Nodding Episodes and High Anion Gap in a 13 Year Old Child with Nodding Syndrome: A Case Report

Article *in* British Journal of Medicine and Medical Research · January 2015

DOI: 10.9734/BJMMR/2015/14595

CITATIONS
6

READS
202

7 authors, including:

David Lagoro Kitara
Gulu University (GU)
110 PUBLICATIONS **820** CITATIONS
SEE PROFILE

Suzanne Gazda
17 PUBLICATIONS **1,217** CITATIONS
SEE PROFILE

Okot Ambrose
2 PUBLICATIONS **10** CITATIONS
SEE PROFILE

Valerie S Palmer
Oregon Health and Science University
91 PUBLICATIONS **2,010** CITATIONS
SEE PROFILE

British Journal of Medicine & Medical Research
6(8): 851-858, 2015, Article no.BJMMR.2015.260
ISSN: 2231-0614

SCIENCEDOMAIN *international*
www.sciencedomain.org

Nodding Episodes and High Anion Gap in a 13 Year Old Child with Nodding Syndrome: A Case Report

David Lagoro Kitara[1*], Suzanne Gazda[2], Eger Ambrose[3], Okot Ambrose[4] Collines Angwech[5], Valerie Palmer[6] and Peter Spencer[6]

[1]Department of Surgery, Faculty of Medicine, Gulu University, P.0.Box 166, Gulu, Uganda.
[2]Neurologist, President and Co-founder for Hope for HumaNs, Saint Antonio, Texas, USA.
[3]Faculty of Business and Development Studies, Gulu University, P.0.Box 166, Gulu, Uganda.
[4]Faculty of Education and Humanities, Gulu University, P.0.Box 166, Gulu, Uganda.
[5]Social Worker, Hope for Humans, Odek Nodding Syndrome rehabilitation centre, Gulu, Uganda.
[6]Department of Global Health and Neurology, Oregon Health and Sciences University, Oregon, USA.

Authors' contributions

This work was carried out in collaboration between all authors. Author DLK designed the study, wrote the protocol, and wrote the first draft of the manuscript. Author SG managed the literature search, data analysis; authors EA and OA managed the research process, literature search, data analysis; authors CA,VP and PS did the literature search, data collection and management of NS patients. All authors read and approved the final manuscript.

Article Information

DOI:10.9734/BJMMR/2015/14595
Editor(s):
(1) Toru Watanabe, Department of Pediatrics, Niigata City General Hospital, Japan.
Reviewers:
(1) Anonymous, Morocco.
(2) Mohamed Hamdy Ibrahim, Neurology Department , Faculty Of Medicine , Ain Shams University , Egypt.
(3) Kevin M. Boehm, Department of Emergency Medicine, St Mary Mercy Livonia Hospital, Livonia, USA.
(4) Kuti Bankole Peter, Paediatrics and Child Health, Obafemi Awolowo University, Ile-Ife, Nigeria.
(5) Anonymous, Iran.
(6) Dirk Dhossche, Psychiatry, University of Mississippi Medical Center, USA.
Complete Peer review History: http://www.sciencedomain.org/review-history.php?iid=907&id=12&aid=7714

Case Study

Received 7th October 2014
Accepted 10th November 2014
Published 9th January 2015

ABSTRACT

Introduction: Nodding syndrome is an unknown neurological disorder affecting children in Northern Uganda, South Sudan and Southern Tanzania. The patient in our case report is, to the best of our knowledge, the first with the syndrome that has been serially followed up for more than three months and the information obtained provides important clue to the possible risk factor to the syndrome.

**Corresponding author: Email: klagoro@gmail.com, klagoro@yahoo.co.uk;*

Case Presentation: A 13-year-old boy diagnosed in Atanga Health Centre III using World Health Organization (WHO) surveillance case definition as probable Nodding syndrome was referred to Gulu Regional Referral Hospital with pyomyositis of abdominal wall muscle and head nodding which was not responding to treatment. Serial anthropometry and laboratory investigations including, haematology, clinical chemistry, biochemistry and muscle biopsy were conducted in a period of 3 months and compared to the nodding episodes. Complete blood count showed leucocytosis with immature granulocytes and atypical lymphocytes mainly during the infective phase of the pyomyositis but returned to normal as a result of the surgical procedure, Incision, Drainage and Debridement (I, D & D) of pyomyositis of the anterior abdominal wall muscle combined with administration of antibiotics and analgesics.

The liver enzymes were high throughout the period of admission in Gulu Hospital. The renal parameters and serum electrolytes were within normal ranges during the nodding free periods but it was deranged during the nodding episodes. Abdominal ultrasound scan showed a focal mass on the right internal and external oblique muscles of the abdominal wall. Histology of the muscle showed a non-specific inflammation of the abdominal muscles with mass necrosis of the muscle and thrombosed blood vessels. These findings highlight the concurrent existence of pyomyositis in a child with Nodding Syndrome but whose nodding episodes were pronounced during the periods with imbalanced electrolyte pattern and with high anion gap.

