Case Report

Nager's Syndrome: A Rare Congenital Disorder with Multidisciplinary Clinical Management

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ABSTRACT

This is a case of 4 yr male patient came with complaints of abnormal posturing, lethargy was seen with decreased activity, fever, and vomiting (5 episodes). Physical assessment shows Small head, Down slanting palpebral fissure, Low set ears, Frontal bossing and preaxial limb defect. MRI demonstrated metopic craniosynostosis (trigonocephaly) and midbrain asymmetry. He initially managed by keeping nil per oral (NPO). Intravenous fluids (DNS and 3% normal saline) were administered to maintain hydration and correct electrolyte imbalance. Ondansetron, ranitidine, saline nasal drops, intravenous Ceftriaxone and vitamin B12 supplementation were given as part of supportive management. Nutritional support was initiated as a part of multidisciplinary management approach, and the patient was closely observed for improvements and related possible complication secondary to nager syndrome.

Keywords: Acrofacial dysostosis type 1 (AFD1), Nager's syndrome, cranioskeletal abnormalities, preaxial limb defect, SF3B4gene mutation.

INTRODUCTION

Nager's syndrome – is a rare genetic disorder. Its is also called as acrofacial dysostosis type 1 (AFD1). Since 1948 after the discovery of Nager's syndrome approximately 100 cases have been reported.[2] The main cause of Nager syndrome is mutation in the SF3B4 gene a component of spliceosome which is responsible for processing pre m RNA,[4] here both autosomal recessive and autosomal dominant inheritance pattern have been seen spontaneously.[6] It is described as AFD1 due to presence of malformation of cranioskeletal and pre axial limb defects commonly absence of the thumb and hypoplasia.[6,7] The cranioskeletal abnormalities includes downward slanting of palpebral fissures, lower eyelids, mid face retrusion, cleft palate, ear abnormalities, micrognathia. The limb defects include radial elements of forelimbs, hypoplasia or agenesis of thumb.[2,6] The major problem faced by infants is upper airway obstruction causing respiratory and feeding difficulties.[9]

The standard diagnosis for Nager syndrome is assessment of patient's clinical features and history. The confirmation test is based on genetic testing of both child and parent,[2] even though patients with Nager syndrome are reported to have normal intelligence some patients with intellectual disability and developmental delay are also seen.[4] This disorder doesn't have any cure but multidisciplinary care like tracheostomy, gastrostomy, craniofacial surgery, airway management like noninvasive ventilation (NIV) can be done.[2]

CASE REPORT

A 4-year-old male child was admitted to the Department of Pediatrics, Karnataka Medical College and Research Institute (KMCRI), Hubballi, on 5 July 2026 for further evaluation and multidisciplinary management of his underlying congenital condition.

Chief Complaints

According to the mother, the child presented with the following chief complaints - Abnormal posturing since morning, lethargy was seen with decreased activity since two days, fever since one day, and vomiting since one day (5 episodes).

Previous Admission History

The patient had a history of multiple previous hospital admissions. At the age of 7 months, he was admitted to Karnataka Medical College and Research Institute (KMCRI), Hubballi, for evaluation of developmental delay. Magnetic resonance imaging (MRI) of the brain was performed, and further evaluation was advised at Shri Dharmasthala Manjunatheshwara (SDM) Hospital.

At 9 months of age, the patient was admitted again following a history of head trauma. A computed tomography (CT) scan of the brain was performed and revealed no significant abnormality.

The patient was subsequently admitted at the age of 1 year and 12 months with a history of poor weight gain for approximately 4–5 days and was evaluated accordingly.

Later, the patient was admitted to a city clinic in Hubballi with complaints of fever and loose stools for approximately 3–4 days and received appropriate symptomatic management.

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Antenatal History:

The patient's mother was diagnosed with hypothyroidism during pregnancy and was initiated on thyroid hormone replacement therapy with thyroxine 12.5 µg once daily. The maternal thyroid disorder and corresponding treatment were documented as part of the patient's antenatal history and were considered relevant to the overall clinical assessment.

Clinical Features and Their Relevance to Nager's Syndrome

Affected Part	Clinical Finding	Relevance to the Case
Head	Small head size (microcephaly)	May be associated with craniofacial developmental abnormalities and contributes to the overall dysmorphic phenotype.
Eyes	Down-slanting palpebral fissures	Represents a characteristic craniofacial dysmorphic feature and may occur as part of the facial phenotype in Nager's syndrome.
Ears	Low-set ears	Indicates abnormal external ear development, consistent with the craniofacial anomalies commonly observed in Nager's syndrome.
Face	Frontal bossing	Reflects an abnormal craniofacial morphology and contributes to the characteristic facial appearance.
Limb	Left thumb absent (preaxial limb anomaly)	A significant limb abnormality associated with Nager's syndrome, which characteristically involves preaxial limb defects affecting the radius and/or thumb.
Skin	White macule measuring approximately 0.5 × 0.5 cm over the left upper thigh	An incidental cutaneous finding documented during examination; it is not considered a characteristic feature of Nager's syndrome and should be reported separately from the syndrome-associated anomalies.

