Case Report :

Neuro-Psychological Profile of Velocardiofacial Syndrome - A Case Report

Priyanka Shukla[1], Debasish Padhi[2], K. S. Sengar[3]

ABSTRACT:

Velocardifacial (VCFS) is congenital problem with the physical and psychological anomalies having significant positive correlation with various psychiatric/neuropsychological problems. Most commonly reported is schizophrenia 25% followed by ADHD 20%. Apart from these psychiatric co morbidities, number of cognitive impairments is also common in the cases of Velocardiofacial syndrome.

The objective of this case history presentation is to discuss neurocognitive functions of the cases with such rare entity. To find out the neuropsychological profile and cognitive impairment detail psychological evaluation was done. On psychological evaluations patient was cooperative and participated actively in testing. Results support the view that such patients are having significant difficulty in the area of cognition and suspected anomalies in the functioning / lesion in the multiple area of the brain. Results further reveals the deficits in the area of memory, attention, visuospatial ability, intelligence, social skills and overall in personality. VCFS is complex problem related to physical, congenital cardiac anomalies and multiple psychiatric symptoms need multimodal intervention approach including behavioural, cognitive and neuropsychological rehabilitation for the management of the syndrome.

Key words: ***Velocardiofacial Syndrome, Schizophrenia, Neurocognitive, Congenital, ADHD***

Introduction:

Velocardiofacial Syndrome (VCFS) was described first clinically by Kirkpatrick and DiGeorge in the 1960s and later on by Shprintzen and colleagues in the 1970s. The physical phenotype of VCFS is highly heterogeneous, with 180 possible clinical manifestations. It has significant cognitive / physical involvement as it was defined as a constellation of immunologic deficiencies secondary to thymus, hypoplasis and hypocalcaemia, secondary to hypoparathyrodism. The most common ones are-congenital anomalies present in about 75% of patients who have VCFS. The most prevalent are tetralogy of Fallot, ventricular septal defect with pulmonary atresia, persistent truncus arteriosus, and interrupted aortic arch. On screening of patients with cardiac anomalies, 3% to 15% had the chromosomal deletion indicative of VCFS (Marino, Mileto and Digilio, 2005). ***VCFS understand by palate anomalies (velo) congenital cardiovascular defects (cardio) and mild facial dysmorphism (facial).*** Abnormal facies are common in VCFS and are characterized by hypoplastic alae nasi, prominent nasal root, long narrow face with flat cheeks, narrow eye opening, small mouth and retruded chin, and small-cupped ears. Palatal abnormalities are present in up to 75% of patients. Most affected patients have insufficiency of the palate, with cleft palate being less common and cleft lip being rare. Clinically, the cleft anomalies in VCFS cause hypernasal speech, (Kirscher, 2005). Other physical features of VCFS include tortuous retinal vessels, growth retardation, juvenile rheumatoid arthritis, and urinary system anomalies. Since its inception in early 1960s researchers discovered that VCFS is extremely wide and includes more than 180 possible congenital anomalies.

Though the reported prevalence of VCFS is around 1 in 10000 but the magnitude of the problem may be severe as the actual prevalence of the VCFS is difficult to ascertain because the diagnosis of VCFS is only possible through cytogenetic test and high cost of FISH *(Flurscence in Situ Hybridization)* test is not allowing the people and clinicians as well for easy excess of such testing. It is proved that the VCFS is caused by chromosome 22 at band 22q 11.2. Therefore some clinicians are in favor of renaming the syndrome as 22q11.2 deletion syndrome.

The VCFS and psychiatric problems have been found positively correlated. Especially VCFS and schizophrenia are highly associated as 25% persons suffering from VCFS develop schizophrenia. Overall 79 % cases of VCFS reported for having psychiatric

disorders mainly ADHD, Anxiety disorder and also Mood disorder. They also share common problem like social isolation / withdrawals, social rejection, low self esteem, and deficits in social skills (Basset A S, Chow EW, Abdel Malik et al, 2003).

