International Journal of Research and Review
www.ijrrjournal.com E-ISSN: 2349-9788; P-ISSN: 2454-2237

Case Report

Behavioural Phenotype of Fragile X Syndrome - A Case Study

Yogender Kumar Malik[1*], Manoj Kumar[2*], Ruchita Shah[3*], Poonam Adlakha[4]**

[1]Senior Resident, [2]Junior Resident, [3]Assistant Professor, [4]Senior Resident,
[*]Department of Psychiatry and [**]Pathology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Corresponding Author: Yogender Kumar Malik

ABSTRACT

Behavioral phenotypes are syndromes with a chromosomal or genetic etiology, comprising both physiological and behavior manifestations. Behavioral phenotypes are likely to be dynamic, changing during development and aging. Behavioral phenotypes of intellectual disability syndromes are extreme phenotypes and are rare or absent in the general population. Fragile X syndrome (FXS) is the most common worldwide cause of inherited intellectual disability. We hereby describe behavioural phenotype of fragile X syndrome in a pair of male siblings

Key words: Fragile X-syndrome, *Behavioral phenotype,* Intellectual disability.

INTRODUCTION

The behavioral phenotype refers to a characteristic pattern of social, linguistic, cognitive, and motor observations consistently associated with biological/ genetic disorder. [1] Behavioral phenotypes of intellectual disability syndromes are extreme phenotypes and are rare or absent in the general population. [2] Fragile X Syndrome (FXS) is an X- linked dominant disorder caused by the amplification of a CGG repeat in the 5′ untranslated region of the FMR. Rare but most common inherited cause of intellectual disabilities. [3] FXS present with a wide range of developmental, behavioral or emotional dysfunctions along with neuropsychiatric symptoms. The presentation varies by gender with males more severely affected. [4] Studying about typical behavior of behavioral phenotype increased the understanding in investigating the new or more specific treatment options for mental or behavioral disorders. We hereby describe male siblings with behavioural phenotype of fragile X syndrome with psychiatric symptoms.

Clinical Cases

Sibling 1

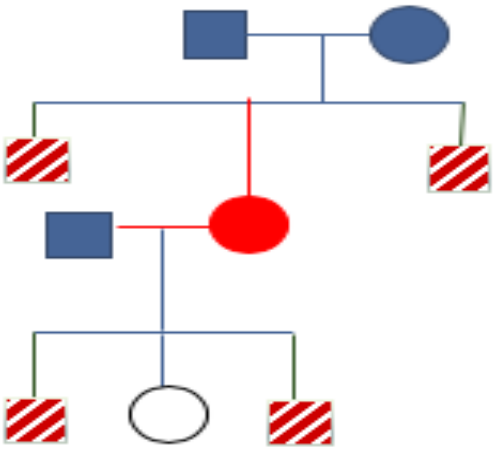
17-year old boy (offspring of a woman with FXS carrier status) presented with deficit in intellectual, emotional and behavioral functioning with classical physical characteristics. History and mental status examination was suggestive of behaviour phenotype as excessive shyness, constantly anxious, separation anxiety, scared, excessive fear to noises, reminiscent of social phobia, gaze aversion, pervasive ignoring, inappropriate laughing, tactile defensiveness, difficulty in willingness and social interaction, clinging behaviour, aloof, lack of curiosity about the environment and irritability typically provoked by environmental stressors. Phenotypically the

boy appeared large forehead with frontal bossing, large and anteverted ears, intraoral ogival palate, dental hypo mineralization, crowded teeth, high arch palate, joint hyperlaxity, hypotonia and unilateral macro orchidism. On psychological assessment his intellectual quiescent was 21. Parents were psycho educated about the illness and disability certification provided to them. The pre vocational training started as a part of rehabilitation management.

Sibling 2

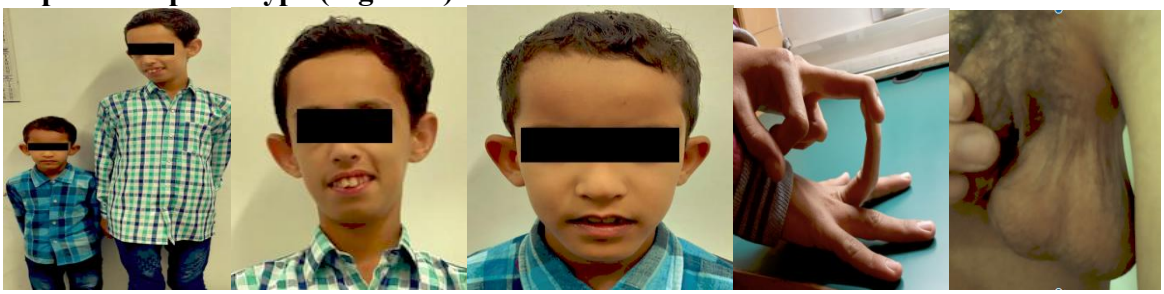
8-year old boy (offspring of a woman with FXS carrier status) presented with deficit in language, intellectual, emotional and behavioral with characteristics physical appearance. History and mental status examination was suggestive of no spontaneous initiation of speech and communication, monotonous speech, use language phrase inappropriately, difficulty in conveying simple things, pointing nonverbal communication, fearful, agoraphobic, inattentive, frequent temper tantrums, repetitive and stereotypic behavior and inappropriate laughing and crying. Phenotypically the boy appeared large forehead with frontal bossing, large and anteverted ears, crowded teeth, high arch palate, smooth skin and joint hyperlaxity. On psychological assessment his intellectual quiescent was 35. Parents were psycho educated about the illness and disability certification provided to them. The pre vocational training started as a part of rehabilitation management.