In conclusion: Nodding syndrome is an unknown neurological disorder affecting children whose nodding episodes are probably related to the high Anion Gap metabolic acidosis.

Keywords: Nodding syndrome; high anion gap; metabolic acidosis; Gulu; Northern Uganda.

1. INTRODUCTION

Nodding syndrome is a neurologic disorder of an unknown aetiology that has recently been reported among children in several sub-Saharan African countries and primarily among internally displaced persons [1-4]. The primary and characteristic feature is a paroxysmal "spell" in which the head bobs forward 15-20 times repeatedly over a period of a minute; in most cases the children appear unresponsive during the episodes [3,4]. The illness has a clustering of onset mainly between the ages of 5 and 15 years [4]. The affected children are stunted, malnourished, dehydrated, mentally retarded, have seizures and nodding [4,5].

We present a case of a 13 year old school boy with NS who developed primary Pyomyositis of internal & external oblique muscles of the anterior abdominal wall and was hospitalized at Gulu Regional Referral Hospital, Northern Uganda for 3 months and during the period his anthropometry, haematology, biochemistry, clinical chemistry, and Nodding episodes were closely and serially observed, compared and monitored for any relationships.

2. CASE PRESENTATION

A 13-year-old boy was diagnosed as a probable Nodding syndrome using WHO epidemiological surveillance case definition and was referred from Atanga HC III in Pader district to Gulu Regional Referral Hospital where he was enrolled for inpatient management and undergoing nutritional rehabilitation at the nodding syndrome treatment center. He came with a history of progressive swelling and pain in the right anterior abdominal and lumbar regions. The swelling and pain was associated with a high grade fever which was constant and only partially relieved by analgesics which also had antipyretic properties which relieved the condition of the patient. These symptoms were not associated with vomiting, constipation, yellow eyes, loss of appetite, weight loss or urinary symptoms. The patient reported a history of falling from a tree during one of the nodding episodes 2 years prior to admission and hit his abdomen onto a tree branch. On further probe on his childhood history, his mother reported that he was born normally at home by a Traditional Birth Attendant (TBA) in one of the Internally Displaced peoples (IDP) camps. She reported that there was an uneventful pregnancy which was carried to term and delivery by Spontaneous vaginal delivery (SVD). During her pregnancy at the IDP camps, she had exclusive feeding on relief food provided by United Nations World food program (UNWFP) which composed of beans, yellow posho and cooking oil and denied history of ingestion of herbs or traditional medications which may have caused adverse events during and after the pregnancy. Her child was said to have had a normal physical, cognitive and social childhood development similarly to her other normal children before the onset of nodding which began three years after she returned home from the IDP

camps in 2009. The child was enrolled in Atanga NS rehabilitation and treatment centre and was being managed on Carbamazepine, multivitamins, food supplement and Ivermectin. She reported that in spite of these medications the child continued to have partial seizures and nodding at least twice a day and had since dropped out of school.

On general examination, he was moderately dehydrated, febrile (t^{o}=38.0^{o}C), no anaemia (Hb=13.5 g/dl) and moderately wasted (weight for age with BMI=15.82 Kg/M^2). There was a right lumbar and anterior abdominal wall mass which was tender, indurated, non-fluctuant with a shinny skin. The spleen and liver were not palpable. There was no bilateral renal angle or supra-pubic tenderness. The rectum was full of faecal material which was of normal colour and texture. The anal tone was normal and the examining finger was stained with normal stool.

Haematological investigations were conducted and showed neutrophilia, lympocytosis, monocytosis and eosinophilia and there were immature granulocytes and atypical lymphocytes seen on the peripheral film report at admission but these returned to normal when the pus in the anterior abdominal muscles was evacuated. Other laboratory results including liver function parameters (ALT, AST) which were consistently elevated over the period while serum albumin and total protein levels were low at admission but returned to normal levels with food rehabilitation. Renal function parameters (serum creatinine, blood urea and nitrogen level) were normal throughout the study period, while serum electrolytes (K+, Na+, Cl-, $HC0_3^-$) varied over the period and it was observed that high Anion Gap was associated with nodding episodes (Table 1).

Abdominal Ultrasound showed inflamed internal and external oblique muscles of the anterior abdominal wall, the spleen and Liver were of normal echogenicity but liver was mildly enlarged. The patient underwent Incision, Drainage and Debridement (I, D & D) of the affected muscle at Gulu Regional Referral Hospital, Department of Surgery and the wound was left open for 14 days and thereafter secondary wound closure was conducted. A biopsy of the muscle affected was taken for histological analysis. He received supplementary food rehabilitation and his seizure medication was changed to Sodium Valproate 200mg twice a day under direct observation therapy (DOTS) and close monitoring of the vital signs and nodding episodes.