On Clinical Examination

On clinical examination, the patient exhibited multiple dysmorphic features. Craniofacial examination revealed a small head, down-slanting palpebral fissures, low-set ears, and frontal bossing. Examination of the limbs demonstrated congenital absence of the left thumb, representing a preaxial limb anomaly. Dermatological examination revealed a well-defined, hypopigmented macule measuring approximately 0.5 × 0.5 cm over the left upper thigh. These findings were documented as part of the patient's overall dysmorphic and congenital phenotype.

ANTHROPOMETRIC ASSESSMENT

Anthropometric assessment revealed **Severe Acute Malnutrition (SAM)**. The patient demonstrated significant growth faltering, with anthropometric parameters suggestive of severe nutritional deficiency. Weight, height/length, and other relevant anthropometric indices were assessed and interpreted according to age- and sex-specific standards.

Vital Signs at Admission

Parameter	Recorded Value	Clinical Interpretation
Temperature	37.0°C	Afebrile
Pulse Rate (PR)	112 beats/minute	Within the expected range for age
Respiratory Rate (RR)	26 cycles/minute	Within the expected range for age
Blood Pressure (BP)	80/50 mmHg	Low-normal for age; clinical correlation advised
SpO_2 (Oxygen Saturation)	99%	Adequate oxygen saturation
GRBS (Glucose Level)	114 mg/dL	Within an acceptable range

At the time of admission, the patient was **afebrile and maintaining adequate oxygen saturation**, with a pulse rate of 112 beats/minute and respiratory rate of 26 cycles/minute. Blood pressure was recorded as 80/50 mmHg, and the random blood glucose level was 114 mg/dL.

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Systemic Examination and Clinical Relevance

System	Examination Findings	Relevance to the Present Case
Cardiovascular System (CVS)	Normal S1 and S2 with no audible murmur	No clinically evident cardiovascular abnormality was detected. This finding helps document the absence of associated cardiac involvement in the present case.
Respiratory System (RS)	Bilateral normal vesicular breath sounds with no added sounds	No respiratory abnormality was evident on examination. This is relevant because craniofacial and mandibular abnormalities in Nager's syndrome may predispose patients to airway and respiratory complications.
Central Nervous System (CNS)	Patient was conscious and responsive. Higher mental functions were below the expected level for age, consistent with developmental delay	Developmental delay was an important clinical feature in this patient and was documented as part of the overall neurodevelopmental assessment. The reduced age-appropriate higher mental functioning warrants further developmental and neurological evaluation.
Per Abdomen (P/A)	Abdomen was soft and non-tender, with no palpable hepatomegaly or splenomegaly	No clinically evident abdominal organ involvement was identified. This finding helps establish that there was no significant hepatosplenomegaly or abdominal abnormality at the time of examination.

Dysmorphic and Limb Examination

Examination	Clinical Findings	Relevance to the Present Case
	• Small head (microcephalic appearance) • Down-slanting palpebral fissures • Low-set ears • Frontal bossing	These craniofacial dysmorphic features contribute to the characteristic abnormal facial phenotype observed in the patient and are relevant to the clinical assessment of Nager's syndrome, a congenital craniofacial disorder.
	• Congenital absence of the left thumb	The absent left thumb represents a **preaxial limb anomaly**, which is a significant clinical feature of Nager's syndrome. Thumb abnormalities, often associated with radial-ray defects, are characteristic of the disorder and support the clinical diagnosis.

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Hematological Investigations

Investigation	Observed Value	Reference Range*	Interpretation	Relevance to the Case
Hemoglobin (Hb)	11.6 g/dL	~11.0–14.0 g/dL	Within normal range	No significant anemia was evident on evaluation.
Total Leukocyte Count (TLC)	17,700/µL	~5,000–15,000/µL	Mildly increased	May indicate a mild inflammatory or infectious response; clinical correlation is required.
Neutrophils	77.6%	~30–60%	Increased	Neutrophilia may suggest an acute inflammatory/infective response and should be interpreted along with clinical findings.
Lymphocytes	8.7%	~30–60%	Decreased	Relative lymphopenia may accompany an acute inflammatory or infectious process.
Packed Cell Volume (PCV/Hematocrit)	36.8%	~31–41%	Within normal range	Indicates preserved hematocrit without evidence of significant anemia or hemoconcentration.
Platelet Count	3.53 lakh/µL	~1.5–4.5 lakh/µL	Within normal range	No thrombocytopenia or thrombocytosis was identified.
ESR	23 mm/hour	~0–15 mm/hour	Increased	Suggests a nonspecific inflammatory response and requires correlation with the patient's clinical condition.

