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Original Article

Beyond The Mask: Understanding And Caring For Child With Kabuki Syndrome

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ABSTRACT

Kabuki Syndrome (KS) is a rare genetic disorder characterized by distinctive facial features, developmental delay, intellectual disability, growth abnormalities, and multiple congenital anomalies. The syndrome was first described in Japan and affects various organ systems, resulting in lifelong healthcare needs. It is an uncommon developmental chromatinopathy caused by mutations in genes that regulate chromatin remodeling and gene expression. The principal genes implicated are KMT2D (12q13.12), encoding a histone H3K4 methyltransferase typically associated with autosomal dominant inheritance and frequent de novo variants, and KDM6A (Xp11.3), encoding a histone H3K27 demethylase with X-linked transmission. Both proteins act within the ASCOM epigenetic complex; disruption of their complementary methylation activities leads to broad transcriptional dysregulation during embryogenesis. Clinically, KS manifests with a recognizable facial gestalt, congenital heart disease, skeletal anomalies, renal malformations, immunodeficiency, and neurodevelopmental impairment, necessitating lifelong multidisciplinary care. Advances in next-generation sequencing have enabled accurate molecular diagnosis, improving genetic counselling and early intervention strategies. Despite progress, therapeutic options remain supportive, underscoring the need for further research into targeted epigenetic therapies. This review highlights the genetic basis, clinical spectrum, diagnostic approaches, and management challenges of KS, emphasizing its significance as a model disorder for understanding chromatin-mediated regulation of human development.

Keywords: Kabuki Syndrome, chromatinopathy, developmental disorder, congenital anomaly.

INTRODUCTION

Case Scenario: Kabuki Syndrome in a 5 years old male Child, presenting with complaints of persistent developmental delay, speech impairment, and recurrent infections admitted to Tertiary pediatric hospital, Bhubaneswar, Odisha, India`

History of Past Illness:

Child (patient) born at term, weighing 2.6 kg. Early infancy was marked by feeding difficulties and poor weight gain. Motor milestones were delayed: sat at 10 months, walked independently at 24 months. Speech development remained limited, with only single words by age 5. He experienced recurrent respiratory infections (4–6 episodes per year) and two hospitalizations for pneumonia. Genetic evaluation at age 3.5 confirmed Kabuki syndrome.

On examination:

- Anthropometry: weight 12.5 kg (<3rd centile), height 98 cm (<3rd centile), head circumference 48.5 cm (10–25th centile).
- Dysmorphic features: long palpebral fissures with lateral eversion, arched eyebrows, depressed nasal tip, large ears, high-arched palate.
- Neurological: mild hypotonia, gait instability, poor fine motor coordination.
- Cardiac: soft systolic murmur; echocardiogram showed small secundum ASD (4 mm). disability (IQ 50–60).

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- Genetics: heterozygous de novo pathogenic KMT2D nonsense variant (c.1234C>T, p.Arg412*).

Introduction

Kabuki syndrome is a rare multisystem developmental disorder first described in Japan in 1981. It is most commonly associated with pathogenic variants in the KMT2D gene and less frequently in KDM6A, leading to disruption of chromatin remodeling and transcriptional regulation. Clinically, affected children present with a characteristic facial gestalt arched eyebrow, long palpebral fissures, depressed nasal tip, and large ears alongside growth deficiency, intellectual disability, congenital heart defects, skeletal anomalies, and immune dysfunction. Because of its broad spectrum of manifestations, Kabuki syndrome requires multidisciplinary management involving pediatricians, cardiologists, therapists, audiologists, ophthalmologists, and genetic specialists. Early recognition is crucial to initiate developmental therapies, monitor systemic complications, and provide family counseling.

Epidemiology

Kabuki syndrome is considered an ultra-rare disorder, but reported prevalence varies widely across regions. In Japan, where the condition was first described, estimates suggest approximately 1 in 32,000 live births, while studies in Australia and New Zealand report a lower frequency of 1 in 86,000 births. Globally, the prevalence is thought to range between 1–9 per 100,000 births, though underdiagnosis remains a major challenge due to phenotypic variability and limited access to genetic testing. Importantly, Kabuki syndrome has been documented across all ethnic groups without sex predilection, underscoring its universal distribution. Recent advances in next-generation sequencing have led to increased recognition of atypical cases, including milder phenotypes that may previously have gone unnoticed. This evolving epidemiological picture highlights the need for heightened awareness among clinicians and nurses, as early identification directly influences developmental outcomes and family counselling.