The embryonic origin of physical disease associated with VCFS is impaired migration of the neural crest cells which give rise to mesenchyme of the third and forth pharyngeal arches which further differentiate into face, cleft, thymus, parathyroid glands and cardiovascular system. The region containing the smaller 1.5 million base deletions in VCFS contains 24 genes. It is likely that a haploinsufficiency (missing part) of one or combination of these genes predisposes the individual who has VCFS to the accompanying physical and psychological symptoms. TBX_1 gene have been found responsible for developmental anomalies, common features include thymus and parathyroid glands, hypoplasia, cardiac outflow abnormalities, abnormal facial structure, vertebrae and cleft palate. It also plays significant role in development of arteries. TBX_1 protein potentially contribute in neuropsychiatric and cognitive deficits in VCFS (Mc Darmid H E, Marrow BE, 2002 & Paylor R, Glaser B, Mupo A, et. al., 2006)

Case History:

A case report is presented of Mr. U., 22 years old, male, unmarried, no family history of psychiatric illness, but having past history of two psychotic episodes from since 6 years. The Patient was born out of full term normal delivery at hospital; there is history of delayed milestone development, he took lot of time in learning essential life skills like speaking, taking food, self care, etc. The patient was restless and hyperactive from the childhood but his problem was increased since last 6 years. Most of the time, he keeps on moving here and there and had roaming around tendency. Once he goes outside, never come back by his own. He is over talkative and making big claims, he has the behavioural oddities like teasing the girls of village, his sleep was decreased, and he hardly sleeps 2-3 hours out of 24 hours. He takes his personal care properly but did not bear his responsibilities properly. His pervasive and persistent mood was cheerful. On mental status examination (positive findings), he was kempt and tidy, eye contact was maintained, rapport was established, cooperative attitude, decreased reaction time with increased productivity of speech, restlessness, affect cheerful, appropriate and communicable, delusion of grandiosity, impaired judgment, grade one insight was present. No H/o Tics, mannerism, stereotypy was reported.

Mr U was assessed for his multiple functioning on following tests:

- PGI –Battery of brain dysfunction (PGI-BBD)
- Wechsler Adult Performance Intelligence Scale (WAIS)
- Stanford Binet Intelligence Scale,
- Vineland-Social Maturity Scale (VSMS)
- Luria-Nebraska Neuropsychological Battery (LNNB)
- Rorschach Inkblot Test
- Human Figure Drawing Test (HFDT)
- Indian Disability Evaluation and Assessment Scale (IDEAS)
- Conner's Rating Scale,
- Young-Mania Rating Scale (Y-MRS)

Results: The following tests findings of assessment has been drawn and are being presented -

Attention Patient has poor level of attention and unable to focus attention n task (concentration) and on PGI-BBD; significant level of cognitive dysfunctions was elicited.

I Q His intellectual and social adaptive functioning was on the border line level. Performance IQ is poor than Verbal IQ

Human Figure Drawing
- Moderate level of cognitive impairment.
- Poor self concept, low energy, high aspiration
- Hostility,
- Regression and organicity

On Rorschach
- Poor Productivity
- Quick reaction time
- Conservative processing approach
- Uses the fantasy for reality in stressful situation
- Serious meditational impairment.
- Highly vulnerable to loss of control and unable to cope with the stress.
- Has an avoidant extratensive style.
- Tendency to economize and avoid complexity.
- Prone to use his feelings more directly in decision making by merging them with his thought.

- Poor human empathy and
- Reserved interest level

Neuropsychological deficits on LNNB
- Impaired Visuo-spatial skills
- Deficits in expressive speech
- Intact writing ability on written material but inability to write on auditory commands/stimulus.
- Disruption on reading ability
- Mild dysfunctions on arithmetic
- Dysfunction in short term memory and intermediate memory.

- **Findings on Young Mania Rating Scale, Corner's Rating Scale and IDEAS** suggests:
  - Manic like symptoms,
  - ADHD like symptoms and
  - Moderate level of disability on social functioning.

Discussion:

