

CASE REPORT

A CHILD WITH ADVANCED MUCOPOLYSACCHARIDOSIS PRESENTING WITH SEVERE BEHAVIOURAL PROBLEMS

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Abstract

Objective: Clinicians are less familiar with clinical presentation of rare disorder like mucopolysaccharidosis (MPS), especially as presentation is complex and varied with different subtypes of this disorder. This case report highlights severe behavioural problems and non-recognition of MPS by clinicians. Though behavioural problems, hyperactivity and aggression are common in children suffering from mental disability, they are also seen in rare metabolic disorders like MPS. **Methods:** We have reported a seven year old girl who presented with severe episodes of hyperactivity, poor social interaction, impaired understanding of speech and delay as well as regression in developmental milestones is presented along with the investigations and treatment given. **Results:** Initially, the child was thought to be suffering from intellectual subnormality and/or pervasive developmental disorder. However, radiological studies showed x-ray findings suggestive of MPS. Her developmental history, physical findings, hearing loss as noted on BERA further supported this diagnosis. Due to financial constraints of the family detailed investigations (enzyme assays) to know the exact type of MPS could not be done. Behavioural problems had to be managed with low dose clonazepam and carbamazepine. **Conclusion:** It is worth considering metabolic disorders as one of the important differential diagnosis in any child presenting with developmental problems, dysmorphic facies along with behavioural problems. *ASEAN Journal of Psychiatry, Vol. 16 (1): January – June 2015: XX XX.*

Keywords: Mucopolysaccharidosis (MPS), PDD, Mental Retardation

Introduction

A child presenting with severe behavioural problems is often a challenging situation for a psychiatrist. In absence of significant intellectual subnormality, differential diagnoses like autism spectrum disorders, emotional disorders, and conduct disorder are considered.

Mucopolysaccharidosis (MPS) is a rare but serious metabolic disorder. Type – III disorder is seen in 1 in 2500 live births, while other types are further rare (1 in 100,000).

Prevalence may be underestimated due to under diagnosis of this condition. Very few cases have been reported from Indian population.[1,2,3] It is caused by the absence or malfunctioning of lysosomal enzymes needed to break down Glycosaminoglycans [3,4]. These accumulate in cells, blood and connective tissue which results in permanent progressive cellular damage affecting appearance, physical abilities, mental development and functioning of various organ systems. The child usually presents between 3 – 6 years, with dysmorphic features and deterioration of mental and intellectual

functioning [5]. Diagnosis is clinically suspected based on presenting complaints and facial appearance. Laboratory investigations are needed to confirm the diagnosis. Currently management of this disease is directed more towards symptomatic relief rather than the actual cure. Enzyme replacement therapy has proved useful to some extent. Administration of genistein, a soy-bean derived isoflavone, ameliorates disease severity in MPS III to some extent, by inhibition of Glycosaminoglycan synthesis. Bone marrow transplant and umbilical cord blood transfusion have been tried with limited success [6 - 8].

This paper focuses on identification and psychiatric management in this condition.

Method and results

Case history

A 6 years and seven months old girl was brought by her parents to Psychiatry clinic of this general hospital with the complaints of inability to understand speech and remaining aloof. Social interactions had recently reduced significantly. Delayed developmental milestones were noted on detailed assessment especially language and fine motor developmental milestones. Sudden episodes of hyperactivity and aggressive behaviour mainly towards self were also reported.

On further questioning some regression of language milestones was noted while her gross motor function development was relatively normal. Her mother reported, when her daughter turned 2 years old she started to feel concerned about her ability to understand and get involved in routine social interactions. She was unable to play with other children or do any kind of group activity due to her behavioural problems. She ran around the house, repeatedly clapped her hands and hit on her head. These symptoms worsened with time. At the time of presentation she was able to walk and run without support, however she had trouble climbing stairs. She had not achieved a mature pincer grasp and was unable to write or perform other activities requiring fine motor control. She used to say bi-syllables and a few meaningful words, but her speech and the ability to understand it deteriorated with time. She had not achieved bowel or

bladder control. She slept well except for on and off disturbances and she also has a good appetite, but needed assistance to eat food.

She stayed with her parents and sibs and did not have a family history of any major disease. Her 4 year and 9 year old brothers were apparently healthy.

The patient had coarse, dysmorphic facial features. She was hyperactive and occasionally engaged in self harming behaviour like head banging. She was admitted in the psychiatry ward for her uncontrollable motor activities that were mostly meaningless. Due to facial dysmorphic appearance she was referred to a paediatrician for further assessment.

Investigations

She was advised various investigations by paediatrician in view of possible inborn error of metabolism. Ultrasonography of abdomen showed mild diffuse hepatomegaly. ECG findings were suggestive of ASD. BERA showed mild hearing loss in right ear and moderate loss in left ear. B type tympanogram was seen on impedance audiometry. X- ray hand AP- Proximal ends of metacarpals were pointing. X- ray PBH- Acetabular roof was horizontal. (hypoplastic inferior ilium). Neck of bilateral femur was shortened with widened femoral epiphysis. X- ray Thoracolumbar spine AP and Lateral- Vertebrae had beaking and fish mouth appearance. All these X-ray findings were suggestive of MPS. MRI brain was suggestive of diffuse cerebral atrophy.