The patient continued to have regular follow-up in the surgical ward; seizures and nodding stopped completely from the time of intervention in the hospital where food rehabilitation and seizure control was achieved over a period of one month. With these interventions, the child had neither seizures nor nodding episodes and the child returned to near normal life. Serial measurements of the hematological and clinical chemistry findings 2 weekly showed that the renal function parameters were normal although the serum electrolytes varied throughout the period while the liver enzymes were elevated and remained high throughout the observation period (Table 1).

The patient consistently remained in a seizure and nodding free period during the time when the anion Gap remained normal until when he developed a watery diarrhoeal three months after admission. The diarrhoea was controlled in 2 days and suddenly caused a change in his electrolyte pattern as seen in the laboratory recording 2 days after the onset of the diarrhoea and thereafter a raised Anion gap which was followed by recurrent episodes of nodding and sometimes seizures which occurred at least twice a day.

3. DISCUSSION

The true incidence and prevalence of Nodding Syndrome in Northern Uganda is unknown. The socio-demographic characteristic of this child reflected similar findings to those children with NS previously investigated in Northern Uganda [3,5]. They are generally from poor families and are malnourished [3,5,6,7]. This patient had been receiving medications for symptomatic management of Nodding syndrome with anticonvulsants, multivitamins, Ivermectin, Folic Acid and albendazole from Atanga health center III for over ten months but still continued to have nodding episodes plus seizures at least twice a day. This child developed Pyomyositis of the muscle of the anterior abdominal wall which was managed by surgical incision, drainage and debridement, analgesics and antibiotics administration.

The emphasis of this paper was the serial laboratory investigations over the period of the hospitalization which observed that nodding episodes were associated with an increased anion Gap as shown by the laboratory results (Table 1).

Table 1. Shows the socio-demographic characteristics and the serial laboratory results of a 13 year old nodding syndrome patient

Variables	Dates					Normal values
	2/12/2012	12/12/2012	19/12/2012	31/12/2012	30/1/2013	
Age (years)	13 years	Same	Same	Same	Same	
Sex	Male	Same	Same	Same	Same	
Level of education	P.3	Same	Same	Same	Same	
Religion	Catholic	Same	Same	Same	Same	
Weight (Kg)	31.0	32.0	36.0	37.5	35.5	
Height (M)	1.40	1.41	1.41	1.41	1.41	
BMI	15.8	16.1	18.1	18.9	17.9	18.5 - 24.9 Kg/M^2
Temperature (ºC)	38.0	38.4	37.1	36.8	36.9	36.1-37.2ºC
Pulse rate (beats/minute)	100	103	80	78	80	60-80 beats/minute
Respiratory rate (/minute)	23	25	20	19	20	15-20 breaths/minute
HIV status	Negative	Negative	Negative	Negative	Negative	
Nodding & seizure status	**Present**	**Absent**	**Absent**	**Absent**	**Present**	
Haematological results						
WBC	19.6	20.91	9.64	6.5	5.4	3.0-15.0x103 /uL
RBC	5.3	5.01	4.23	4.22	4.23	2.5-5.5x106 /uL
Hb	13.5	13.10	11.1	11.3	11.4	10.0-17.0 g/dL
Hct	40.5	37.6	32.5	32.8	33.1	26.0-50.0%
MCV	80.2	75	76.8	76.9	77.2	86.0-110.0 fL
MCH	26.8	26.1	26.2	26.4	26.5	26. -38.0 pg
MCHC	35.4	34.8	34.2	34.9	35.1	31.0-37.0 g/dL
PLT	218	216	292	296	299	150.0-400.0x103 /uL
RDW-SD	37.6	37.1	38.8	39.2	39.1	37.0-54.0 fL
RDW-CV	14.7	14.1	14.8	14.9	15.1	11.0-16.0%
PDW	12.8	12.5	13.1	13.5	13.6	9.0-17.0 fL
MPV	10.9	10.8	10.9	11.2	11.4	9.0-13.0 fL
P-LCR	31.7	31.4	33.2	33.7	33.8	13.0-43.0%
PCT	0.25	0.23	0.32	0.35	0.38	0.17-0.35%
Neutrophils	10.97	12.02	3.48	1.21	0.52	1.5-7.0x103 /uL
Lymphocytes	5.22	5.47	4.57	4.12	3.85	1.0-3.7x103 /uL
Monocytes	2.6	2.6	0.85	0.42	0.34	0.0-0.7x103 /uL
Eosinophils	0.78	0.79	0.72	0.72	0.65	0.0-0.4x103 /uL
Basophils	0.03	0.03	0.04	0.03	0.04	0.0-0.1x103 /uL

Table 1 continues ……..

