Case Report

Trisomy 21- A Case Report with Literature Review

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A B S T R A C T

Introduction: Down's syndrome is the commonest chromosomal abnormality, named after John Langdon Down who described its clinical description in 1866. It is the most prevalent genetic disease worldwide , appearing in about 1 in 400-1500 newborns with huge medical and social cost. It is caused by trisomy of whole or part of chromosome 21.

Case report: This present case report highlights the clinical presentation of 19yrs old patient with Down's Syndrome,.we have also emphasized an overview of Down's syndrome.

Conclusion: It has effects on most body systems, giving rise to a variety of characteristic clinical features and greater risk of other medical conditions such as congenital heart defects, respiratory disease, leukemia , Alzeihmer's disease and Hirschsprung disease, etc..

Keywords: Down's Syndrome, Trisomy 21, Systemic Manifestations, Gene Karyotyping, Intellectual Impairment

INTRODUCTION

Down's syndrome is the common genetic cause of intellectual disabilities worldwide causing several delayed psychomotor development and large numbers of patients throughout the world encounter various additional health problems, including heart defects, respiratory infections, gastrointestinal anomalies, weak neuromuscular tone, hypothyroidism,dysmorphic features of the head, neck and airways, characteristic facial and physical features, audiovestibular and visual impairment, hematopoietic disorders and Alzheimer disease[1].The incidence of trisomy is influenced by maternal age and differs in population (between 1 in 319 and 1 in 1000 live births .All patients with Down's syndrome have a degree of intellectual impairment ranging from mild to severe. Screening for DS is an important part of routine prenatal care[2]. Diagnostic hypothesis of DS include chromosome analysis (karyotype examination) which can be performed in the pre and postnatal period. As present there is no cure for cognitive impairment in downs disease [3].Scientists have identified specific genes that are involved in the formation of various clinical characteristic features. These advances in turn may help to develop targeted therapy for persons with trisomy 21. The use of prophylactic measures and respiratory syncytial virus (RSV) prophylaxis , additional immunizations are preventive interventions to be undertaken[4]. Recent advancement in medical treatment with social support has increased the life expectancy for DS population. In developed countries, the average life span for DS population is upto 60 years.[5]

CASE REPORT

A 19yr old female patient reported to the department of Oral Medicine and Radiology with her mother, presenting with chief complaint of deposits on her teeth and wanted to clean her teeth. Her history of presenting illness revealed, she has halitosis and bleeding gums on brushing. Patient's medical history disclose that she was diagnosed with Down's syndrome with gene karyotyping test at the age of 1. Her test report revealed KARYOTYPE- 47,XX,+21 with abnormalities, numerical type-Trisomy 21 was given.

Examination of other systemic illness was not contributory. Her habit history revealed that she has tongue thrusting habit for past 10 yrs.Family history of the patient revealed consanguineous marriage of parents. Patient has one elder brother , four years older to her, who is apparently normal and all other family members are normal.

On general examination, the patient is conscious, not well oriented to time and place and responds to only few basic questions by action. The stature of the patient is short with short neck. Patient's mother also revealed there was delay in milestone achievement of her daughter. There is marked difficulty in speech and in pronouncing some words and learning difficulty are also noted. History of mouth breathing is also seen .The gait of the patient is abnormal with her feet wide apart and turned outwards. The BMI of the patient was found to be 26.7 and she was overweight.

On examination of the head and neck region(FIGURE-1), facial asysmmetry noted, with presence of scar tissue on her forehead region in the centre. Proptosis of the eyes seen, hypertelorism , broad nose, flat nasal bridge, low set

ears, incompetent lips, tongue protrusion in normal resting position noted.

Intraoral findings (FIGURE-2) of the patient revealed clinically missing teeth 12,22 and 37,transposition of upper first premolar 14 and 24, retained deciduous 54 and 64 and altered morphology of the canine 23 is also noted. Anterior cross bite and open bite seen on occlusion. Her periodontal status was poor with inflammation of the gingiva and gingival recession in relation to upper and lower anteriors with grade II mobility of 11,21,31,32,41,42.

With the above findings, provisional diagnosis of generalized chronic periodontitis was given and other diagnosis includes Down's syndrome and malocclusion.