The VCFS is complex congenital anomalies / problem caused by physiological and genetic abnormality, commonly associated with multiple psychiatric conditions. Studies of school aged children shows that already in childhood, individual who had VCFS had high psychiatric morbidity with multiple behavioural and cognitive abnormalities more commonly ADHD, anxiety disorder, mood disorder and schizophrenia the findings of the present study are in similar track where it is apparent that this case has shown borderline level of social and daily living skills and social adaptive functioning. The individual suffering from VCFS most often share the common risk factor such as social isolation and rejection by family members and otherwise too may also be contributing factor for impairment in social isolation, persistent low self evaluation, and poor interaction with environment. The findings of present case study on LNNB suggests lesion in left hemisphere and the possible involvement of left temporal lobe, might be responsible for poor attention process, and difficulty in organizing the things in proper useful manner. The findings are consistent with Bish JP et al. (2005). The MRI findings of the children having VCFS is in favor of abnormal activation of the parietal cortex and the researchers proposed that a parietal dysfunctions in individual who have VCFS may impair their ability to orient visual cues and contribute to an overall executive dysfunctions (Gothelp D, Hoeft F, HinardC, et al, 2007). The result of the present study shows the evidence of poor intellectual functioning of the case, discrepancy in verbal and performance IQ as the verbal IQ is more than performance IQ. The full scale IQ of present case is on borderline category. These findings are further consistent with the study of Swillen, Devriendt and Legius (1997). The average full-scale IQ score in individuals with VCFS is in the mid- 70s, within the borderline-intelligence range, in 25% to 40% of subjects intelligence is in the mental retardation range. Cross-sectional studies in children who had VCFS indicated an 8 - to 10-point higher verbal IQ (VIQ) than performance IQ (PIQ) (Campbell and Swillen, 2005) whereas in adults, VIQ was 3.6 points lower than PIQ, (Henry, Amelsvoort and Morris, 2002). The evidence of decline of VIQ scores in adults is confirmed by longitudinal study (Gothelf D, Elliez S, Thompson T et al, 2005).

The cognitive profile of subjects who have VCFS is characterized by relative strength in the area of reading, spelling and weakness in visuospatial memory and arithmetic. The cognitive level task requires the shift of attention cognitive flexibility and working memory functions mainly dealt by frontal cortex and caudate nucleus and task related to visuospatial numerical ability by posterior parietal cortex is found impaired as the findings of LNNB clearly indicate the possible lesion in the posterior area of temporal lobe and adjacent area of the parietal lobe as well. The findings are consistent with the findings of Eliez S, Barnea-Goraly N, Schmitt J E et al (2002) and Simon T J, Beardon C E, Mc- Ginn DM et al, (2005). The individual having VCFS also manifest deficient skills in various area, poor self concept, poor decision making, presence of hostility/ aggression might be considered as resultant of lesion/deficits / involvement of various significant areas of the brain which platys very significant role either independently or conjointly with other areas on above neurocognitive / sociocognitive functions. The findings of the study also reveal the manic like symptoms and ADHD like symptoms. VCFS have increased rate of affective disorders. Mood swings are common. About two third children and adolescents reported the problem of bipolar disorder (Poplas D F, Feadda G L, Veit S et al, 1996, Fenstien C, Eliez S Blacy C et al 2002).

Since the VCFS is not simple entity rather it's a complex set of physical, psychological, neurological and physiological problems. In individuals with VCFS physical, psychiatric and neurocognitive deficits vary widely in scope and severity. Because of the complexity of the problems the management is another challenging task for clinicians/ psychiatrist as antipsychotic medicines most

often produce multiple side effects. Because schizophrenia and ADHD is most common psychiatric co-morbidities with VCFS, the question arises whether to provide stimulants medication. There are multiple concerns regarding the use of stimulants/antidepressants/ antipsychotics in subjects having VCFS because of their congenital cardiac anomalies and the use of such medicines can increase the risk of hypertension and tachycardia. In such condition apart from pharmacological (psychotropic or otherwise) multimodal treatment approach is required, including behavioural intervention, cognitive rehabilitation, social skill training and parental guidance in cases of children to be considered inevitable part of management of VCFS syndrome.

Conclusion: Velocardiofacial Syndrome (VCFS) was described in 1960s with multiple physical, psychological and congenital cardiac anomalies. Further researches supported the view of common co morbidities of psychiatric disorders and multiple cognitive deficits and neurological involvement as well. Such complex conditions produce the difficulty on diagnostic clarification and challenge for clinician in management process of such syndrome. It needs the sharp skills of clinician to identify the problem symptoms for arrival of specific diagnosis and use of multimodal approach of intervention for the management of multiple physical, cognitive, psychiatric, behavioural and social problems. Sometimes in case of children parental counseling and family counseling in case of adulthood onset of problem may also become essential to deal with problem successfully in totality.

