Bangladesh Journal of Medicine (BJM)
ISSN : 1023 - 1986
eISSN : 2408 - 8366

CASE REPORT

A GIRL PRESENTED WITH LEARNING DIFFICULTY AND POOR SCHOOL PERFORMANCE: A CASE REPORT

AMINUR RAHMAN[1], MD. DAHARUL ISLAM[2], MD. EKHLASUR RAHMAN[3], ZAHED ALI[4], FIROZ AHMED QURAISHI[5]

Abstract:

DiGeorge Syndrome (DGS) which is also known as chromosome 22q11.2 deletion syndrome is a primary immunodeficiency caused by the deletion of chromosome 22. Its main features include dysmorphia, hypoparathyroidism, hypocalcemia, hypoplasia or aplasia of the thymus, cardiac anomalies, renal anomalies, and behavioral/ psychiatric issues. This incurable syndrome could be treated for its complications to increase the quality of life. With the advancement of technology, DGS can now be identified in childhood itself where FISH is the main diagnostic method used. A case report of a 7 year-old girl who visited the learning difficulty, poor memorization,poor school performance and socialization problems is presented here. On the evaluation of his case, DiGeorge Syndrome was confirmed.

Keywords: *Learning difficulty; Chromosome 22q11.2 deletion; DiGeorge syndrome; Dysmorphia; Hypocalcemia; Hypoparathyroidism; Microdeletion*

Received: 09.02.2023 *Accepted: 10.04.2023*
DOI: https://doi.org/10.3329/bjm.v34i2.65617

Citation: *Rahman A, Islam MD, Rahman ME, Ali Z, Quraishi FA. A Girl Presented with Learning Difficulty and Poor School Performance: A Case Report. Bangladesh J Medicine 2023; 34: 147-150.*

Introduction:

DiGeorge syndrome (DGS) is one of the most common chromosomal disorders with an estimated incidence of 1 in 4,000-6,000 live births.[1,2] It is usually sporadic; however, autosomal dominant inheritance has been reported in 10-20% of the patients. The phenotypic expression shows wide variability.[2,3] Congenital heart defect, typical facial appearance, immune deficiency due to thymic hypoplasia, palatal cleft, velofacial dysfunction, hypocalcemia associated with hypoparathyroidism, developmental and behavioral problems are the main features associated with the syndrome.

So we report a 7 years old girl with 22q11.2 DS who presented with Learning Difficulty and socialization Problems, a condition which is unusual for this age and usually is in the differential diagnosis in early childhood.

Case report:

A 7-year-old girl born to unrelated healthy parents was attend at a pediatrician with learning difficulty, poor memorization and socialization problems . She was referred to the Department (OPD) of Neurology in Sir Salimullah Medical College Mitford Hospital, Bangladesh. Following psychiatric assessment, the

1. Assistant Professor, Dept. of Neurology, Sir Salimullah Medical College, Dhaka-1100, Bangladesh.
2. Associate Professor, Dept. of Medicine, Sir Salimullah Medical College, Dhaka-1100, Bangladesh.
3. Professor, Dept of Paediatrics, Anwer Khan Modern Medical College, Dhaka-1205, Bangladesh.
4. Professor, Department of Neurology, Sir Salimullah Medical College, Dhaka- 1100, Bangladesh.
5. Professor, Department of Neurology, Anwer Khan Modern Medical College, Dhaka-1205, Bangladesh.

Address of Correspondence: Dr. Aminur Rahman, Assistant Professor, Dept. of Neurology, Sir Salimullah Medical College, Dhaka-1100, Bangladesh. E-mail: draminur@yahoo.com

patient was referred endocrinology department at the pediatric hospital for evaluation of possible hypoparathyroidism. The patient's mother reported that she was inattentive, poor school performance and asocial. The girl had a medical history of mild recurrent numbness in his hands in the past 2 years. There is no history of recurrent infection.

During the physical examination, mild facial dysmorphism was seen prominent nose prominent nose, antimongoloid slant, telecanthus, ocular hypertelorism, and long face (Figure: 1) .The voice was hypernasal. Chvostek and Trousseau signs were positive. Systemic findings were otherwise normal.

The laboratory investigations revealed a serum calcium level of 6.6 mg/dL (Normal 9-10.5 mg/dL), phosphorus 8 mg/dL (Normal: 2.4 to4.1 mg/dL) parathormone level of 8 pg/mL (normal: 10-65), 25-hydroxyvitamin D level of 25 ìg/L, and urine calcium/ creatinine ratio of 0.01. His thyroid hormone levels were within the reference range (Table: 1). The thymus was not visualized at scintigraphic evaluation bur her immunologic studies revealed normal. The echocardiography of the patient revealed normal. Ultrasonography of the left kidney has demonstrated a cortical cyst which is again a feature of DGS. Fluorescence in situ hybridization (FISH) analysis, showed the chromosome 22q11.2 deletions. This diagnosis, suggested by the clinical and biochemical findings, was found to be associated with 22q11.2 DS, which was shown by FISH as a heterozygote deletion. Calcium replacement therapy, combined with active vitamin D was started.