Etiology and Genetics of Kabuki Syndrome

1. Genetic Basis

KMT2D gene (Kabuki syndrome type 1)

- Located on chromosome 12q13.12.
- Encodes a histone H3 lysine 4 (H3K4) methyltransferase.
- Responsible for adding activating methylation marks to histones, promoting gene transcription.
- Accounts for ~75–80% of cases.
- Inheritance: autosomal dominant, but most cases are de novo (new mutations not inherited from parents).

KDM6A gene (Kabuki syndrome type 2)

- Located on chromosome Xp11.3.
- Encodes a histone H3 lysine 27 (H3K27) demethylase.
- Removes repressive methylation marks, allowing gene activation.
- Accounts for ~5–10% of cases.
- Inheritance: X-linked dominant; males often more severely affected.Other Genetic Insights

Genotype–phenotype correlation:

- KMT2D variants → more frequent congenital heart defects, immune dysfunction.
- KDM6A variants → more severe intellectual disability, growth deficiency.
- Rare reports of mosaicism and familial inheritance exist, but most cases are sporadic.
- Emerging evidence suggests additional genes (e.g., RAP1A, HNRNPK) may produce Kabuki-like phenotypes, though these are less common

Major genes implicated in Kabuki syndrome

Gene	Syndrome	Chromosome	Main protein function	Inheritance
KMT2D	KS type 1	12q13.12	Histone H3K4 methyltransferase	Autosomal dominant
KDM6A	KS type 2	Xp11.3	Histone H3K27 demethylase	X-linked

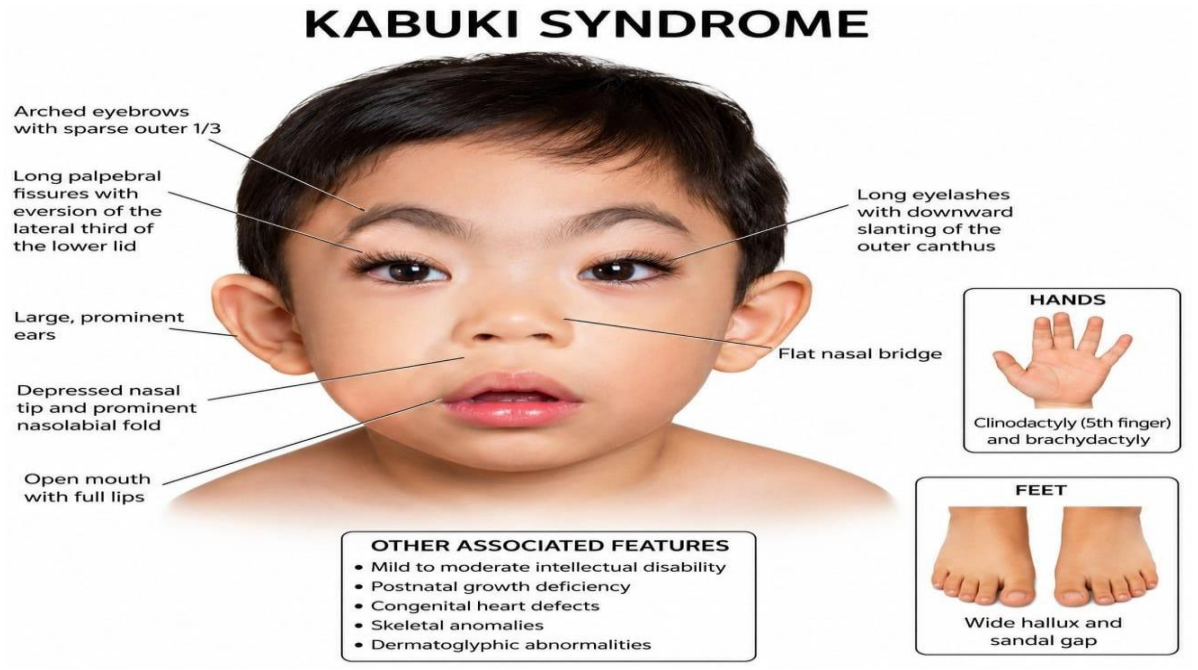

Figure-1, Clinical Features of kabuki Syndrome

Clinical Manifestations

Kabuki syndrome is characterized by a distinctive facial gestalt and multisystem involvement. Common features include:

- Craniofacial features: arched eyebrows with sparse lateral third, long palpebral fissures with eversion of the lower eyelid, depressed nasal tip, large prominent ears, flat nasal bridge, long eyelashes, and open mouth with full lips.
- Skeletal anomalies: clinodactyly of the fifth finger, brachydactyly, wide hallux, sandal gap, joint hyperlaxity, scoliosis.
- Growth and development: postnatal growth deficiency, global developmental delay, intellectual disability (mild to moderate).
- Cardiac anomalies: congenital heart defects (ASD, VSD, coarctation of aorta).
- Renal anomalies: hydronephrosis, structural malformations.
- Immune dysfunction: recurrent respiratory infections, hypogammaglobulinemia (especially low IgA).
- Neurological: hypotonia, poor coordination, seizures in some cases.

- Sensory issues: hearing loss due to recurrent otitis media, vision problems (strabismus, coloboma).
- Other: dermatoglyphic abnormalities, feeding difficulties, cleft palate, dental anomalies.

Diagnosis and Investigations

Diagnosis is based on clinical recognition of characteristic features supported by genetic confirmation.

1. Clinical Diagnosis

- Recognition of the facial gestalt and associated anomalies.
- Use of diagnostic criteria (e.g., dysmorphic features + developmental delay + congenital anomalies).
- Differential diagnosis: other syndromes with overlapping features (Noonan, CHARGE, etc

2. Laboratory and Imaging Investigations

- Genetic testing:
- Clinical exome sequencing or targeted gene panel.
- Pathogenic variants in KMT2D (Kabuki syndrome type 1) or KDM6A (Kabuki syndrome type 2).
- Cardiac evaluation: echocardiography for congenital heart defects.
- Renal evaluation: ultrasound for hydronephrosis or anomalies.
- Immunology: serum immunoglobulin levels (IgA, IgG, IgM).
- Developmental assessment: standardized scales (Bayley, IQ testing).
- ENT/Audiology: hearing assessment, tympanometry.
- Ophthalmology: vision screening for strabismus, coloboma.
- Other labs: CBC, metabolic panel to rule out associated conditions.

Medical Management

- Cardiac: annual cardiology surveillance; surgical closure if ASD enlarges.
- Renal: periodic ultrasound; nephrology follow-up.
- Immune dysfunction: monitor immunoglobulins; prophylactic antibiotics if severe; strict vaccination schedule.
- Growth/nutrition: dietitian input; calorie-dense feeding; feeding therapy; gastrostomy if severe.
- Developmental delay: physiotherapy, occupational therapy, speech therapy; individualized education plan.
- ENT/hearing: audiology screening; tympanostomy tubes; hearing aids if needed.
- Vision: ophthalmology follow-up; corrective lenses or surgery for anomalies.
- Genetic counseling: explain de novo mutation, low recurrence risk; family support.

NURSING MANAGEMENT

Growth and Development

Assessment: Monitor developmental milestones regularly.

Interventions: Provide age-appropriate stimulation, encourage play, collaborate with physiotherapist/occupational therapist, and educate parents on home activities.

Goal: Maximize developmental potential and independence.

Nutrition and Feeding

Assessment: Observe swallowing, feeding patterns, and weight gain.

Interventions: Offer small frequent feeds, maintain upright position during feeding, refer to dietitian/speech therapist, monitor for aspiration.

Goal: Maintain adequate nutrition and growth.

Respiratory Care

Assessment: Monitor respiratory rate, effort, oxygen saturation, and breath sounds.

Interventions: Position for optimal ventilation, suction as needed, encourage fluids, observe for infection signs.

Goal: Maintain clear airway and stable respiratory status.

Communication Support

Assessment: Evaluate speech and language ability

Interventions: Encourage verbal interaction, use simple instructions, allow response time, introduce pictures/gestures, refer for speech therapy.

Goal: Improve communication and social interaction.

Mobility and Physical Function

Assessment: Check muscle tone, strength, and mobility.

Interventions: Assist ambulation, encourage physiotherapy exercises, ensure safety precautions, promote physical activity at developmental level.

Goal: Enhance mobility and prevent injury.

