Case Report

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Dentistry Section

Oral and Clinical Manifestations of DiGeorge Syndrome with Primary Hypoparathyroidism: A Case Report

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ABSTRACT

DiGeorge syndrome is an autosomal dominant inherited disorder caused by a deletion of chromosome 22q11.2. It is a multisystem condition, classically presenting with a triad of congenital heart defects, hypoplasia of the parathyroid glands and thymus, and congenital immunodeficiency. The present article reports a 24-year-old female with a DiGeorge syndrome with primary hypoparathyroidism, with emphasis on craniofacial and extraoral features, which included a hypoplastic mandible, flattened forehead, bulbous nose, and flattened nasal bridge. Radiographic findings revealed a thickened calvarium, frontal calcifications, and sutural diastasis. Early diagnosis and intervention, including genetic testing, can significantly improve patient outcomes.

Keywords: Congenitally missing teeth, Enamel hypoplasia, Frontal calcifications, Hypertelorism, Primary hypoparathyroidism, Sutural diastasis

CASE REPORT

A 24-year-old female patient presented to the Department of Oral Medicine and Radiology with a chief complaint of swelling on the right side of her face for the past two weeks. She reported a history of throbbing, intermittent pain in the same region, which had begun one week earlier. The pain was aggravated while eating and relieved by medication. The patient noticed swelling in the area but was uncertain whether it had increased in size.

Her parents reported a medical history of primary hypoparathyroidism, with ongoing treatment including Vitamin D3, calcitriol capsules, and daily calcium supplementation for the past 20 years. Laboratory investigations performed one month prior revealed a serum calcium level of 8.8 mg/dL and a serum phosphorus level of 7.3 mg/dL. The parents also reported that the patient had experienced intermittent vomiting and mild breathing difficulties since birth.

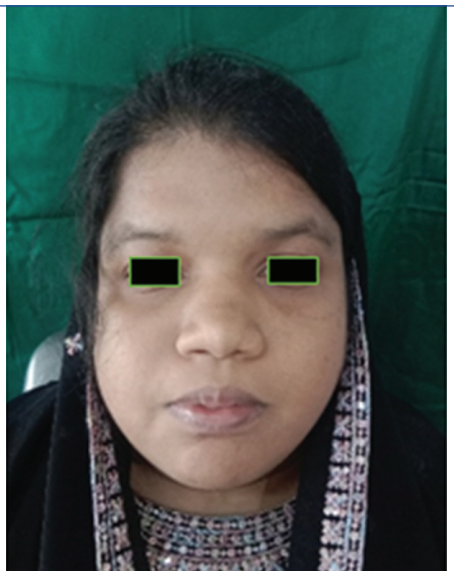
At 14 days of age, she developed generalised body stiffness and was admitted to the hospital, where hypocalcaemia was diagnosed. She was treated with calcium carbonate tablets twice daily and 0.5 mcg of alfacalcidol once daily for two months. Subsequently, cytogenetic testing—including Fluorescence In Situ Hybridization (FISH) and karyotype analyses—was advised at the age of eight. The FISH study revealed a deletion at the 22q11.2 region, and genetic testing confirmed a microdeletion of 22q11.2, establishing a diagnosis of DiGeorge syndrome.

The patient was born to non-consanguineous parents and had a delayed attainment of motor and speech milestones. She experienced menarche at the age of 15. Family history was non-contributory; she has two siblings (one brother and one sister) with no relevant medical history.

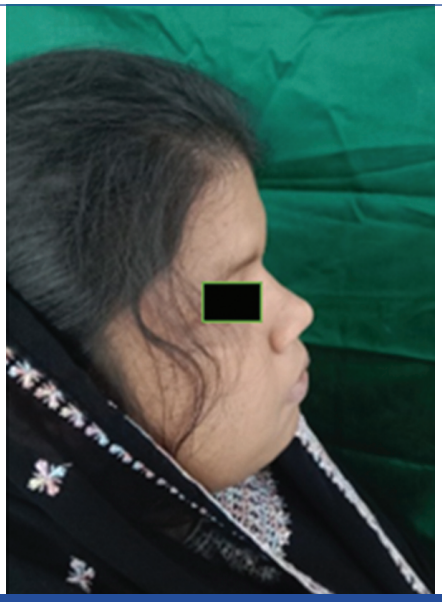
On general examination, the patient was conscious, coherent, cooperative, and well-oriented to time, place, and person. She appeared obese but well-nourished.