Laboratory Findings and Analysis:

Table-I : *Interpretation of laboratory findings*

LaboratoryInvestigation	Result	Normal Level
Serum Calcium	6.6 mg/dL	9 – 10.5 mg/dL
Phosphorus	8 mg/dL	2.4 – 4.1 mg/dL
Alkaline phosphatase (IU/L)	244	145-420
Magnesium (mg/dL)	1.9	1.5-2.3
Albumin (g/dL)	4.8	4.0-5.3
Parathormone (PTH)	8 pg/mL	10 – 65 pg/mL
25-hydroxyvitamin D	25 ìg/L	>30 ìg/L
Urine Calcium/ Creatinine ratio	0.01	<0.14
CD3+ (CD16+56+)	60-68%	58-82%
Thyroid Hormones	Normal	

Table-II : *Findings of the patient*

Features of DiGeorge syndrome	Patient
Dysmorphic findings	Subtle Hypoplasia
Thymic hypoplasia/aplasia	Absent
Recurrent infection	Yes
Hypoparathyroidism	Absent
Heart defect	No
Renal involvement	Cortical cyst

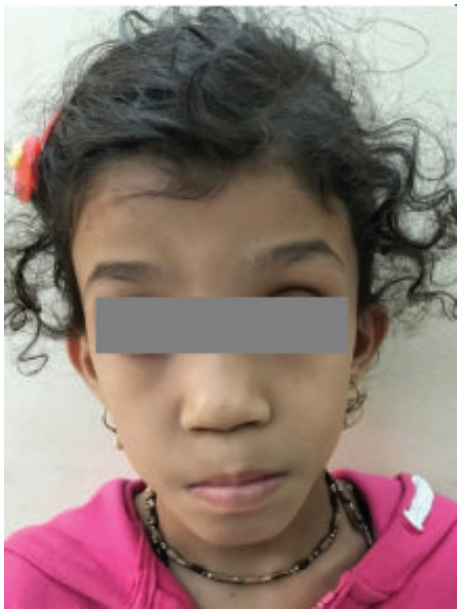

Figure 1 *A girl with DGS - prominent nose, antimongoloid slant, telecanthus, ocular hypertelorism, and long face*

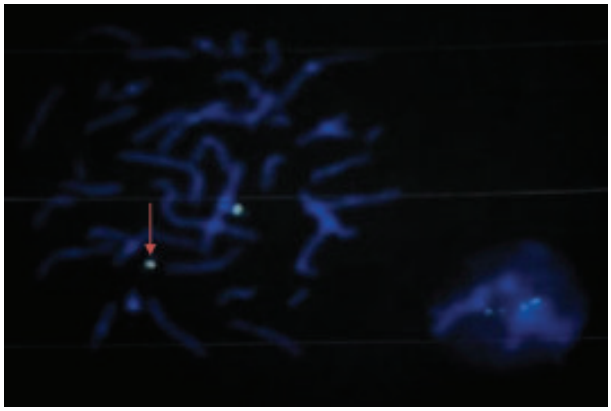

Figure 2. *FISH analysis with the Zygolight SPEC HIRA probe specific to Di-George region, arrow shows a deletion of chromosome 22q11.2*

Discussion:

Hypoparathyroidism and the resulting hypocalcemia are among the main features of 22q11.2 DS, and are observed in 70 of individualities with this deletion. [4, 5] The hypocalcemia may be of variable inflexibility. In the severest cases, the hypocalcemia is natural. Still, latent hypoparathyroidism is more common than patient cases with characteristic hypocalcemia.[6, 7] In the most cases, hypocalcemia resolves around one time of age, but recurs in in childhood or in adolescence. In latent hypoparathyroidism, PTH is secreted in sufficient amounts in in basal states, and serum calcium (Ca) and phosphorus (P) situations are normal. However, when Ca intake is not sufficient, especially when Ca requirements are high such as the case in infancy, adolescence or pregnancy, PTH secretion becomes inadequate and hypocalcemia becomes evident as recurrent numbness.[7, 8.]Mild recurrent numbness in his hands in the past 2 years in our case were presumably related to latent hypoparathyroidism, which came decompensated during puberty, due to increased calcium demand that wasn't met by an acceptable PTH response.

DGS can be associated with generalized anxiety, phobias, attention deficit hyperactivity disorder; autism, social isolation in children severe psychopathology, in adults including bipolar disorder and schizophrenia in adults. Cognitive disabilities are seen in 40 to 46% of individuals with 22q11.2 deletion and the majority of them are mild to moderate [9]. For this reason, it is possible for patients with undiagnosed DGS to first be admitted to a psychiatry department. So our patient had cognitive disabilities and social isolation. Another manifestation of our case was velopharyngeal dysfunction, which redounded in hypernasal voice and deceleration in speech development.