REFERENCES:-

- Baset A S, Chow EW, Abdel Malik et. al. (2003). The schizophrenia phenotype in 22q11deletion syndome. *American Journal of Psychiatry*, 160: 1580-6.
- Bish JP, Firrante SM, Mc Donald – McGinn D, et al. (2005): Maladaptive conflict montoring as evidence for executive dysfunction in children with chromosome 22q11.2deletion syndrome. *Dev Science*; 8:36-43.
- Campbell LE, Swillen A. The cognitive spectrum in velo-cardio-facial syndrome. In: *Velocardio- facial syndrome: a model for understanding microdeletion disorders*. Cambridge (MA): Cambridge University Press; 2005. p. 147–64.
- Conner, C.K.(1997). *Conner's Parent Rating Scale-Revised*. North Tonawanda, NY: Multi Health System.
- Doren Gothelf (2007); Velocardiofacial Syndrome; Child and Adolescents Psychiatric Clinics of N America; 16;677-693.
- Eliez S, Barnea-Goraly N, Schmitt JE et.al. (2002): Increased basal ganglia volume in velo-cardio-facial syndrome (deletion 22q11.2). *Biological Psychiatry*; 52:68-70.
- Exner J.E. (1991). *The Rorschach: A comprehensive system*. Volume 1: Basic foundation (2nd edition). New York: Wiley
- Feinstein C, Eliez S, Blasey C, et al. Psychiatric disorders and behavioral problems in children with velo-cardio-facial syndrome: usefulness as phenotypic indicators of schizophrenia risk. *Biol Psychiatry* 2002; 51:312–8.
- Gothelf D, Hoeft F, Hinard C (2007): Abnormal cortical activation during response inhibition in 22q11.2 deletion syndrome; *Human Brain Mapp*. in press
- Gothelf D, Eliez S, Thompson T, et al. COMT genotype predicts longitudinal cognitive decline and psychosis in 22q11.2 deletion syndrome. *Nat Neuroscience*, 2005; 8:1500-2.
- Henry JC, Van Amelsvoort T, et al. (2002); An investigation of the neuropsychological profile in adults with Velocardiofacial syndrome (VCFS). Neuropsychologia; 40:471-8.
- Kirkpatrick JA Jr., Di George AM (1968); Congenital absence of the thymus. American Journal of Roentgenol Radium Ther Nucl Med; 103: 32-7
- Kirscher RE. (2005): Palatal anomalies and velopharyngeal dysfunction associated with velo-cardio-facial syndrome. *In: Velo-cardio-facial syndrome: a model for understanding micro deletion disorders*. Cambridge (MA): Cambridge University Press, pp. 83–104.
- Marino B, Mileto F, Digilio MC, et al.(2005): Congenital cardiovascular disease and velo-cardio-facial syndrome. In: Murphy KC, Scambler PJ, editors. *Velo-cardio-facial syndrome: a model for understanding micro deletion disorders*. Cambridge (MA): Cambridge University Press; pp. 47–82.
- Mc Dermit HE, Morrow BE (2002): Genomic disorder on 22q11. *American Journal of Human Genetics*; 70:1077-1088.
- Paylor R, Glaser B, Mupo A et al. (2006): Tbx1haploinsufficiency in linked to behavioural disorders in mice and humans. *Proc Natl Acad science*; 103:7729-34.

- Papolos DF, Faedda GL, Veit S, et al. (1996); Bipolar spectrum disorders in patients diagnosed with velo-cardio- facial syndrome: does a hemizygous deletion of chromosome 22q11 result in bipolar affective disorder? *Am J Psychiatry*; 153:1541–7.
- Ramalinga Swami, P. (1974); *The Measurement of intelligence among Adult Indians*. New Delhi: National Council of Education Research and Training.
- Shprintzen RJ, Goldberg RB, Lewin ML, et al.(1978); A new syndrome involving cleft palate,cardiac anomalies, typical facies, and learning disabilities: velocardio-facial syndrome. *Cleft Palate* J;15:56–62
- Simon TJ, Bish JP, Bearden CE, et al.(2005); Amultilevel analysis of cognitive dysfunction and psychopathology associated with chromosome 22q11.2 deletion syndrome in children. *Dev Psychopathology*, 17:753–84
- Swillen A, Devriendt K, Legius E, et al. (1997); Intelligence and psychosocial adjustment in velocardiofacial syndrome: a study of 37 children and adolescents with VCFS. *J Med Genet*; 34:453–8.
- Young, R.C., Biggs, J.T., Ziegler, V.E. (1978); A Rating Scale for Mania: Reliability, Validity, and Sensitivity. *British Journal of Psychiatry*, 133: 429-435.

Authors

1. Priyanka Shukla
   Research Officer, Dept. of Clinical Psychology
2. Debasish Padhi
   Senior Resident, Department of Psychiatry
3. K. S. Sengar
   Associate Professor, Dept. of Clinical Psychology,
   Ranchi Institute of Neuropsychiatry and Allied Sciences (RINPAS), Kanke, Ranchi.

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