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CASE REPORT

Kabuki Syndrome- A Case Report

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***ABSTRACT*:**
Kabuki syndrome is a rare, multisystem disorder characterized by multiple abnormalities including distinctive facial features, growth delay, varying degrees of intellectual disability, skeletal abnormalities, and short stature.Here we are presenting a 5-year old boy diagnosed as a case of Kabuki syndrome on the basis of its characteristic features.
Key words: Kabuki syndrome, clinical features, chest infection.

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INTRODUCTION:

Kabuki syndrome is a rare, multisystem disorder characterized by multiple abnormalities including distinctive facial features, growth delay, varying degrees of intellectual disability, skeletal abnormalities, and short stature.[1,2] First described in Japan, Kabuki syndrome is known to occur in all ethnic groups and affects males and females in equal numbers. The incidence of is unknown but has been estimated to be somewhere between 1 in 32,000-86,000 individuals in the general population. Here we are presenting a 5-year old boy diagnosed as a case of Kabuki syndrome on the basis of its characteristic features.[3,4] The distinctive facial features included arched eyebrows; long eyelashes; long palpebral fissures with everted outside edges; a flat, broadened tip of the nose; and large protruding earlobes. He also had history of recurrent respiratory infections and was found to have tubular bronchiectasis affecting both lungs with peribronchial thickening in both the lungs on HRCT Chest. Subsequently, given recurrent respiratory infections with a normal immunological status respiratory infections are frequent in KS and possibly due to immune system dysfunction.

CASE REPORT:

A 5-year old first order boy was admitted to the Pediatric Department of MGM Hospital, Kamothe, Navi Mumbai, Maharashtra, India, with complaints of cough, cold and fever from one month. He was born out of a non-consanguineous marriage by normal vaginal delivery after term gestation to a primigravida mother. There was history of failure to gain weight and developmental delay.

The current weight was 12.6kg with a birth weight of the baby was 2.8kg. His height was 89cm and head circumference was 48cm.(all the parameters <3 SD) The boy had not attained developmental milestones like unable to talk in sentences but wa able to run and understand verbal instructions. He had generalized hypotonia and facial dysmorphism with high arched eyebrows sparse laterally, long palpebral fissures with everted lower eyelids, long eyelashes accompanying microcephaly. His nose was broad with depressed tip, and ears were prominent and protruding. His weight-for-length ratio was significantly at below the 5th percentile. He exhibited a delay in gross motor skills. A clinical diagnosis of KS was proposed

On auscultation he had bilateral wheeze and lower zone bilateral crepitations. His chest X-ray revealed bilateral haziness in bilateral lower zone and was started on IV antibiotics and nebulizations. USG chest revealed left sided minimal pleural effusion. USG Abdomen showed no abnormalities. 2 D ECHO was normal. He suffered from recurrent pneumonia, an immunologic evaluation was performed including: levels of total Ig and IgG subclasses,

lymphocyte classes, lymphocyte proliferation assays and specific antibody responses, showing normal data. A chest CT scan with iv injection of iodine contrast agent was performed, diffuse small and large airways disease is seen. Tubular bronchiectasis wirhperibrochial thickening is seen in both the lungs, most marked in lower lobes with mucoid impaction.

Clinical features

- 5 years boy came with h/o recurrent respiratory infection since birth and failure to thrive.
- He had generalized hypotonia and facial dysmorphism.
- His weight-for-length ratio was significantly below the 5th percentile.
- He exhibited a delay in gross motor skills.
- His chest xray revealed bilateral haziness in bilateral lower zone.
- USG chest revealed left sided minimal pleural effusion.
- USG Abdomen showed no abnormalities.
- 2 D ECHO was normal .
- he suffered from recurrent pneumonia, an immunologic evaluation was performed showing normal data.
- HRCT chest revealed Tubular bronchiectasis wirhperibrochial thickening is seen in both the lungs, most marked in lower lobes with mucoid impaction.