Family pedigree (Figure 1)



The two-generation- family history of intellectual disability and typical characteristics of fragile X syndrome genetically younger brother has full mutations more than 200 repeats CGGG at FMR1 locus. Mother has borderline to mild intellectual disability as a carrier and two maternal uncles have similar behavioral and physical phenotype as in siblings.

The patient's phenotype (Figure 2)



Note the typical facial features of fragile X-syndrome, such as the elongated
Face, prominent mandible, large anteverted ears, crowded teeth, joint hyperlaxity, and macroorchidism.

DISCUSSION

The cognitive, behavioral and physical phenotype of FXS varies by sex, with males more severely affected because they have only one X chromosome. [5] Physical characteristics may include a long, narrow face, high arched palate, prominent ears, and enlarged testicular volume as seen in index case. [6,7] The FXS phenotype typically involves a variety of psychiatric symptoms, including intellectual disability, features of autism, attention deficit/

hyperactivity disorder, anxiety, and aggression most of them also seen in index case. [8]

Behavioral phenotypes are likely to be dynamic, changing during development and aging. The development of Alzheimer's disease with age is a classic example of behavioral and cognitive phenotype of Down syndrome. [1] So it is important that clinicians are able to anticipate the impact of aging on behavior, ability, and mental health and that they are aware of the likely future medical complications. As we know FXS is an example of a genetic disorder that shows anticipation (more severe presentation in successive generations in families). Like in index case both the sibling are male so there are chances of developing more and severe form of neuropsychiatric manifestation in near future, need to be have proper assessment and management of presenting symptoms. The index case also has the syndrome in two maternal uncles and mother as carrier. So the diagnosis of fragile X syndrome should be considered during genetic counseling of every individual with mental disability or in intellectual disability "syndromes" to prevent future complications and more severe presentation in successive generations.

CONCLUSIONS

Fragile X syndrome as a pathology in which the cognitive and behavioral phenotype plays a role in children's education and social life, should be diagnosed in early childhood to allow adequate management and genetic counseling for the family. As fragile X syndrome present with wide range of psychiatric manifestations so appropriate assessment is important but can be challenging in the majority of patients with intellectual impairment. Further research is needed in order to treating psychiatric manifestations.

REFERENCES

1. O'Brien, G., & Bevan, R. (2011). Recent advances in behavioral phenotypes as they affect adults. Advances in Mental Health and Intellectual Disabilities, 5;5–14.
2. E. Tsakanikos and J. McCarthy. Handbook of Psychopathology in Intellectual Disability: Research, Practice and Policy; 2014.
3. Terracciano A, Chiurazzi P, Neri G. Fragile X syndrome. Am J Med Genet C Semin Med Genet. 2005;32-7.
4. Tsiouris JA, Brown WT. Neuropsychiatric symptoms of fragile X syndrome: pathophysiology and pharmacotherapy. CNS Drugs. 2004; 687-703.
5. Fryns JP, Jacobs J, Kleczkowska A, van den Berghe H. The psychological profile of the fragile X syndrome. Clin Genet. 1984;131–4.
6. R. J. Hagerman and P. J. Hagerman, Fragile X Syndrome: Diagnosis, Treatment, and Research, Johns Hopkins University Press (JHU Press), Baltimore, Md, USA, 2002.
7. S. A. Kidd, A. Lachiewicz, D. Barbouth et al., "Fragile X syndrome: a review of associated medical problems," Pediatrics, 2014.
8. Tranfaglia MR. Fragile X syndrome: a psychiatric perspective. Results Probl Cell Differ. 2012;281–95.

How to cite this article: Malik YK, Kumar M, Shah R et.al. Behavioural phenotype of fragile X Syndrome - a case study. International Journal of Research and Review. 2019; 6(8):41-43.

******