Extraoral examination: Gross facial asymmetry was observed, with a broad nasal bridge, bulbous nasal tip, hypertelorism, retrognathic mandible, and flattened forehead [Table/Fig-1,2]. Trigonocephaly, a dolichofacial growth pattern, and a convex facial profile were noted. No digital abnormalities or hearing deficits were observed. On clinical examination, both Chvostek's and Trousseau's signs were absent.

Intraoral examination: Grossly decayed teeth were observed in the maxillary and mandibular posterior regions. Congenitally

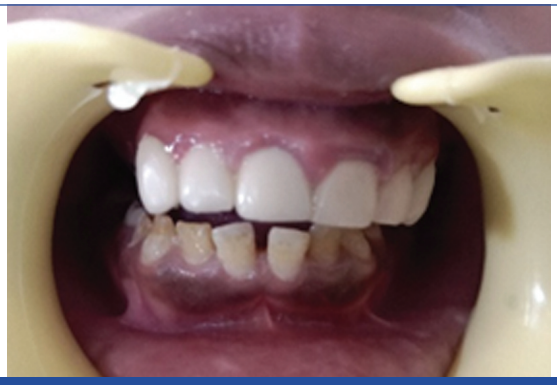


[Table/Fig-1]: Showing bulbous nose, flattened forehead, broad nasal bridge.



[Table/Fig-2]: Showing the facial profile of the patient.

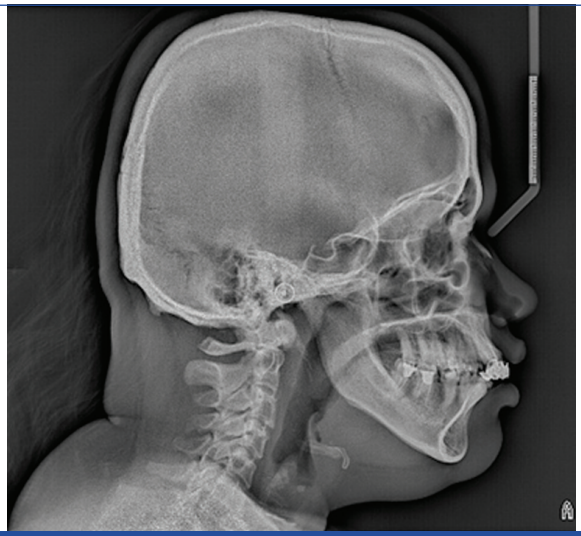
missing teeth were noted with respect to 36 and 46. Microdontia was present in the lower anterior teeth, and a fixed partial prosthesis was observed in relation to teeth 13, 12, 11, 21, 22, and 23 [Table/Fig-3].



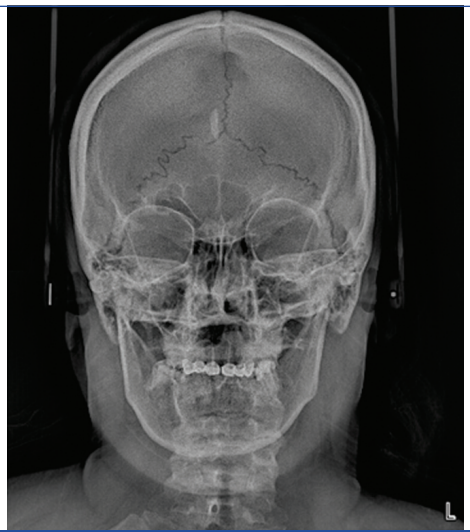
[Table/Fig-3]: Showing the microdontia in lower anterior teeth and fixed prosthesis in upper anterior teeth.

