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Phobic anxiety disorder in hereditary hyperekplexia – Comorbidity or a coincidence: Case reports of two siblings

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Abstract

Hyperekplexia (startle disease) is a rare non-epileptic neurological entity resulting from gene mutation. The onset of this disorder is usually in infancy, but can be delayed until early adulthood. Patients with this disorder usually have normal mental development. Patients with hyperekplexia may present with symptoms ranging from sub-syndromal anxiety, to symptoms of syndromal anxiety disorder. This case report is about two siblings with hyperekplexia, in whom phobic anxiety disorder was a prominent manifestation.

INTRODUCTION

Familial or hereditary hyperekplexia is an infrequent disorder, which usually presents with abnormal startle reaction to auditory or somatosensory stimuli.[1] This disorder exists in two clinical forms – "major form" and "minor form". Hyperekplexia is associated with genetic mutation of alpha-1 subunit of glycine receptor which can be either dominant or recessive.[1-3] In some studies it has been found that the above genetic mutation is linked more to the "major" form of hyperekplexia rather than the "minor" form.[4-6] Both "major" and "minor" forms of hyperekplexia have excessive startle reaction, but the "minor" form of hyperekplexia differs from the "major" form by not having generalized stiffness in the course of the disorder.[4] Jerky muscle stiffness usually resolves itself by the end of the first year of life whereas the startle response to auditory and somatosensory stimuli usually persist for life.[5] The "minor" form of hyperekplexia is associated with behavioural manifestations and is of neuropsychiatric significance.[6]

Hyperekplexia may follow familial or sporadic pattern.[2] Chromosome 5 is associated with this disorder.[7-9] Usually the disorder presents in infancy, with minimal impairment to mental development.[3,13] Clonazepam is effective in the treatment of hyperekplexia.[1,2,9,11] Familial hyperekplexia is frequently associated with serious falls, which in the long run may produce hesitant gait disorder and phobic disorders (particularly fear of open spaces).[5,12,13] Neuropsychiatric co-morbidities like specific phobia are also associated with "stiff-man syndrome" which is a similar condition of exaggerated startle response.[14,15]

In this case report, hyperekplexia and its associated neuropsychiatric manifestations in two biological siblings are discussed.

CASE REPORTS

Patient 1

This 25 year old male previously diagnosed with familial hyperekplexia by a neurologist was referred for evaluation of his morbid fear of heights, which was insidious in onset and present since childhood. Further history revealed that since infancy, the patient used to fall suddenly and injured himself whenever there was any loud noise. After each fall, stiffening of all the limbs was observed, which was followed by complete relaxation of muscles over the next 4-5 minutes. Due to rigidity he would fall with arms adducted and thus could not protect himself. Because of the disorder patient had incurred multiple injuries to his face and head. He was treated with clonazepam (1mg/day) for the last 6 years during which frequency of falls had declined. The patient also had a history of myoclonic seizures during his childhood which were well controlled with sodium valproate (1 gram/day).

On evaluation of the psychiatric history, it was found that the patient had a morbid fear of heights. Since childhood, he was reluctant to climb stairs and look down from heights. His mother noticed

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that as a child, the patient would not look down from her lap and would always cling to her neck. As he grew up, he avoided going on the roof. He reported that he used to feel dizzy when he suddenly gazed downwards. The dizziness was not associated with nausea or vomiting, and was relieved by looking up or straight ahead.

Since the past 6 years he was on regular treatment by a neurologist, following which his fear gradually reduced and he had no difficulty in looking down or climbing stairs. However, his fear of falling essentially led him to avoid heights completely.

His antenatal and perinatal histories were not contributory. There was no developmental delay. Patient was intellectually normal and was pursuing management studies. Family history revealed similar symptoms in his biological sister (Patient 2). Neurological examination, systemic examination and routine investigation were within normal limit. His CT scan (head) and EEG did not reveal any abnormality. Psychometric assessment revealed anankastic and impulsive traits. After clinical assessment, a diagnosis of specific phobia (acrophobia) had been made based on the ICD-10 criteria. He was prescribed escitalopram (10mg/day), and treated with behaviour therapy.

