Case Report

Type 1 Diabetes with Nodding Syndrome

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Nodding syndrome is an epileptiform encephalopathy- a type of neurodegenerative disorder. It's commonly seen in certain parts of African countries (Sudan, Tanzania) where children between 3 to 18 years of age are affected. It's characterized by head nodding, stunted growth, delayed puberty, seizures, endocrine dysfunction, cognitive decline & behavioural problems. Exact etiology is not known but potential reasons could be: nematode infection, malnutrition. MRI brain reveals diffuse atrophy of cerebral & cerebellar areas while EEG shows generalised spike wave or mutifocal spike wave discharges. Treatment includes antiepileptic therapy, nutritional rehabilitation, psychiatric counselling and physiotherapy. Here, we want to report the first case of Type 1 Diabetes who presented with Nodding syndrome from India.

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Key words **: Type 1 diabetes, Nodding syndrome, Cerebral atrophy.**

Case Report

18 years old female patient was referred to our clinic for management of uncontrolled sugar with multiple episodes of hypoglycaemia. She also had complained of involuntary movements of head as well as both upper limbs. As patient was not much responsive to our questions so further history was given by her parents. First head nodding got started about one & half year before. It was gradual in onset with few episodes of head nodding per minute but since last 4 months it was markedly increased in frequency. She was having vertical & sometimes horizontal head nodding episodes 25-30 per minute which disappeared during sleep. She also had coarse movements in both hands since last 1 year. They were asymmetrical in nature (Affecting right hand more than left). No cranial nerve palsy was noted. No history of fever or convulsions, chronic illness (except Type 1 Diabetes) observed till present.

Examinations — On Examination, she had lean & thin built up. Her height was stunted. Marked wasting was noted in all four limbs. She had no menses & had all features of delayed puberty. She used to keep herself isolated except when she wanted any kind of help or when she wanted to eat, she used to speak few words. Her both pupils were reactive to light. Deep tendon reflexes were not elicitable. Bilateral extensor plantar response was noted. Cog wheel rigidity was noted in all four limbs.

In past she had similar complain about 4 years back. At that time only head nodding was there which persisted for about 1 year for which they consulted physician & it disappeared after 1 year. Due to cognitive decline,she was dropped out from school after 7th class.

Editor's Comment :

- Nodding syndrome (NS) can be observed even in India. We need to identify more such cases where undernutrition is quite prevalent.
- Type 1 Diabetes with Nodding syndrome: First case reported from India.
- By early identification, we can manage them in better way as they need multimodal approach which helps to improve quality of life & empower them to live independently.

Her birth weight was around 1.8 Kg. She was a preterm baby delivered at 7 months pregnancy by normal vaginal delivery. She had no other siblings.She remained markedly undernourished during her childhood.

Regarding diabetic history, she was first diagnosed as type 1 diabetic when she was 10 years of age. She had very poor control of diabetes which might be due to lack of education, financial constrain & cognitive decline. She got admitted for Diabetic Ketoacidosis (DKA) four times in past 3 years. Currently, she was on premix insulin (30/70) & she had HbA1c of 10.5%. She also had frequent episodes of hypoglycaemia on premix insulin.

Her height was 142 cm, weight: 31.3 Kg with Body Mass Index (BMI) of 15.5 Kg/m^2. Vitals were within normal limits.

Blood investigations were done. Her HbA1c was 10.6% (<7%- well controlled) with c peptide of 0.2 ng/ml (0.92–3.73 ng/mL). All other reports were within normal limits. HIV serology was negative.

Fundus was suggestive of mild Non-proliferative Diabetic Retinopathy (NPDR) otherwise rest other findings were normal. EEG Report was found to be normal. MRI Brain revealed marked cerebral atrophic changes with prominent sulcal space and ventricular system. As compared to previous MRI brain which was done 1 year before, there was mild increase in atrophic changes (Figs 1-3).