The patient was advised to undergo an intraoral periapical radiograph of the 17 region, which revealed an ill-defined radiolucency involving the periapical area, suggestive of a chronic periapical abscess. For further evaluation of other teeth and the skull region, an orthopantomograph, lateral cephalogram, and Posteroanterior (PA) view were advised.

The lateral cephalogram and PA view demonstrated a thickened calvarium, frontal calcifications, and sutural diastasis [Table/Fig-4,5]. The orthopantomograph revealed congenitally missing teeth

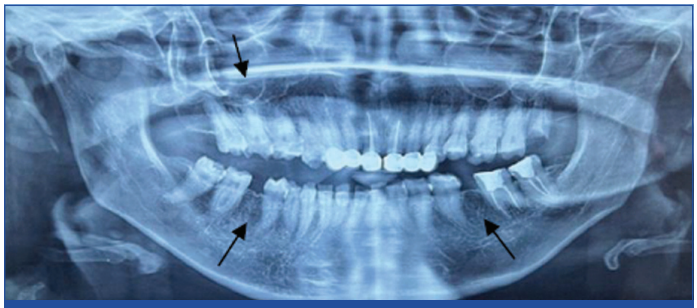


[Table/Fig-4]: Showing the lateral cephalogram with thickened calvarium.



[Table/Fig-5]: PA view of skull indicates the calcifications in the calvarium. Fusion of the frontal sutures was noted.

in relation to 36 and 46, along with generalised enamel hypoplasia [Table/Fig-6].



[Table/Fig-6]: Periapical abscess i.r.t 17.
Congenitally missing teeth, i.e., 36 and 46, noted (as per the patient's history).

The patient was subsequently advised to undergo endodontic management of tooth 17 and aesthetic restoration of the decayed teeth in the maxillary and mandibular posterior regions.

DISCUSSION

DiGeorge syndrome is a primary immunodeficiency resulting from abnormal development of the third and fourth pharyngeal pouches during embryonic life [1]. It is a rare genetic disorder caused by microdeletion of the 22q11.2 region (DGS1) [2]. Case reports have highlighted neuroinflammation and oxidative stress in individuals affected by this syndrome [1], and attention deficit problems have been reported in children with DiGeorge syndrome [2]. Additionally, case reports describe DiGeorge syndrome in patients with mild intellectual disability and psychosis [3].

In this case, oral manifestations included microdontia, anodontia, enamel hypoplasia, and dentinal caries. DiGeorge syndrome is typically characterised by the clinical triad of cardiac abnormalities, thymic hypoplasia or aplasia, and hypoparathyroidism-induced hypocalcaemia. In this patient, a prior diagnosis of DiGeorge syndrome had already been established. Medical history revealed ongoing treatment for hypoparathyroidism-induced hypocalcaemia, while other cardiac anomalies and thymic hypoplasia or aplasia had been ruled out.

The incidence rate of DiGeorge syndrome is approximately 1:3000 live births [3,4]. Deletion of chromosome 22q11.2 can result in several genetic conditions, including conotruncal facial anomaly, velocardiofacial syndrome, Shprintzen syndrome, DiGeorge syndrome, and CATCH 22 syndrome, each exhibiting distinct clinical features [4]. Diagnosis of DiGeorge syndrome is made based on the presence of characteristic clinical features in conjunction with 22q11.2 deletion and is typically pursued only when clinical suspicion exists [5].

The prevalence of latent or recurrent hypoparathyroidism in patients with 22q11.2 deletion is not well-documented in the literature. DiGeorge syndrome arises from developmental defects of the pharyngeal apparatus, a transient embryonic system present only in vertebrates, composed of tissue bulges (pharyngeal arches) separated by epithelial invaginations (pharyngeal pouches) [5]. These developmental anomalies lead to the classic features of DiGeorge syndrome, including congenital heart defects, hypoplasia of the parathyroid glands and thymus, congenital immune deficiency, and renal abnormalities [6].