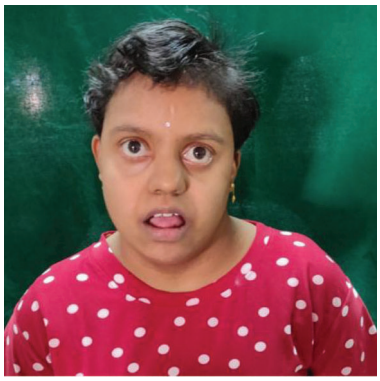

Figure-1: Profile

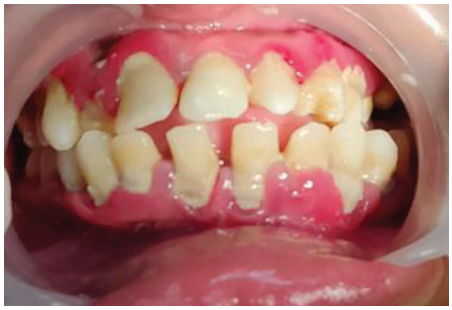

Figure-2: Intra oral

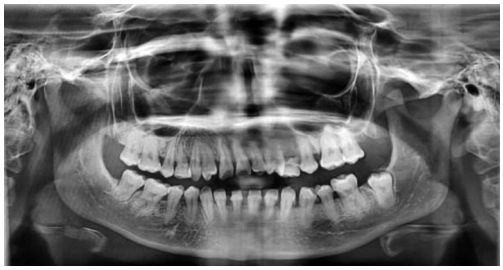

Figure-3: OPG

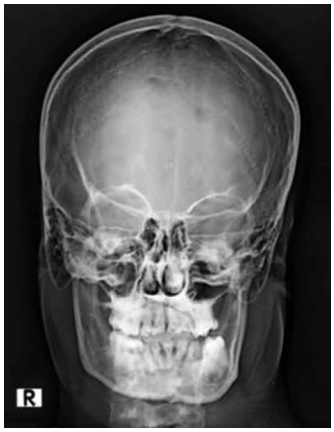

Figure-4: PA skull

General manifestations
1. Short stature
2. Broad and short hands,feet and digits
3. Joint laxity
4. Muscle hypotonia

Table-1: General manifestations

Craniofacial manifestations
1. Brachycephaly
2. Frontal prominence
3. Occipital flattening
4. Flat face with large anterior fontanelle and open sutures
5. Depressed nose, rounded nose tip, flat, broad and short nose, Prognathism.
6. Slanting of the eyes
7. Ocluarhypertelorism
8. Epicanthic folds
9. Strabismus

Table-2: Craniofacial manifestations

Craniofacial manifestations
1. Trachea-smaller size is one of the contributing factor.
2. Recurrent pneumonia
3. OSA
4. Chronic intermitten hypoxia, respiratory acidosis
5. Pulmonary embolism, pulmonary edema
6. Pulomonary hypertension occur because of lung vasculature, overabundance of anti angiogenic factors-tissue inhibitor of MMP3, amyloid protein precursor, endostatin which decrease the vascularity
7. Acute lung injury

Table-3: Respiratory changes

Cardiovascular disease
1. Atrioventrivular septal defects
2. Tetralogy of fallot
3. Patent ductus arteriosus
4. Mitral prolapse, valvular regurgitation.

Table-4: Cardiovascular disease

Manifestations-other systems
1. Presenile dementia.
2. Protuberant abdomen, duodenal atresia
3. Hypospadia
4. Crptorchism
5. Delayed puberty
6. Hirschsprung disease
7. Polydactylia, syndactylia
8. Leukemia
9. Epilepsy
10. Hypothyroidism
11. Hypogenitalism

Table-5: Manifestations of other system

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Oral manifestations
1. Incompetant lips, angulacheilitis
2. Macroglossia
3. Fissured tongue, Geographic tongue
4. Tongue protrusion
5. Hypodontia-permanent third molars, second premolars and lateral incisors in the order.
6. Malocclusion
7. Teeth-malformed, enamel hypoplasia, microdontia
8. High arched narrow palate
9. Cleft palate/cleft lip
10. Alkaline pH- resistance to tooth decay.
11. Taurodontism
12. Severe periodontal disease without any apparent cause.
13. Weekend immune system- candida infections
14. Bruxism
15. Cystic hygroma

Table-6: Oral manifestations

Radiographic findings
1. Thinning of the cranial vault
2. Delayed closure of sutures
3. Defective ossification along the sutures.
4. Absence of frontal sinuses
5. Hypoplasia or aplasia of maxillary sinuses
6. Poorly developed air sinuses
7. Decreased intraorbital distance
8. Small rudimentary nasal bones
9. Vestibular dysplasia
10. Stenosis of external auditory canal
11. C1-C2 dislocation

Table-7: Radiographic findings

Further , patient was subjected to OPG and PA SKULL.
Her OPG findings (FIGURE-3) revealed generalized crestal bone loss of about 3mm above the CEJ in upper teeth and 3mm below the CEJ in the lower teeth suggestive of periodontitis. Structural alteration of the root of upper central incisor in relation to 11,21, retained deciduous teeth 54 and root stumps 64, transposition of 14,24 and 23 and there is bulbous enlargement of root in relation to 37 and 47 suggestive of hyercementosis.