DYSMORPHIC FEATURES

- high arched eyebrows sparse laterally
- long palpebral fissures with everted lower eyelids
- long eyelashes accompanying microcephaly
- His nose was broad with depressed tip
- ears were prominent and protruding

Figure 1: HRCT revealing bilateral Tubular bronchiectasis wirh peribrochial thickening is seen in both the lungs, most marked in lower lobes with mucoid impaction

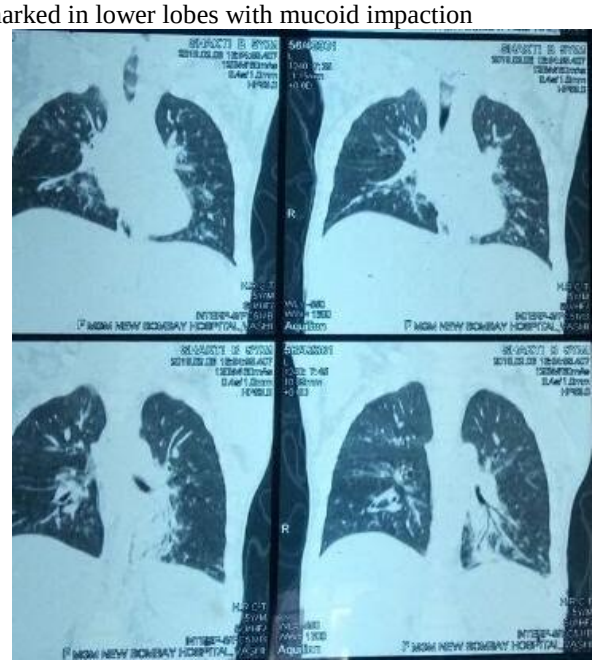


Figure 2:

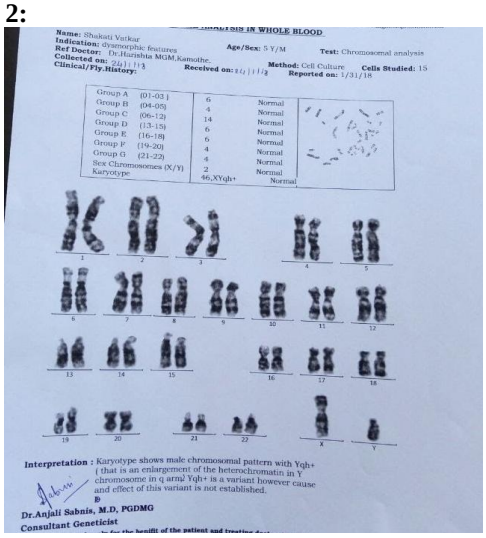


Figure 3: HRCT revealing bilateral Tubular bronchiectasis wirh peribrochial thickening is seen in both the lungs, most marked in lower lobes with mucoid impaction

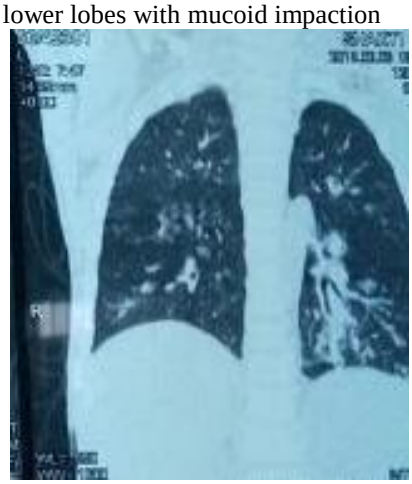
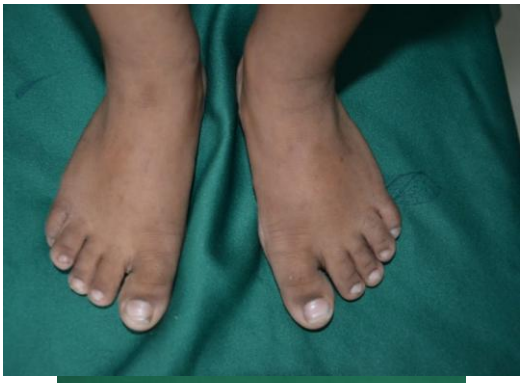
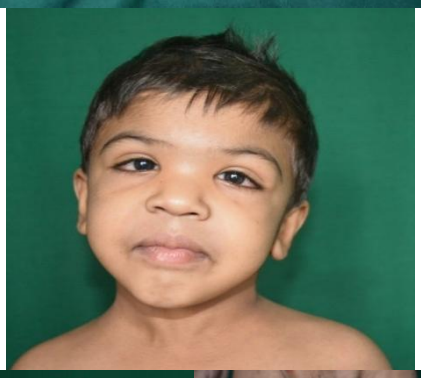
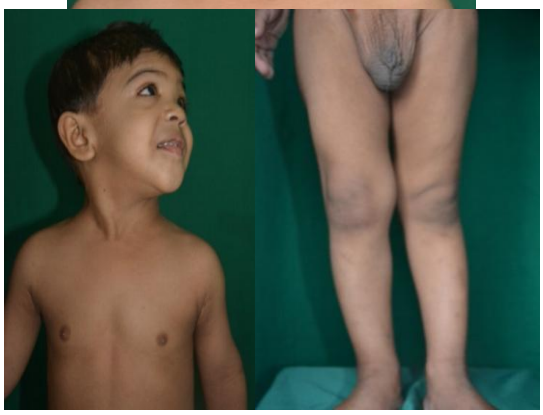