Congenital conotruncal cardiac defects involving the truncus aorticus were reported in 70% of patients with DiGeorge syndrome. The most common cardiac anomalies include interrupted aortic arch, tetralogy of Fallot, atrial septal defect, and ventricular septal defect [7]. In this case, cardiac anomalies were ruled out during diagnosis in childhood.

Hypocalcaemia, caused by primary hypoparathyroidism, has been reported in approximately 60% of patients [8]. Hypocalcaemia associated with clinical features such as cardiac defects and

immunodeficiency is a strong predictor of DiGeorge syndrome. Common presentations of hypocalcaemia include muscle cramps, numbness, tetany, focal or generalised seizures, prolonged QT interval, and hypotension. Chvostek's and Trousseau's signs may also be positive [9]. In our case, the patient had a history of muscle cramps, tetany, and generalised seizures during childhood, for which she received medication. Currently, she does not exhibit any of these typical signs or symptoms.

Although immunodeficiency is uncommon in adults, it can occur in 70-80% of children with DiGeorge syndrome. Thymic hypoplasia results in a low T-cell count, which may lead to immunodeficiency [10-12]. Immunocompromised patients may experience systemic fungal infections, recurrent viral respiratory infections, and recurrent bacterial illnesses. In this case, the patient has not reported any recent chest infections or other bacterial or fungal infections.

Research on DiGeorge syndrome has identified several intraoral characteristics, including bifid uvula (11%), high palate (22%), cleft palate (22%), enamel hypomineralisation and hypoplasia (22%), dental wear (22%), caries (22%), and malocclusion, which was the most common trait (44%) [4].

DiGeorge syndrome is also associated with neurodevelopmental conditions such as attention-deficit/hyperactivity disorder, autism spectrum disorder, intellectual disability, communication problems, and specific learning disorders [13-15].

Candelo et al. reported a series of nine patients in which acute heart failure, low birth weight and height, and episodes of infection and seizures were observed. Oral manifestations included anodontia, dental crowding, granular enamel with pits on the vestibular surface, and misalignment of the teeth between the dental arches [14].

Chen X et al., reported a case of a 35-year-old male with clinical features including moon-shaped face, dysmorphic facial features, low nasal bridge, hypertelorism, short palpebral fissures, asymmetrical ear size and shape, left helix curving ventrally, and hypogonadism [16].

Several methods exist for diagnosing 22q11.2 deletions. Conventional techniques include Chromosomal Microarray (CMA) and Fluorescent In Situ Hybridisation (FISH). Individuals with an unusual or distal deletion that excludes the proximal region (LCR A-B) may not be detected by FISH, which is specialised for identifying deletions of the 22q11.2 gene. CMA uses a microarray platform with DNA probes to detect chromosomal copy number imbalances across the genome [17].

Differential diagnoses for DiGeorge syndrome include: Smith-Lemli-Opitz syndrome - commonly associated with polydactyly and cleft palate. Oculo-Auriculo-Vertebral (Goldenhar) syndrome - characterised by ear anomalies, heart defects, vertebral anomalies, and renal abnormalities. Alagille syndrome - presents with butterfly vertebrae, congenital heart disease, and posterior embryotoxon. VATER association - includes heart disease, vertebral, renal, and limb anomalies. CHARGE syndrome - may involve any combination of congenital heart disease, palatal abnormalities, choanal atresia, coloboma, renal anomalies, growth deficiency, ear anomalies/hearing loss, facial palsy, developmental differences, genitourinary anomalies, and immunodeficiency [17].

CONCLUSION(S)

Hypoparathyroidism in patients with 22q11 deletion/DiGeorge syndrome may be the earliest and sometimes the most dramatic clinical manifestation of the disease. Although symptoms may resolve within the first year of life, recurrence is possible. Conversely, patients with 22q11 deletion may harbor latent hypoparathyroidism that can be unmasked later in life. Therefore, lifelong monitoring of parathyroid function is recommended for all patients with 22q11 deletion.

