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Available online at: http://www.iajps.com *A Case Report*

VCFS SYNDROME IN A CHILD OF 7-YEAR-OLD: A CASE REPORT

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Abstract:

Velocardiofacial syndrome (VCFS), also referred to as DiGeorge syndrome or 22q11 deletion syndrome, is a complex genetic disorder characterized by the congenital absence of the thymus and the parathyroid gland. This condition typically presents with a triad of congenital heart disease, endocrinopathy featuring hypocalcaemia, and primary immunodeficiency. Beyond this classic triad, VCFS exhibits pleiotropic abnormalities and diverse clinical manifestations, often leading to facial dysmorphism and palate alterations. Patients with VCFS are particularly susceptible to recurrent respiratory or gastrointestinal infections. In cases where thymic aplasia is observed, prophylactic antibiotic therapy and thymic transplantation are essential for effective management, while in other instances, expectant management strategies are employed. The recognition and understanding of these facets of VCFS are critical for comprehensive patient care and effective interventions. In this case study, we present a 7-year-old male who came to our clinic for a routine well-child evaluation. The presence of distinctive dysmorphic traits raised concerns about the possibility of VCFS, but we couldn't conclusively confirm this diagnosis due to the patient's discontinuation of follow-up.

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INTRODUCTION:

Velocardio-facial syndrome (VCFS) is a genetic syndrome with multiple anomalies, inherited in an autosomal dominant manner. It is characterized by a microdeletion on chromosome22 at band q11.2, which is detected using Fluorescent-In-Situ Hybridization (FISH). VCFS is the most frequent human microdeletion syndrome (Saitta et al., 2004) [1,2]. Its estimated prevalence is approximately 1 in 2000 surviving newborns (Shprintzen, 2008). The term "surviving" is used because the actual incidence of the disease may be higher, as VCFS is linked to congenital anomalies like the Potter sequence, leading to the population prevalence not reflecting the true disease burden [3].

Over 180 clinical and psychiatric features have been associated with VCFS (Robin and Shprintzen, 2005) [4]. The sole defining characteristic is the presence of the 22q11.2 deletion on FISH. Our case involves a 7-year-old boy who visited our clinic for a well-child check-up. He displayed dysmorphic features that raised suspicion of VCFS, but definitive confirmation through genetic testing was not possible due to loss to follow-up.

CASE PRESENTATION:

Here we present the case of a 7-year-old boy who visited our outpatient clinic for a routine well-child check-up. During the visit, the boy comfortably sat in a chair, and his parents expressed concerns about his poor school performance and the possibility of intellectual impairment, as they had observed that he was slow to grasp certain concepts. An IQ test was conducted, revealing mild intellectual impairment. Upon further inquiry, his parents mentioned that he had difficulty sitting still and that his teachers had noticed he frequently interrupted and blurted out answers in class.

Upon close examination of his face and oral cavity, it became evident that he had a retrognathic mandible with crowding of the lower mandibular teeth **(Fig 1**) and a narrow palatal vault **(Fig 2).** Additionally, he displayed a long and narrow face, narrow down-slanting palpebral fissures, and midface hypoplasia. The posterior displacement of his mandible resulted in his inferior lip being covered by the upper lip. Furthermore, he exhibited a hypoplastic philtrum with a thin upper lip **(Fig 3).** He also had thin, elongated fingers, with a normal arm span to height ratio. During chest examination, we identified the presence of pectus excavatum **(Fig-5).** The boy's speech had a hyper nasal quality, although his parents did not report any difficulties with feeding. All laboratory tests, including serum calcium levels, came back normal. An Echocardiogram was conducted and yielded unremarkable results.