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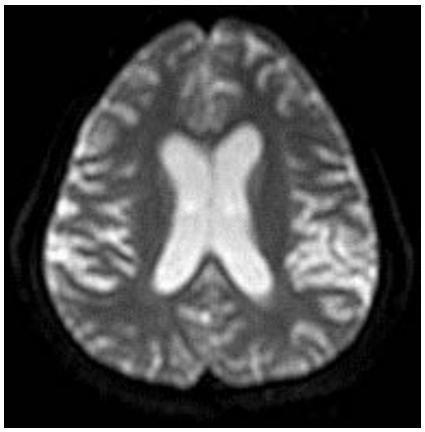

Fig 1

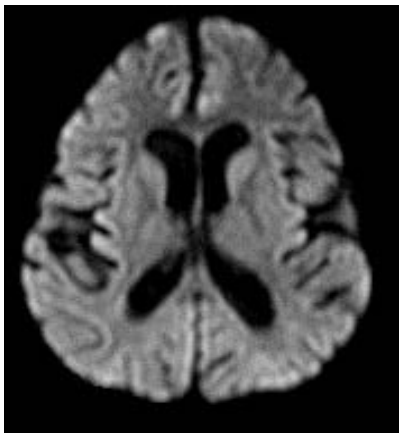

Fig 2

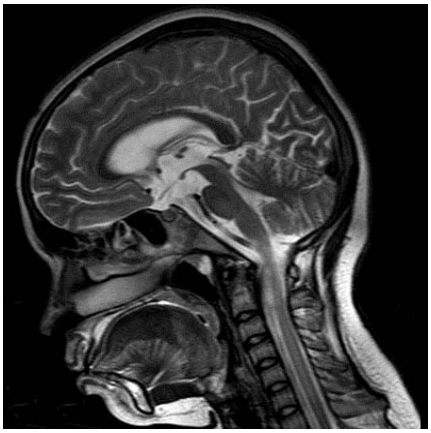

Fig 3

Figs 1-3 — All MRI images are showing features of cerebral atrophy

She was diagnosed as confirm case of Nodding syndrome based upon clinical features & brain imaging. After consulting neurophysician, she was started on Tablet valproate 287 mg, propranolol 40 mg & topiramate 25 mg (All three tablet to be taken once a day). Other supportive management including physiotherapy, psychiatric counselling &nutritional rehabilitation was made. At 3 months follow up, her head nodding & rigidity of limbs improved but it was not completely resolved. She was now involved more with outer environment & used to help her parents in household work. Overall, her psychiatrics features also improved & she seemed to be in better position than before treatment.

For diabetes, we stopped premix insulin & started her on basal bolus regimen. She was treated with regular human insulin 6 units before each meal & glargine 12 units at 10 pm. Self monitoring of blood glucose was explained to her parents. Dietary recall was made & right insulin injection technique was explained. She was in touch with us over teleconsultation & her insulin units were titrated as per her sugar readings. At 3 months follow up, her sugar was relatively controlled with HbA1c of 7.8% & no hypoglycaemia further. She also gained weight of about 4 kg.

Discussion

Nodding syndrome (NS) is a type of neuro-degenerative disease characterised by epileptic encephalopathy. Certain parts of African countries where there is high risk of malaria & onchocerca volvulus (River blindness) transmission like Tanzania, Southern Sudan & Uganda are significantly affected with this syndrome[1].

Etiology

Exact etiology is not known but poverty & malnourishment are frequent association. As compared to normal individuals, increased rate of systemic infection is found with O. volvulus although Polymerase Chain Reaction (PCR) testing of brain & CSF fluid has been found to be negative which excludes Central Nervous System (CNS) infection. There is possible chance of molecular mimicry to antigen “leiomodin-1” which is considered to be present on O.voluvulus[2,3].

Case Definitions[4] (Table 1)

Table 1

Case Category	Criteria	
Suspected case	Head nodding developed in normal subject	
Probable case Requires 2 major & 1 minor criteria	Suspected case with Major criteria: - Onset of nodding between 3 to 18 years Age - Frequency of nodding 5–20 per minute.	one of the following minor criteria:- - Delayed puberty - Psychiatric symptoms. - Other neurological issues* - Nodding Triggered by food/cold - Stunted growth - Clustering in space or time with similar cases
Confirmed case	Probable case with documentation of nodding episode that is: - Observed by expert Medical person, or - Videotaped, or - EEG/EMG	

*Other neurologic abnormalities include cognitive decline, school dropout because of cognitive or behavioral problems, other seizures or neurologic abnormalities.

Clinical presentation

Most common age group affected is of 3 to 18 years. Peak incidence is around 10 years of age. Peculiar feature of this disease is head nodding with frequency of 5-20/min. Studies done on NS revealed that there are five stages[5] (Table 2).

Nodding can precede or even accompany stage of seizures. Evaluation of stages is variable & it may differ in individual cases. NS can be considered a proconvulsive stage as nodding gets triggered by cold or food[6].

