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**Case Report**

# Hyperekplexia in a neonate: a seizure mimicker

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## ABSTRACT

Hyperekplexia is an exaggerated startle to external stimuli associated with generalized increase in tone seen in a normal newborn with both sporadic as well as genetic predisposition. This is an uncommon neurological entity that is often confused with seizure in infancy. To date about 150 cases have been reported in the literature. We report a 6-week-old infant with characteristic intermittent generalized tonic spasm misdiagnosed as seizure disorder and was on phenobarbitone. With characteristic stiffening episode and exaggerated startle without habituation on tapping the nose we came to a clinical diagnosis of Hyperekplexia or Stiff baby syndrome or Startle disease. The child was started on Clonazepam to which he responded remarkably with decreased startle reflex. The aim of this case reporting is to through insight to this disease entity when we see an intermittent hypertonic infant.

**Keywords:** Clonazepam, Exaggerated startle, Hyperekplexia, Stiff baby Syndrome

## INTRODUCTION

Hyperekplexia or Stiff baby syndrome or Startle disease is a rare early neonatal onset, potentially treatable, neurological disorder, characterized by a triad of an exaggerated startle reflex in response to tactile or auditory stimuli followed by short periodical generalized stiffness and nocturnal myoclonus.[1] It was first described by Kirstein and Silfverskiold in 1958.[2] This is congenital disorder with major and minor forms.[3] Major includes the triad and minor if stiffness is absent. Hyperekplexia exhibits both autosomal recessive and dominant inheritance with mutations in several genes involved in glycinergic neurotransmission.[4] Hyperekplexia can have severe consequences such as sudden infant death due to laryngospasm and cardiorespiratory failure. The symptoms tend to resolve after infancy; however, adults may have increased startle-induced falls or nocturnal muscle jerks with association of umbilical hernias and congenital dislocation of the hip.[5]

## CASE REOPRT

We report a case of a 6-week-old, 5$^{th}$ order male infant born out of nonconsangious marriage whose mother complained of brief episodes of stiffening of body for few minutes several times a day which started 5days after birth. The baby was born by normal vaginal delivery at term, cried immediately after birth, was on exclusive breast feeding with good sucking and swallowing reflexes. This is not associated with fever, lethargy, loose stools, difficulty in breathing, alteration of colour of body. The blood glucose, electrolytes (Sodium, Potassium, Calcium), Urea and Creatinine were in the normal range as per age. On proper history taking the parents informed that these stiffening episodes were exaggerated by minor stimuli like touch which showed no improvement despite taking phenobarbitone at proper dosage. At the time of presentation, the child was alert, normothermic, with age appropriate head circumference, length and weight. The child has intermittent jittery with

hypertonia of body with no feeding difficulties. On lightly tapping the bridge of the nose with a finger when the child is calm, there was an exaggerated startle response with symmetrical myoclonic jerking of limbs which did not habituate with repeated stimulation at intervals of one second. Transfontalle ultrasonography showed no structural anomaly of brain. Cerebrospinal fluid study was done to rule out the possibility of meningitis. Thyroid function test revealed euthyroid status. So, based on the above case scenario a clinical diagnosis of hyperekplexia was done. The infant was started on clonazepam after, withdrawal of phenobarbitone. Few weeks later there was a dramatic improvement with no stiffening episodes with normal muscle tone and decreased startle response to touch stimuli. Clonazepam was continued upto 6months then gradually tapered over another one month.

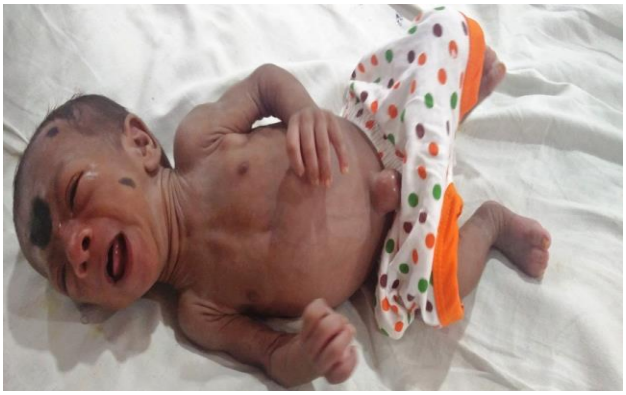

**Figure 1: Depicts the increased tone in all the limbs and association with umbilical hernia.**

## DISCUSSION

Startle reflex, a normal reticular and cortical reflex is elicited in normal newborns and infants to a minor degree.[6] Hyperactivity of cortical neurons, abnormalities of the inhibitory systems of the brain and abnormalities of the serotoninergic pathways are among the proposed mechanisms for hyperekplexia.[7] Mutations in the glycine receptor alpha 1 subunit gene (GLRA1) is seen in 30% of hyperekplexia cases.[8] Linkage analysis has mapped a gene for this disorder to chromosome 5q 33-35. The inheritance is mainly autosomal dominant with variable penetrance, and both major and minor forms may be seen in the same family.[9] Rarely, hyperekplexia may present antenatally with abnormal intrauterine movements and a peculiar fetal position.[10]

The early manifestations include abnormal responses to unexpected auditory, visual, and so esthetic stimuli such as sustained tonic spasm, exaggerated startle response and fetal posture with flexion of forearm and legs, clenched fists, anxious stare and prominent nocturnal myoclonus at times associated with apnea.[11] Consistent generalised flexor spasm in response to tapping of the nasal bridge (without habituation) is the clinical hallmark of hyperekplexia which was seen in our case. The increased tone is apparent only when the infant is awake.[12] These spasms are usually accompanied by normal electroencephalogram, evoked potential test and nerve conduction velocity.[7,13] Electro-myography (EMG) may indicate periodic sustained muscle contraction with intermittent quiet periods with a prominent long latency C response has also been described.[11] A simultaneous EEG-EMG may help discriminate movement artifacts.[14] The differentials include myoclonic epilepsy, psychogenic movement disorder, Isaac syndrome, Schwartz-Jampel syndrome, Gilles de la Tourette, congenital stiff person syndrome and culture specific startle syndromes such as jumping Frenchman of maine. Clonazepam, a gamma aminobutyric acid (GABA) receptor agonist, is the treatment of choice for hypertonia and apnea episodes.

However, may not influence the degree of stiffness significantly. A simple manoeuvre (Vigevano) like forced flexion of the head and legs towards the trunk is known to be life-saving when prolonged stiffness impedes respiration. No definite guidelines exist regarding duration of therapy, but the drug can be tapered slowly once the symptoms subside.[15]

What is known? Hyperekplexia is a known hereditary neurological disorder presenting as exaggerated startle in newborn along with episodes of generalised hypertonia. This entity is also known as Stiff Baby Syndrome.

What is new? Hyperekplexia is an uncommon entity which is usually diagnosed as seizure disorder in infancy. Simple clinical tool like tapping the nose eliciting exaggerated startle (non-habituating) will clinch the diagnosis, thus preventing unnecessary neuroimaging. Clonazepam is the best drug to improve such exaggerated startle episodes and to be tried in each and every case of hyperekplexia.

## CONCLUSION

Although a rare entity, we must think about Hyperekplexia when we see a hypertonic newborn. This case report reflects this to be a purely clinical entity with minimal investigation to rule out organic entity and a single drug that can remarkably improve the outcome. In most cases, fear of falling and toddling gait normalizes in adolescence. Diagnosis of such entity prevents unnecessary exposure to anti-epileptic medication to the child.

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