Patient 2

This 19 year old female was the younger sister of Patient 1. She had similar history of falls in response to loud noises since infancy, and was diagnosed as familial hyperekplexia. She was referred to the adult Psychiatry Out Patient Department for her fear of heights and walking alone in open spaces. As with her brother, she had a fear of heights and walking alone since childhood. She had multiple falls whenever she walked on uneven surfaces, as a result she avoided walking alone. She used to fall with arms adducted, which prevented her from protecting herself. She was treated with clonazepam (1mg/day) for the past 4 years by a neurologist. With this treatment, the hyperekplexia was under control, but the fear of heights and walking alone persisted. The EEG and CT scan (head) were within normal limits. Unlike her brother, her fears did not improve when the treatment of hyperekplexia was initiated. There was no significant past history of medical or psychiatric illness. There was no evidence of birth asphyxia or birth related trauma. The patient did not have any developmental delay. She was average in studies. There was no history of any substance use. After assessment, a diagnosis of specific phobia (acrophobia) was made on the basis of ICD-10 diagnostic criteria. She was given escitalopram (10mg/day) and behaviour therapy.

In both Patient 1 and 2, the behaviour therapy was done by graded exposure to anxiety provoking situations (heights) following a hierarchy. The combined pharmacotherapy and behaviour helped to reduce the phobic symptoms in both patients.

DISCUSSION

Hyperekplexia is infrequently encountered in clinical practice, so many clinicians have little awareness about this disorder. Clinicians should be aware of the clinical manifestations of hyperekplexia, as the diagnosis is entirely clinical.[9] The condition is often mistaken for epilepsy.

Anxiety disorders, particularly phobic anxiety disorders are common in patients with hyperekplexia. As patients with hyperekplexia have an increased risk of sustaining injury due to repeated falls, they usually develop anxiety to social situations, open spaces, closed spaces and heights in anticipation of danger. They usually avoid such situations. In the long run, the avoidance behaviour becomes consolidated leading to significant impairment in day to day life. A prolonged disorder would lead to stronger avoidance behaviours thus leading to significant impairment. Early identification and appropriate psychiatric intervention of the anxiety disorder, particularly phobic symptoms, can improve the quality of life.

A question might arise; “Is the anxiety disorder in patients with hyperekplexia a co-morbidity or just a coincidence?” Existing literature suggests that anxiety and phobic symptoms frequently occur in patients with hyperekplexia.[5,12,13] These anxiety symptoms seem to be a reaction to the anticipatory fear of falling, but at times it is out of proportion to the danger, thus leading to a syndromal diagnosis of phobic anxiety disorder. Due to the rarity of hyperekplexia, its associated co-morbidities (particularly neuropsychiatric co-morbidities) are poorly studied. The author belief that co-existence of phobic anxiety disorder in patients with hyperekplexia is not merely by chance. It is more likely to be a psychiatric co-morbidity. So patients of hyperekplexia (particularly those having prolonged history of falls) should be routinely screened for anxiety disorders.

In our patients, both pharmaco-therapeutic

and non-pharmaco-therapeutic treatments were tried. The patients were given selective serotonin reuptake inhibitor (SSRI), which is an approved medication for phobic anxiety disorder.[14] At the same time, behavioural therapy was attempted in the form of graded exposure to anxiety provoking situations. The patients have been regularly follow up in our Psychiatry and Neurology Out Patient Departments for 7 months. They showed significant response to the treatment. Non-pharmacological modalities of treatment like cognitive behaviour therapy, systematic desensitization, flooding are also effective in treatment of phobic anxiety disorder.[15]We belief that a combined pharmacotherapy and non-pharmacotherapy approach is the best approach to manage phobic anxiety disorder in hyperekplexia. Since stiff-man syndrome and hyperekplexia are similar conditions on their clinical presentation and co-morbidity association[16, 17], the management approach to phobic anxiety disorder in stiff-man syndrome may also be similar to that of hyperekplexia.

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