Discussion

This patient was brought to the clinic very late in the course of her disease. Initially, due to the nature of her symptoms she was admitted as a case of pervasive developmental disorder with mental retardation. After investigations the diagnosis was reviewed as a presentation of MPS type III. Developmental delay and behavioural problems like hyperactivity and aggression are commonly seen in mucopolysaccharidosis Type III [7]. Autistic features, cognitive decline and presentation with behavioural problems are common with Type IIIB of this disorder [8, 9, 10]. Unfortunately in this case urine glycosaminoglycan screen or serum enzyme

assay could not be done. When parents were informed about the condition, they expressed concern about her symptomatic management only. They were reluctant for any costly investigations, once the child was behaviourally better.

Low dose of various antipsychotic drugs has been reported to be effective in management of behavioural problems though response is unpredictable and side effects are common [7,10]. This patient too had extra pyramidal symptoms with low dose Risperidone (0.25 mg) as well as Aripiprazole (1.25mg) and low dose Clonazepam (0.25mg) had to be given for activity control. Low dose Carbamazepine (50 mg twice a day) was also administered. Use of Carbamazepine to manage inpatient child aggression has been studied, recommended and documented in literature [11].

The patient has two brothers who do not have any similar symptoms. There is a 67% chance of them being carriers of this autosomal recessive disease and they were in need of genetic counselling for the future [12]. Parents of children with MPS face a lot of psychosocial problems in their life. Handling aggressive behaviours, making home "safe" to avoid injuries, financial stress are to be faced by these grieving parents. Parents may often need psychiatric help [9]. Parents of this child were also counselled regarding all these issues. They were explained about genetic transmission, handling everyday problems, prognosis and psychosocial support was provided.

The prognosis of MPS depends on the particular type affecting the patient because each type is associated with specific co-morbidities and estimated lifespan is variable as well though child usually survives till second decade. Specific treatment/cure is limited so a very well organized management plan is needed for such patients. The patient will need timely follow up to access presence of corneal clouding, joint stiffness, increased hearing loss, cardiovascular disease and obstructive airway disease. A team approach to tend to the patients needs involving a pediatrician, ophthalmologist, orthopedic surgeon and a physical and occupational therapist is beneficial.

Since this disease can present with symptoms seen in a number of psychiatric and developmental disorders it is difficult to diagnose at an early stage. The differential diagnosis of an inherent metabolic disorder should always be considered in a child presenting with behavioural problems.

Conclusion and Clinical Implications

Rare condition like MPS should also be considered in a child presenting with behavioural problems, who appears intellectually subnormal. Early diagnosis can improve chances of effectiveness of newer treatments available. Symptomatic treatment with psychotropic drugs is helpful for the child and genetic counselling helpful for planning subsequent pregnancy. Drug treatments as well as psychosocial support for psychological distress and burnout in parents are deemed necessary. Early identification of these cases is possible with high level of clinical vigilance, which will improve survival and quality of life of both child and parent alike.

References

1. <http://emedicine.medscape.com/article/1115193>. Date of accessed: 10/6/2014
2. Gadve SS, Sarma D, Saikia UK Short stature with umbilical hernia – Not always due to Cretinism: A report of two cases Indian J Endocr Metab 2012;16: 453 – 6.
3. Gauri Shankar Shah, Tania Mahal and Subodh Sharma ; Atypical clinical presentation of mucopolysaccharidosis type II (Hunter syndrome): a case report. Journal of Medical Case Reports 2010, 4:154 doi:10.1186/1752-1947-4-154.
4. Leo Galvin, Alan O'Hare, Reuben Grech, Seamus Looby; Hurler syndrome (Mucopolysaccharidosis type I) ; *BMJ Case Reports* 2013; doi:10.1136/bcr-2012-008148.
5. Martin R, Beck M, Eng C, Giugliani R, Harmatz P, Mufioz V, Muenzer

- J: Recognition and diagnosis of mucopolysaccharidosis II (Hunter syndrome). *Pediatrics* 2008, 121(2):377-386.
6. Maryam Banikazemi, Mucopolysaccharidosis Type I—e-medicine specialities, Updated: Apr 14, 2009.
 7. Cleary MA, Wraith JE Management of Mucopolysaccharidosis Type III Archives of Disease in Childhood 1993; 69: 403-406.
 8. Marlies J Valstar, Jan Pieter Marchal, Martha Grootenhuys, Vivian Colland and Frits A Wijburg Cognitive development in patients with Mucopolysaccharidosis type III (Sanfilippo syndrome) Orphanet Journal of Rare Diseases 2011, 6:43 doi:10.1186/1750-1172-6-43.
 9. Jacqueline Brady, Aditi Trehan, Dennis Landis, Camilo Toro Mucopolysaccharidosis type IIIB (MPS IIIB) masquerading as a behavioural disorder BMJ Case Reports 2013; doi:10.1136/bcr-2013-009592.
 10. Sema Kalkan Ucar, Burcu Ozbaran, Nagehan Demiral Zeki Yuncu Serpil Erermis, Mahmut Coker Clinical overview of children with mucopolysaccharidosis type III A and effect of Risperidone treatment on children and their mothers psychological status Brain and Development Volume 32, Issue 2, February 2010, Pages 156–161.
 11. Deshmukh P, Kulkarni G, Barzman D Recommendations for pharmacological management of inpatient aggression in children and adolescents Psychiatry (Edgmont) Feb. 2010; 7(2): 32 – 40.
 12. Tuschl K, Gal A, Paschke E, Kircher S, Bodamer OA Mucopolysaccharidosis Type II in females: case report and review of literature. *Pediatr Neurol* 2005, 32:270-272.

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