REFERENCES

[1] Meghi M, Micangeli G, Tarani F. Neuroinflammation and oxidative stress in individuals as affected by Di-George Syndrome. Int J Mol Sci. 2023;24(4):4242.
[2] Lowe C. DiGeorge syndrome: A case report of a child with attention deficit and socialization problems. J Med Case Rep Case Series. 2021;2(6):10087.
[3] Altshuler E, Saidi A, Budd J. DiGeorge syndrome: Consider the diagnosis. BMJ Case Rep. 2022;15(2):e245164.
[4] Fomin AB, Pastorino AC, Kim CA, Pereira CA, Carneiro-Sampaio M, Abe-Jacob CM. DiGeorge Syndrome: A not so rare disease. Clinics (Sao Paulo). 2010;65(9):865-69.
[5] Kobrynski LJ, Sullivan KE. Velocardiofacial syndrome, DiGeorge syndrome: The chromosome 22q11.2.2 deletion syndrome. Lancet. 2007;370:1443-52.
[6] Shprintzen RJ, Higgins AM, Anstshel K, Fremont W, Roizen N, Kates W. Velo-cardio-facial syndrome. Cur Opin Pediatr. 2005;17:725-30.
[7] Goodship J, Cross I, Liling J, Wren C. A population study of chromosome 21q11 deletions in infancy. Arch Dis Child. 1998;79:348-51.
[8] Baldini A. Hypoparathyroidism in DiGeorge syndrome. Clinical Cases in Mineral and Bone Metabolism. 2004;1(2):103-05.
[9] Ryan AK, Goodship JA, Wilson DI, Philip N, Levy A, Seidel H, et al. Spectrum of clinical features associated with interstitial chromosome 22q11 deletions: A European collaborative study. J Med Genet. 1997;34(10):798-804.
[10] Marino B, Digilio M, Toscano A, Anaclerio S, Giannotti A, Feltri C, et al. Anatomic patterns of conotruncal defects associated with deletion 22q11. Genet Med. 2001;3:45-48.
[11] Choi JH, Shin YL, Kim GH, Seo EJ, Kim Y, Park IS, et al. Endocrine manifestations of chromosome 22q11.2 microdeletion syndrome. Horm Res. 2005;63:294-99.
[12] McDonald-McGinn DM, Sullivan KE, Marino B, Philip N, Swillen A, Vorstman JA, et al. 22q11.2 deletion syndrome. Nat Rev Dis Primers. 2015;1:15071.
[13] Khaleque A, Bhandarkar R. Digeorge syndrome, schizophrenia, intellectual disability and borderline personality disorder: A case report. Clinical Medicine Insights: Psychiatry. 2023;14
[14] Candelo E, Estrada-Mesa MA, Jaramillo A, Martinez-Cajas CH, Osorio JC, Pachajoa H. The oral health of patients with DiGeorge syndrome (22q11) microdeletion: A case report. Appl Clin Genet. 2021;14:267-77.
[15] Karali Z, Karali Y, Cekic S, Altinok B, Bodur M, Bostanci M, et al. Neurocognitive evaluation of patients with DiGeorge syndrome. J Pediatrneurol. 2024;10:012.
[16] Chen X, Yang L, Li J, Huiwen T. Hypoparathyroidism and late-onset hypogonadism in an adult male with familial 22q11.2 deletion syndrome: A case report with 3-year follow-up and review of the literature. BMC Endocr Disord. 2022;22:278.
[17] Mustillo PJ, Sullivan KE, Chinn IK, Notarangelo LD, Haddad E, Davies EG, et al. Clinical practice guidelines for the immunological management of chromosome 22q11.2 deletion syndrome and other defects in thymic development. J Clin Immunol. 2023;43(2):247-70.

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