Investigation

EEG: There is no uniformity in pattern of EEG. Interictal epileptic discharges can be of (1) generalised slow spike-wave (2) Multifocal spike- wave (3) poly spike-wave. Study done at Tanzania suggested 44% of subjects with abnormal EEG having 2.5 Hz generalised spike wave discharges. One of the studies from Sudan involving 32 children showed generalised recurrent discharges.[7]

MRI Brain : In initial stages, MRI can be normal but as disease progresses, atrophy of cerebral & cerebellar area takes place. Superior & middle frontal gyri with prefrontal cortex are markedly affected with relative sparing of occipital cortex & hippocampus. Neuro-pathological examination has suggested that it is one type of neuro-degenerative disorder due to variable degree of tauopathy with no evidence of nematode microfilaria or any foreign organism[7].

CSF Analysis : Most of the cases it's normal with no cells & protein in it[8].

Treatment

Primary treatment of NS is antiepileptic medications and good nutrition. Phenobarbitone, phenytoin, sodium valproate have been tried in different studies. Positive results obtained from one of the largest studies of Uganda with use of sodium valproate where >70% reduction in seizure frequency was achieved. Benefits of dietary supplementation is beyond doubt. Psychiatric counselling, physiotherapy & physical rehabilitation with management of behavioural issues need to be managed effectively which can make the person independent & empower the patient to live their life in better way[9].

In India, although first case of Nodding syndrome was reported from Department of Paediatrics, Vardhaman Medical College & Safdarjang Hospital[10], our case is unique in that it's the first case of Type 1 Diabetes who presented with Nodding syndrome.

Table 2

Stages	Clinical features
First stage	Blankness, generalised weakness, lethargy, starring (develops in 2 years time)
Second Stage	Head nodding
Third Stage	Different kind of seizures including absence seizures & tonic clonic seizures are observed
Fourth Stage	Cognitive dysfunction, motor dysfunction and psychiatric symptoms
Fifth Stage	Severe disability which may end up in parkinsonian features

References

1 Spencer PS, Palmer VS, Jilek-Aall L — Nodding syndrome: origins and natural history of a longstanding epileptic disorder in sub-Saharan Africa. *Afr Health Sci* 2013; **13:** 176-82.

2 Centers for Disease Control (CDC) — Nodding syndrome – South Sudan, 2011. *MMWR Morb Mortal Wkly Rep* 2012; **61:** 52-4.

3 Colebunders R, Suykerbuyk P, Jacob ST, van Oijen M— Nodding syndrome, other forms of epilepsy, and the Nakalanga syndrome most likely directly or indirectly caused by Onchocerca volvulus. *J Neurol Sci* 2017; **372:** 439-40.

4 WHO — International scientific meeting on Nodding SyndromeWorld Health Organization Kampala 2012.

5 Idro R, Ogwang R, Kayongo E, Gumisiriza N, Lanyero A, Kakooza-Mwesige A, *et al* — The natural history of nodding syndrome. *Epileptic Disord* 2018; **20:** 508-16.

6 Kakooza-Mwesige A, Dhossche DM, Idro R, Akena D, Nalugya J, Opar BT — Catatonia in Ugandan children with nodding syndrome and effects of treatment with lorazepam: a pilot study. *BMC Res Notes* 2015; **8:** 825.

7 de Polo G, Romaniello R, Otim A, Benjamin K, Bonanni P, Borgatti R — Neurophysiological and clinical findings on Nodding Syndrome in 21 South Sudanese children and a review of the literature. *Seizure* 2015; **31:** 64-71.

8 WinklerAS, Friedrich K, Konig R, Meindl M, Helbo R, Unterberger, *et al* — The head nodding syndrome–clinical classification and possible causes. *Epilepsia* 2008; **49:** 2008-15.

9 Idro R, Namusoke H, Abbo C, Mutamba BB, Kakooza-Mwesige A, Opoka RO, *et al* — Patients with nodding syndrome in Uganda improve with symptomatic treatment: a cross-sectional study. *BMJ Open* 2014: 4e;006476

10 Sehgal R, Agarwal N, Gera R — Nodding syndrome- an Indian case. *Afr Health Sci* 2018; **18(3):** 837-41. doi: 10.4314/ahs.v18i3.43. PMID: 30603018; PMCID: PMC6306992.