Infection Prevention

Assessment: Monitor temperature and signs of infection.

Interventions: Maintain hygiene, encourage immunization, educate parents on early signs, avoid exposure to sick contacts.

Goal: Keep child free from preventable infections.

Cardiac Monitoring

Assessment: Observe heart rate, oxygen saturation, activity tolerance, cyanosis, edema, fatigue.

Interventions: Administer prescribed medications, ensure cardiology follow-up.

Goal: Maintain stable cardiovascular status.

Sensory Support

Assessment: Screen hearing and vision regularly.

Interventions: Provide assistive devices, position child for communication, educate parents and teachers.

Goal: Optimize sensory functioning and learning

Caregiver Education and Support

Assessment: Identify caregiver knowledge gaps and anxiety.

Interventions: Explain condition in simple terms, teach feeding and infection prevention, encourage participation in care, provide emotional support, link to support groups.

Nursing Care Plan

Assessment	Nursing Diagnosis	Goals/ Expected Outcomes	Nursing Interventions	Evaluation
Child with feeding difficulty, poor weight gain, hypotonia	Imbalanced nutrition: less than body requirements related to feeding difficulties	Child will maintain adequate nutritional status and show steady weight gain	-Provide thickened feeds or gastrostomy if needed - Collaborate with dietician for high-calorie diet - Monitor weight regularly	Child maintains adequate nutrition and weight gain
Developmental delay, hypotonia, intellectual disability	Delayed growth and development related to genetic disorder	Child will achieve developmental	- Enroll in early intervention programs	Child achieves age-appropriate developmental milestones

		milestones with early intervention	- Encourage play therapy - Provide structured learning activities	
Recurrent ear infections, immune dysfunction	Risk for infection related to recurrent otitis media	Child will remain free from infection during care period	- Monitor for signs of infection - Educate parents on hygiene - Ensure vaccination schedule adherence	No infection episodes during hospitalization
Scoliosis, joint laxity, impaired mobility	Impaired physical mobility related to musculoskeletal abnormalities	Child will demonstrate improved mobility with physiotherapy	-Provide physiotherapy and safe exercises - Positioning to prevent scoliosis progression - Encourage active play	Improved mobility and muscle strength
Speech delay, hearing loss	Impaired verbal communication related to hearing impairment	Child will demonstrate improved mobility with physiotherapy	- Provide hearing aids/assistive devices - Initiate speech therapy - Encourage family interaction	Improved mobility and muscle strength
Parents expressing anxiety about prognosis	Anxiety (family) related to chronic illness	Family will verbalize reduced anxiety and improved coping	- Offer counselling - Connect family with support groups - Provide education about condition and home care	Family demonstrates effective coping strategies

Important Multidisciplinary Care

Children with Kabuki syndrome may require individualized assessment and follow-up involving pediatricians, cardiologists, developmental specialists, physiotherapists, occupational therapists, speech-language therapists, audiologists, ophthalmologists, dentists, dietitians, and genetic specialists, depending on their manifestations.

Priority nursing problems are usually

- Airway/respiratory problems
- Feeding and nutritional problems
- Delayed growth and development
- Impaired mobility
- Communication difficulties
- Risk for infection
- Caregiver knowledge and anxiety

CONCLUSION

Kabuki Syndrome is a rare, multisystem genetic disorder that profoundly impacts growth, development, and overall health. Its etiology lies in mutations of chromatin-modifying genes (**KMT2D** and **KDM6A**), which disrupt transcriptional regulation and lead to diverse clinical manifestations. The case of Aarav Kumar highlights the challenges of delayed milestones, recurrent infections, and congenital anomalies, emphasizing the importance of early diagnosis and multidisciplinary care. Epidemiological data confirm KS as an ultra-rare condition, often underdiagnosed due to phenotypic variability. Genetic insights reveal genotype–phenotype correlations that guide prognosis and management. Clinical manifestations span craniofacial, skeletal, cardiac, renal, neurological, and sensory systems, requiring comprehensive diagnostic evaluations. Medical and nursing management focus on surveillance, supportive therapies, and caregiver education. Priority nursing concerns include airway clearance, feeding difficulties, developmental stimulation, infection prevention, mobility support, and communication enhancement. With coordinated multidisciplinary interventions, children with Kabuki Syndrome can achieve improved developmental outcomes and quality of life.

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