Congenital heart defects and immune deficiency, which are among other findings reported for cases with 22q11 DS, weren't encountered in our case. natural asymmetric crying facies, caused by the absence or hypoplasia of the depressor angulioris muscle on one side of the mouth, has also been reported in 22q11 DS.[2,10] This finding wasn't seen in our case.

There isno phenotype- genotype correlation in 22q11 DS.[7, 10] Wide phenotypic variabilities are seen indeed among family members with the same mutations. [8, 11] Thus early diagnoses may be difficult. A thorough clinical observation is necessary not to over diagnose the cases with atypical findings. It's easy to make the opinion of 22q11 DS in the presence of natural heart blights, palatal disfigurement and characteristic early onset hypocalcemia. Therefore, in the absence of these major findings, as was the case in our case, 22q11 DS must be considered in differential diagnosis of developmental delay,, velopharingeal dysfunction, intermittent attacks of croup, and mild dysmorphic features. Beforehand opinion may prompt early operation of learning difficulties.

Conclusion:

Hypocalcemia due to latent hypoparathyroidism in late childhood and in puberty should be considered in the differential diagnosis of 22q11 DS.

Conflict of Interest:

The authors stated that there is no conflict of interest in this study

Funding:

This research received no external funding.

Consent:

For the purpose of publishing this case report and any related photos, the parents are written informed consent was acquired.

Acknowledgments:

The authors were grateful to the staffs of the Department of Neurology in Sir Salimullah Medical College Mitford Hospital, Bangladesh.

References:

1. Devriendt K, Fryns JP, Mortier G, van Thienen MN, Keymolen K. The annual incidence of DiGeorge/velocardiofacial syndrome. J Med Genet 1998; 35:789-790. https://doi.org/10.1136/jmg.35.9.789-a PMid:9733045 PMCid:PMC1051442
2. Driscoll AD, Sullivan EK. DiGeorge syndrome; A chromosome 22q11.2 deletion syndrome. In Primary immunodeficiency diseases. 2nd edition. Oxford Uni. Press 2007;485-495.
3. Al-taie N, Scheuter-Mlaker S, Schlesinger M, Abrahamian H Case report: DiGeorge syndrome presenting with hypoparathyrodism and Learning Difficulties in adulthood. British Journal of Medical Practitioners. 2014;7(4): a730.
4. Jolin EM, Weller RA, Jessani NR, Zackai EH, McDonald-McGinn DM, Weller EB. Affective disorders and other psychiatric diagnoses in children and adolescents with 22q11.2 Deletion Syndrome. J Affect Disord 2009; 119:177-180. https://doi.org/10.1016/j.jad.2009.02.016 PMid:19269692
5. Shprintzen RJ. Velo-cardio-facial syndrome. In: Cassidy SB, Allanson J (eds). Management of genetic syndromes. 2nd ed. New York, Wiley, 2004;615-632. https://doi.org/10.1002/0471695998.mgs051

6. Swillen A, Devriendt K, Legius E, Eyskens B, Dumoulin M, Gewillig M, Fryns JP. Intelligence and psychosocial adjustment in velo-cardio-facial syndrome: a study of 37 infants and children with VCFS. J Med Genet 2007;34:453-458. https://doi.org/10.1136/jmg.34.6.453 PMid:9192263 PMCid:PMC1050966

7. Greig F, Paul E, DiMartino-Nardi J, Saenger P. Transient congenital hypoparathyroidism: Resolution and recurrence in chromosome 22q11 deletion. J Pediatr 1996; 128:563-567. https://doi.org/10.1016/S0022-3476(96)70372-4 PMid: 8618195

8. Scire G, Dallapiccola B, Iannetti P, Bonaiuto F, Galasso C, Mingarelli R, Boscherini B. Hypoparathyroidism as the major manifestation in two patients with 22q11 deletions. Am J Med Genet 1994;52:478-482. https://doi.org/10.1002/ajmg.1320520415 PMid:7747762

9. Van den Berge K, Diderich K, Poddighe P, Berghout A. Symptomatic hypoparathyroidism based on a 22q11 deletion first diagnosed in a 43-year-old woman. Neth J Med 2009;67:102-104

10. M. Digilio, B. Marino, R. Capolino, and B. Dallapiccola, "Clinical manifestations of deletion 22q11.2 syndrome (DiGeorge/Velo-Cardio-Facial syndrome)," Images in Pae- diatric Cardiology, vol. 7, no. 7, pp. 23-34, 2005.

11. D. M. McDonald-McGinn, N. Minugh-Purvis, R. E. Kirschner et al., "The 22q11.2 deletion in African-American patients: an underdiagnosed population?" American Journal of Medical Genetics Part A, vol. 134A, no. 3, pp. 242-246, 2005. https://doi.org/10.1002/ajmg.a.30069 PMid:15754359 PMCid:PMC2810968