PA SKULL Xray(FIGURE-4) of the patient indicates asymmetry of the skull, bilateral aplasia of the frontal sinus and hypoplastic left maxillary sinus.
Final diagnosis of Down's syndrome was given based on clinical and radiographic features along with gene karyotyping test report brought by the patient. Patient was reffered to department of Periodontology for complete scaling and oral hygiene instructions was given .

DISCUSSION

Downs syndrome also called as trisomy 21 syndrome, mongolism and congenital acromicria syndrome. About 1 in 700 live births reported in all races,with equal predilection for male and female. Trisomy 21 represents ,thepresence of all or part of a third copy of chromosome 21. There are three types of Down's syndrome based on the genetic etiology[6], they are as follows,

- Typical type-trisomy-21 with 47 chromosomes (95% cases)
- Translocation type-46 chromosomes- extra chromosomal material translocated to another chromosome (21/22 translocation or 21/21 translocation)-3% cases
- Chromosomal mosaicism -2%

There is marked mild to severe mental retardation noted in these patients with IQ level ranging from 25-50[7]. The chances of getting Down's syndrome increases with increase in maternal age , the incidence of this syndrome at various maternal ages are as follows,

- 15-29 years: 1 in 1500
- 30-34 years: 1 in 800
- 35-39 years: 1 in 270
- 40-44 years: 1 in 100
- Older than 45 years :1 in 50

The various manifestations of Down's syndrome such as general manifestation[8](table-1), craniofacial manifestation(table-2), manifestation of various systems such as respiratory[9](table-3), cardiovascular[10](table-4) and other systems such as central nervous system, gastrointestinal system, endocrine system, genital system are tabulated[11](table-5). The oral manifestations[17](table-6) and radiographic findings [18](table-7)are also tabulated below. In our case report, the supporting clinical features such as hypertelorism, proptosis, flat nasal bridge, broad nose, low set ears, open bite, protrusion of tongue, habit of mouth breathing , short neck, delayed milestone, mental and learning disability and radiographic features such as hypodontia, retained deciduous and aplasia or hypoplasia of sinus are found along with gene karyotype testing, we gave a final diagnosis of Down's syndrome.
The diagnosis of down's syndrome, involves initial screening tests[12],
First trimester combined test- 2 steps:
Blood test which measure the level of pregnancy associated plasma protein –A(PAPP-A) and HCG and Nuchal translucency test which involves ultrasound to measure the nuchal fold thickness on the back of baby's neck. When there is an abnormality, the thickness is increased because of increased fluid collection in the nuchal fold. The next screening test is Integrated screening test, which is done in the first trimester to measure the level of PAPP-A and uses ultrasound to measure the nuchal translucency and in the second trimester, blood levels of alpha fetoprotein, estriol, HCG and inhibin –A are estimated .
Other diagnostic tests performed during pregnancy includes, Chorionic villus sampling (CVS) , in which the cells taken from placenta and fetal chromosomes are analysed which is performed in first trimester (10-13 weeks)[13]. If there is any abnormality detected in the above tests, final diagnostic test Amniocentesis is performed.
In Amniocentesis, the sample of amniotic fluid is withdrawn through a needle inserted into the mother's uterus. This test is done at 15 weeks .Any genetic variation will be intimated to the patient and patient will be subjected to psychological counselling along with her husband regarding the continuation or termination of the pregnancy[14]. In patients who are under InVitro Fertilization treatment, preimplantation genetic diagnosis is being done .

The treatment of Down's syndrome involvemulti disciplinary approach. Early intervention makes major difference in improving quality of life.[15]About 4-12% of patients die in first year of life due to congenital heart defects and respiratory problems. With the advancement in the medical era, the life expectancy these patients are increased upto 60 years leading a normal life.[16]

CONCLUSION

Down syndrome is one of the most common disorders with an estimated 30,000 cases in India every year. Various systemic manifestations which cause deleterious effect over the health of these patients with Down's syndrome[19] With emergence of Covid 19, adults with Down syndrome were around three times more likely to die from covid-19 than the general population, according to research published by Lancet. Genetics and age could modify the infection response to SARS-cov-2 in Down syndrome. Therefore India plans to prioritise people with Down syndrome for covid-19 vaccination, after the US' centre for disease control (CDC), UK and Spain included those with the genetic condition in the list of 'high-risk' individuals[20]

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