Note: Reference ranges may vary according to the laboratory, age, and sex of the patient. Laboratory-specific pediatric reference intervals should be used in the final manuscript.

Overall interpretation: The hematological profile showed mild leukocytosis with neutrophilia and elevated ESR, suggestive of a nonspecific inflammatory response. Hemoglobin, PCV, and platelet count were within the expected range. These findings should be interpreted in conjunction with the patient's clinical presentation and other investigations.

MAGNETIC RESONANCE IMAGING (MRI) FINDINGS

MRI of the brain revealed mild volume loss involving the right cerebral and cerebellar hemispheres. There was asymmetry of the bilateral lateral ventricles, with prominence of the left lateral ventricle compared with the right. The imaging also demonstrated premature closure of the metopic suture, resulting in trigonocephaly, consistent with metopic craniosynostosis.

DIAGNOSIS

Based on the clinical examination, anthropometric assessment, laboratory investigations, previous medical history, and neuroimaging findings, the patient was diagnosed with Nager syndrome associated with global developmental delay and severe acute malnutrition (SAM).

INVESTIGATIONS AND CLINICAL FINDINGS

The diagnostic evaluation included assessment of vital signs, detailed systemic and physical examination, anthropometric assessment, hematological investigations, and magnetic resonance imaging of the brain. Physical examination demonstrated characteristic craniofacial abnormalities and a congenital preaxial limb defect, including absence of the left thumb, supporting the clinical diagnosis of Nager syndrome.

Hematological investigations revealed leukocytosis with neutrophilia and an elevated erythrocyte sedimentation rate (ESR), suggestive of a nonspecific inflammatory or infective process. Anthropometric assessment was consistent with severe acute malnutrition, indicating significant nutritional compromise.

MRI demonstrated metopic craniosynostosis (trigonocephaly) along with mild right cerebral and cerebellar hemispheric volume loss and asymmetry of the lateral ventricles. These neuroimaging findings were considered in conjunction with the patient's documented developmental delay.

MANAGEMENT

Initially, the patient was kept nil per oral (NPO) because of persistent vomiting and poor oral intake. Intravenous fluids, including dextrose normal saline (DNS) and 3% sodium chloride, were administered as clinically indicated to maintain hydration and manage electrolyte disturbances. Supportive treatment included ondansetron for vomiting, ranitidine for gastric protection, saline nasal drops, and intravenous ceftriaxone for suspected infection. Vitamin B12 supplementation was also administered.

Following stabilization, nutritional rehabilitation gradually initiated with close monitoring of feeding tolerance, hydration status, electrolyte balance, anthropometric parameters, and clinical response. The patient was monitored closely for complications associated with severe acute malnutrition, developmental delay, and the multisystem manifestations of Nager syndrome. A multidisciplinary approach involving pediatric, nutritional, neurological, craniofacial, and other relevant specialties was considered essential for ongoing management.

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Medication and Supportive Management Chart

S. No.	Medication / Intervention	Dose	Frequency	Route of Administration	Purpose / Clinical Rationale
1	Nil Per Oral (NPO)	—	—	—	Instituted because of persistent vomiting and poor oral intake, with temporary withholding of oral feeds to reduce aspiration risk and allow gastrointestinal stabilization.
2	Dextrose Normal Saline (DNS)	40 mL/hour	Continuous	Intravenous (IV)	Administered to maintain hydration and provide glucose and fluid support during the period of poor oral intake.
3	Ondansetron Injection	0.8 mL	1-0-1	Intravenous (IV)	Administered for symptomatic control of persistent vomiting and to improve tolerance of subsequent nutritional rehabilitation.
4	Ranitidine Injection	0.8 mL	1-0-1	Intravenous (IV)	Administered for gastric acid suppression and supportive management of gastrointestinal symptoms.
5	Saline Nasal Drops	—	1-0-1	Intranasal (IN)	Used for nasal mucosal hydration and relief of nasal congestion, if present.
6	3% Sodium Chloride (Normal Saline)	2.5 mL/hour	Continuous	Intravenous (IV)	Administered as prescribed for correction/management of electrolyte imbalance under close monitoring.
7	Ceftriaxone Injection	500 mg	1-0-1	Intravenous (IV)	Administered as antimicrobial therapy in view of suspected bacterial infection, supported by leukocytosis and neutrophilia.
8	Vitamin B12 Injection	1 mL diluted in 60 mL normal saline	0-0-1	Intravenous (IV)	Given as vitamin supplementation as part of supportive nutritional management.

