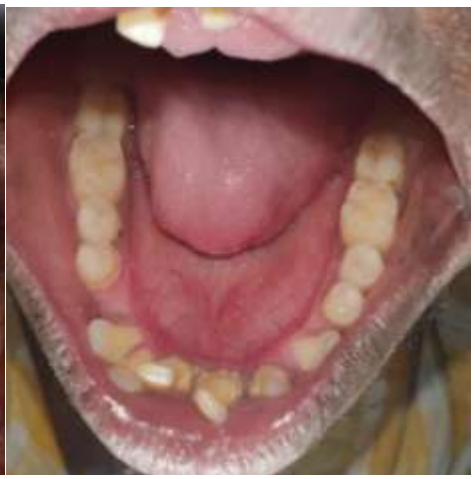

Figure 7:- Intraoral mandible.

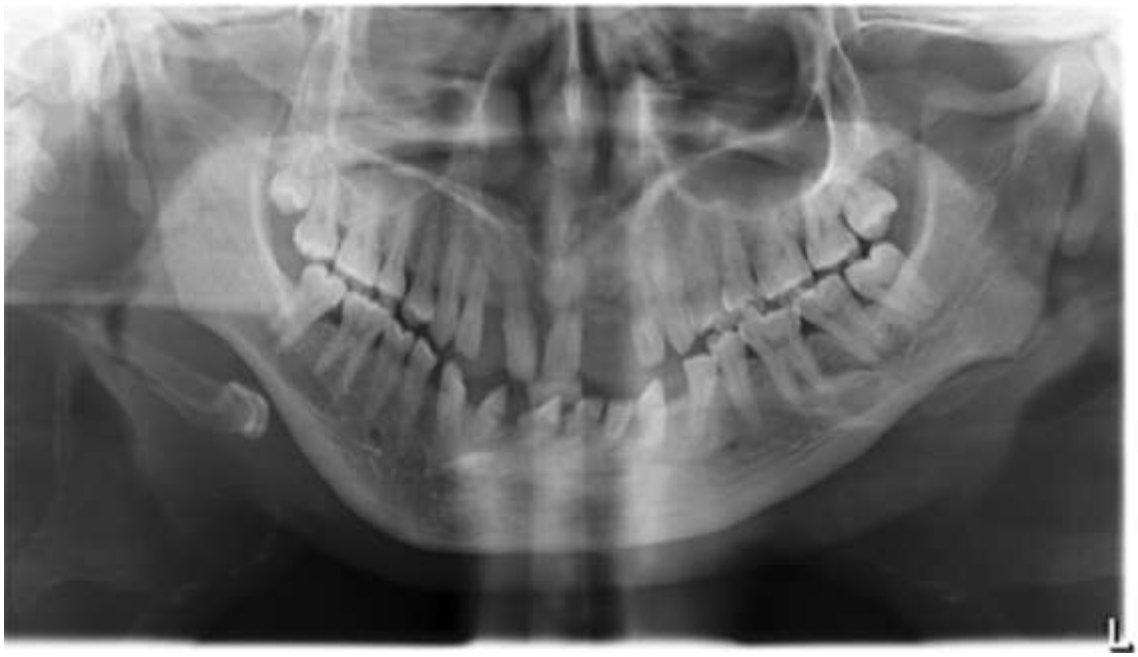

Figure 8:- OPG.