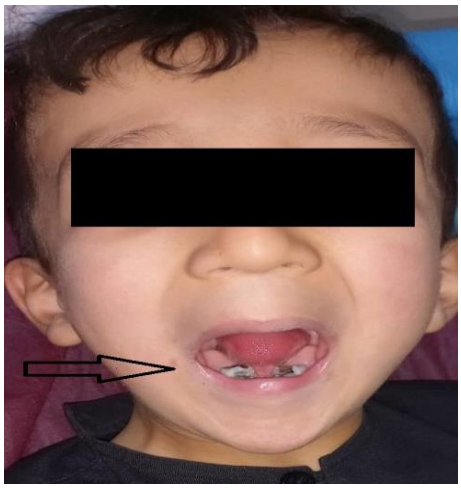

FIGURE:1

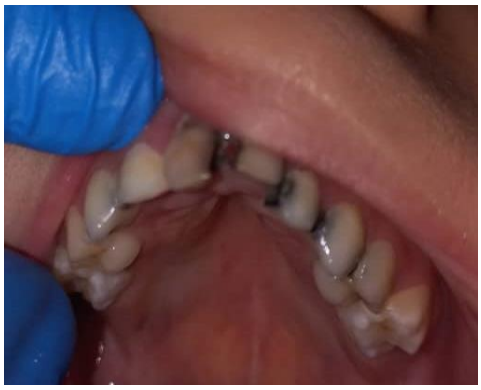

FIGURE :2

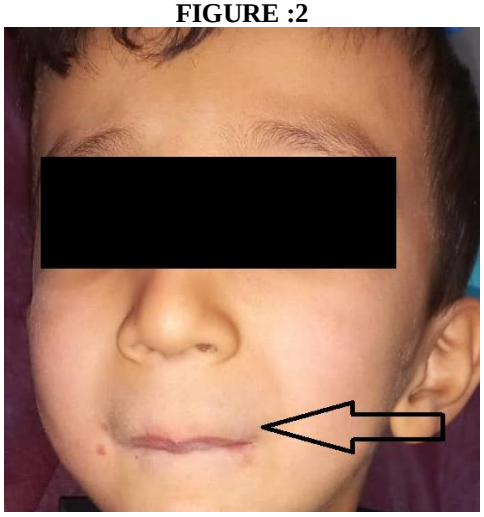

FIGURE:3

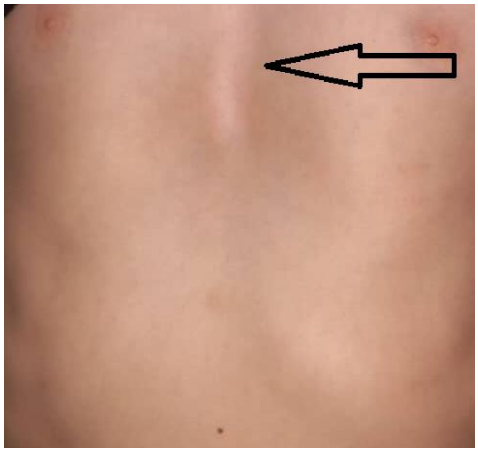

FIGURE:4

Based on his symptoms and the findings from the physical examination, we suggested a probable diagnosis of Velocardiofacial syndrome (VCFS) and advised genetic testing at a local lab. We educated the parents about the disease, including the increased risk of future psychiatric disorders. We also provided genetic counselling, discussing the potential development of VCFS in the offspring of the affected child. Additionally, we referred them to a behavioural therapist and a psychiatrist.

Despite our efforts, the patient has not returned for follow-up after the genetic testing results were expected.

DISCUSSION

VCFS, initially described by Prof Eva Sedluckova in 1955 (Sedluckova, 1955; Sedluckova, 1965) as a condition characterized by hyper nasal speech and facial dysmorphisms, was attributed to congenital shortening of the soft palate [6]. This syndrome is still known by her eponym in Czechoslovakia. Further descriptions by Angelo Di Georgi in 1965 and 1968 highlighted the absence of the thymus, parathyroid glands, and cardiac and aortic arch abnormalities (Di George, 1965; Di George, 1968). In 1978, Sphrintzen expanded on the condition, identifying palatal abnormalities, hyper nasal speech, facial dysmorphisms, congenital heart disease, and intellectual disability, coining the term "velocardiofacial syndrome" (Shprintzen, 1978). The underlying cause of VCFS, deletion of chromosome 22q11.2, was discovered in 1992 (Scambler et al., 1992) [8]

In our case, the patient displayed characteristic dysmorphic features and hyper nasal speech, a consequence of velopharyngeal dysfunction, wherein the velopharyngeal valve's incomplete closure leads to a connection between the nasal and oral cavities. This dysfunction in VCFS can result from various factors, such as cleft palate, palatal and pharyngeal asymmetry, and pharyngeal muscle abnormalities. While our patient did not exhibit palatal abnormalities, the potential presence of an occult submucous cleft palate on the nasal side of the velum could not be excluded due to the lack of a nasopharyngeal endoscopy.

Cardiac abnormalities, hypocalcaemia, and immunodeficiency, typically associated with VCFS, were absent in our patient. However, mild intellectual impairment and symptoms consistent with ADHD were observed. For ADHD management, low-dose methylphenidate is the preferred treatment. Moreover, counselling parents regarding the elevated future risk of bipolar disorder and schizophrenia is essential [3,4]. We also referred the patient to social workers to initiate targeted interventions for managing learning disabilities.

Surgical intervention is inevitably required for managing hyper nasal speech [3]. Genetic testing to confirm the chromosome 22q11.2 deletion is crucial for a definitive VCFS diagnosis. Unfortunately, resource constraints prevalent in our healthcare system present a significant obstacle to arranging affordable genetic testing, making it a challenge to overcome. Therefore, we heavily rely on our best clinical judgment as the most accessible tool. Denying a potential VCFS patient appropriate counselling and management due to resource constraints would be inappropriate. Although the potential for misdiagnosis exists, the benefits in this case outweigh the risks. Interventions such as counselling regarding possible adult-onset psychiatric illnesses, genetic counselling for reproductive decisions, and early interventions to prevent and manage learning disabilities are low-risk with significant benefits**.**

CONCLUSION:

The case report underscores the significance of recognizing VCFS within the appropriate clinical context, especially when the availability of genetic testing is limited. As the most frequently occurring microdeletion syndrome, VCFS can often be diagnosed based solely on clinical features. It is crucial to ensure that patients do not face a denial of essential counselling and management due to the challenges posed by resource constraints. The presence of low-risk interventions for such conditions necessitates a balanced approach, where clinical judgment becomes a valuable tool, enabling us to provide necessary care and support even when a definitive diagnosis remains elusive.

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