DISCUSSION

Nager syndrome (Nager acrofacial dysostosis) is a rare congenital craniofacial disorder characterized by malformations of the craniofacial structures and limbs, particularly the upper extremities. The condition is associated with variable clinical manifestations, ranging from characteristic facial abnormalities to preaxial limb defects. Due to its rarity and phenotypic variability, only a limited number of cases have been reported in the literature. Nager syndrome is most commonly associated with pathogenic variants in the **SF3B4 gene**, which encodes a component of the spliceosomal complex. In most cases, the disorder occurs sporadically; however, both autosomal dominant and autosomal recessive inheritance patterns have been described.

DIFFERENTIAL DIAGNOSIS

Several congenital syndromes may present with craniofacial abnormalities resembling those observed in Nager syndrome. Important differential diagnoses include Treacher Collins syndrome (TCS), Miller syndrome, Edwards syndrome (trisomy 18), and Goldenhar syndrome (oculo-auriculo-vertebral spectrum).

Treacher Collins syndrome shares several craniofacial manifestations with Nager syndrome, including malar and mandibular hypoplasia and external ear abnormalities. However, the presence of preaxial limb abnormalities, particularly thumb and radial-ray defects, strongly favors Nager syndrome.

Miller syndrome may also demonstrate overlapping craniofacial features; however, it is classically associated with postaxial limb abnormalities, distinguishing it from the predominantly preaxial limb involvement characteristic of Nager syndrome.

Edwards syndrome may present with multiple congenital anomalies, craniofacial abnormalities, growth restriction, and limb abnormalities. However, its characteristic multisystem involvement and chromosomal abnormality distinguish it from Nager syndrome.

Goldenhar syndrome is primarily characterized by craniofacial asymmetry, ocular abnormalities, auricular anomalies, and vertebral defects. The characteristic preaxial limb involvement seen in the present patient is more supportive of Nager syndrome.

In the present case, the congenital absence of the left thumb, together with the observed craniofacial abnormalities, particularly the small head, down-slanting palpebral fissures, low-set ears, and frontal bossing, supported the clinical diagnosis of Nager syndrome. The presence of a preaxial upper-limb defect was particularly useful in differentiating the condition from other craniofacial syndromes, especially Treacher Collins and Miller syndromes.

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MANAGEMENT

Management of Nager syndrome is individualized according to the clinical manifestations and needs of each patient. Because the disorder can involve multiple organ systems and may significantly affect feeding, hearing, speech, development, and limb function, a multidisciplinary approach is essential.

The multidisciplinary team may include pediatricians, clinical geneticists, craniofacial/plastic surgeons, otorhinolaryngologists (ENT specialists), orthopedic surgeons, developmental specialists or psychologists, audiologists, nutritionists, and other rehabilitation professionals. Management may involve correction or reconstruction of craniofacial and limb abnormalities, assessment and management of hearing impairment, nutritional rehabilitation, developmental interventions, and appropriate genetic counselling.

In the present case, management was focused on stabilization, nutritional rehabilitation, management of vomiting and suspected infection, monitoring of developmental status, and multidisciplinary evaluation. The coexistence of severe acute malnutrition and global developmental delay further emphasized the need for individualized nutritional, developmental, and supportive care.

CONCLUSION

Nager syndrome is a rare congenital disorder characterized by distinctive craniofacial abnormalities and preaxial limb defects, most commonly associated with pathogenic variants in the SF3B4 gene. The present case highlights the importance of recognizing characteristic features such as craniofacial dysmorphism and congenital absence of the thumb, particularly in a child presenting with developmental delay and severe acute malnutrition. The associated global developmental delay, severe acute malnutrition, persistent vomiting, poor feeding, and metopic craniosynostosis with trigonocephaly further demonstrate the clinical complexity and multisystem needs of affected children. Early recognition and comprehensive evaluation are essential for timely diagnosis, nutritional rehabilitation, and prevention of complications. Management should be individualized and multidisciplinary, involving pediatric, nutritional, developmental, craniofacial, orthopedic, genetic, and rehabilitative care. Regular follow-up and supportive interventions are important to optimize growth, development, functional outcomes, and overall quality of life in children with Nager syndrome.

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