Figure 4: Clinical features:

- short phalanges
- high arched eyebrows sparse laterally
- long palpebral fissures with everted lower eyelids
- long eyelashes accompanying microcephaly
- nose was broad with depressed tip
- ears were prominent and protruding







DISCUSSION:

In the present study, we describe a patient with KS , suffering from recurrent respiratory infections. Respiratory infections are frequent in KS and possibly due to immune system dysfunction. Immunological studies showed normal data in our patient.The recurrent and severe bronchitis caused multiple hospitalizations, leading to a worsening of the patient's life quality. The chest CT scan Tubular bronchiectasis with peribrochial thickening is seen in both the lungs, most marked in lower lobes with mucoid impaction. Treatment provided was aggressive antibiotic, chest physiotherapy and nebulizations, improving his respiratory performances.

Kabuki syndrome is a rare syndrome characterized by distinct dysmorphic facial features, postnatal growth retardation, intellectual disabilities, skeletal abnormalities, and unusual dermatoglyphic patterns. It is usually detected sporadically and has a wide spectrum of clinical manifestations). Recently identified as a genetic syndrome via whole exome sequencing), KS has been increasingly recognized in the primary care setting, and in many cases, its underlying etiology has been discovered. KS is diagnosed and managed by pediatricians. Liu S et al retrospectively retrieved a series of eight patients from two hospitals in China and conducted Sanger sequencing for all of the patients and their parents if available. The patients generally presented with typical clinical manifestations as previously reported in other countries.[5,6] Uncommon symptoms included spinal bifida and Dandy-Walker malformation. With respect to the mutations, five mutations were found in five patients, including two frameshift indels, one nonsense mutation and two missense mutations. This was the first case series on Kabuki syndrome in Mainland China. Unusual symptoms, such as spinal bifida and Dandy-Walker syndrome, suggested that neurological developmental defects may accompany Kabuki syndrome. Sattur A et al reported a 24-year-old girl of Asian origin diagnosed with Kabuki syndrome based on characteristic clinical features. It is characterized by distinctive facial features (eversion of the lower lateral eyelid, arched eyebrows with the lateral one-third dispersed or sparse, depressed nasal tip, and prominent ears), skeletal anomalies, Dermatoglyphic abnormalities, short stature. They suggested association of cervical arterial disease with this syndrome, which has never been described earlier.[7]Dentici ML et al reviewed the clinical and molecular genetic characteristics of 16 patients presenting a suspected diagnosis of Kabuki syndrome (KS) in the first year of life, to evaluate the clinical handles leading to a prompt diagnosis of KS in newborns. Clinical diagnosis of KS can be challenging during the first year of life, as many diagnostic features become evident only in subsequent years. All patients were clinically investigated by trained clinical geneticists. A literature review was performed using the Pubmed online database and diagnostic criteria suggested by DYSCERNE-Kabuki Syndrome Guidelines (2010) were used (a European Network of Centres of Expertise for Dysmorphology, funded by the European Commission Executive Agency for Health and Consumers (DG Sanco), Project 2006122). Molecular analysis of the known causative genes of KS, KMT2D/MLL2 and KDM6A, was performed through MiSeq-targeted sequencing platform. All mutations identified were validated by Sanger sequencing protocols. Mutations in KMT2D gene were identified in 10/16 (62%) of the patients, whereas none of the patients had KDM6A mutations. Facial dysmorphisms (94%), feeding difficulties (100%) and hypotonia (100%) suggested the clinical diagnosis of KS. No significative differences in terms of facial features were noticed between mutation positive and negative patients of the cohort. Brachydactyly, joint laxity and nail dysplasia were present in about 80% of the patients. Other congenital anomalies were most commonly present in the mutated group of patients, including left-

sided cardiac abnormalities, skeletal, renal and anorectal malformations and hypertricosis.[8-10]

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