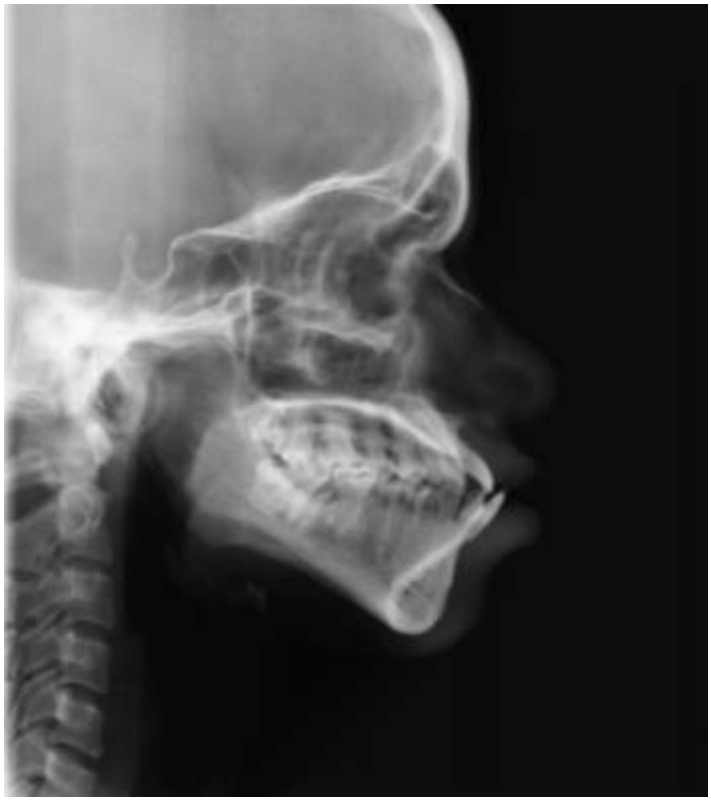

Figure 9:- Lateral cephalogram.

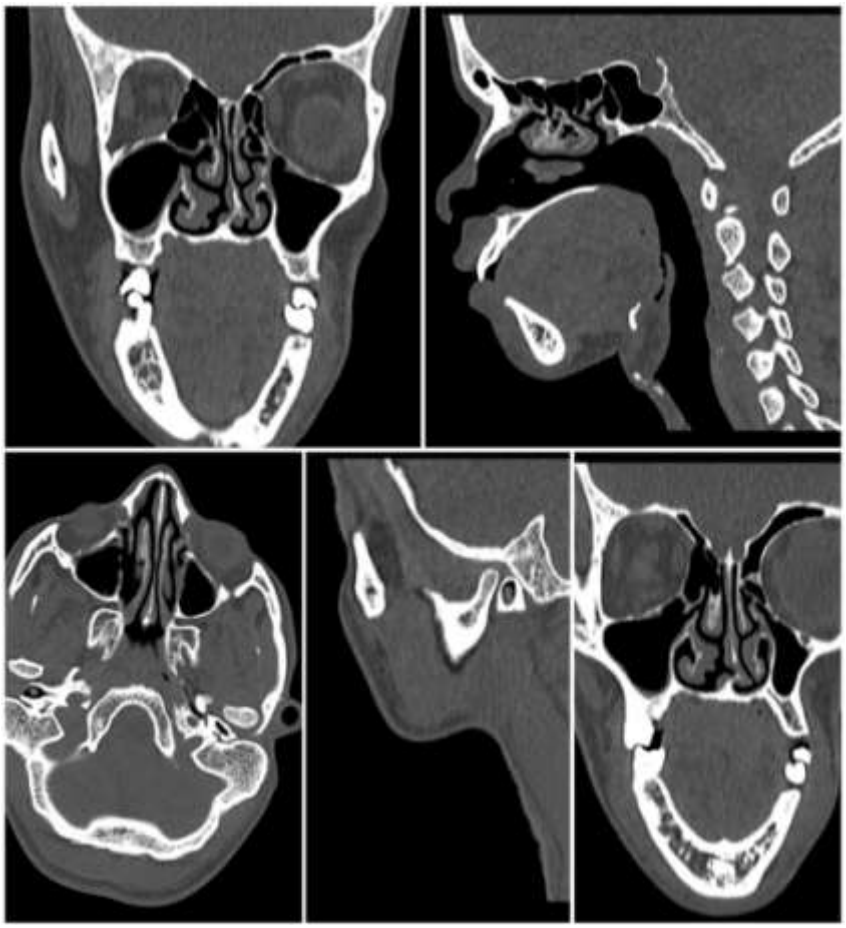

Figure 10:- Computed Tomography.

Figure 11:- Post treatment.

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