Clinical chemistry results						
Renal function tests						
Serum creatinine	0.7	0.7	0.7	0.7	0.6	0.6-1.1 mg/dl
Blood urea nitrogen	15	16	17	25	14	10.0-50.0 mg/dl
Na+	131.8	132	143.3	144.4	142.4	135.0-145.0 mmol/L
K+	3.87	3.85	3.96	3.95	3.64	3.5-5.5 mmol/L
Cl-	98	99	105.4	106.3	101.3	98.0-108.0 mmol/L
$HC0_3$-	11.3	24.5	25.4	26.4	9.8	25.0-30.0 mmol/L
Anion gap	**22.5**	**8.5**	**12.5**	**11.7**	**31.3**	**8.0-16.0mEq/L**
Liver function parameters						
GOT-ASAT	124	125	128	331	311	0.0-37.0 U/L
GPT-ALAT	100	101	102	252	248	0.0-42.0 U/L
Bilirubin-Direct	0.13	0.13	0.13	0.13	0.14	0.0-0.2 mg/dl
Bilirubin-Total	0.2	0.22	0.25	0.44	0.45	0.1-1.2 mg/dl
Serum Albumin	34.2	36.4	43.9	43.5	41.7	38.0-51.0 g/L
Total Protein	53.6	57.4	81.7	67.2	66.5	66.0-87.0 g/L

4. LABORATORY INVESTIGATIONS

4.1 Serum Electrolytes

Serum potassium and chloride remained within normal ranges throughout the period while sodium concentration was initially low at admission but over the month, its concentration returned to normal levels. The serum concentration of bicarbonate was in normal ranges during the nodding free period but was low at admission and at the end of January 2013 when there were frequent seizures and nodding episodes.

4.2 Anion Gap

During the hospitalization, the anion Gap of the child was calculated using the formula [Na+]-[Cl-]+[Hco_3-] and values between 8-16mEq/L was considered normal while those above 20mEq/L was considered high and thus a high anion metabolic acidosis was diagnosed [6,7,8]. The patient had high anion Gap at admission and three months later after the outset of watery diarrhoeal illness when the serum bicarbonate levels were below normal and this was associated with the increased nodding and seizure episodes.

Following this event and other previous observations that cold weather, starvation, bathing with cold water, stress and physical exercises stimulated nodding in NS children; it was perhaps a sign that these activities were increasing acidosis from lactic acid accumulation as a result of those activities. We hypothesized that nodding episodes was associated with high anion Gap metabolic acidosis due to excessive lactic acidosis and since this patient had a normal nutritional status, it was unlikely that the source of acidosis was from chronic starvation as was previously published. This acidosis may have resulted from a probably deranged energy production pathway where excessive acids were produced as by-products of metabolism. It is thought that this may be a result of a dysfunctioning of the mitochondria [8]. A mitochondrial disorder/disease presents with clinical features similar to that of Nodding syndrome such as brain developmental delays, neuro-psychiatric disturbances, mental retardation, seizures, dysautonomia (temperature instability and other dysautonomic problems); muscle weakness, cramping, dysmotility, hypotonia and muscle pains which have been observed in NS children. Mitochondrial disease/disorder may have occurred as a result of environmental contaminations in which children that developed NS may have experienced during or after the IDP camps [8].

4.3 White Blood Cell Counts (WBC)

The total white blood cell count was high at admission and the film report did indicate toxic granules to suggest active infective process at the beginning of the management at Gulu Regional Hospital (Pyomyositis of the muscles of the anterior abdominal wall). The hemoglobin concentration (Hb) of this patient was within normal ranges and reduced following the surgical procedure while the total WBC returned to normal two months after admission.

4.4 Renal Function Parameters

The patient had a normal serum creatinine and blood urea nitrogen levels and this indicated that the renal functions were probably normal and was perhaps unlikely that this patient had any intrinsic renal disease that could have contributed to the high anion gap. The CDC and other studies conducted on children with nodding syndrome in Northern Uganda in 2009 and later also confirmed the absence of intrinsic renal diseases [3,5,6,7,8].

4.5 Liver Function Parameters

The intrinsic liver enzymes AST and ALT were significantly high above the critical clinical threshold and this suggested liver cell injury and may be due to inflammation of the liver. Perhaps some of the anticonvulsant being administered may be culprit to this but it may perhaps be any other unrelated conditions to the anticonvulsants that may have caused the elevated liver enzymes.

4.6 Anthropometry

The anthropometry of the child improved during hospitalization; an indication that the food rehabilitation was making a positive change on the nutritional status of the child as reflected by the improvement in the weight, height, serum albumin, total protein and BMI.

4.7 Muscle Histology

The histology result as shown here on Fig. 1 showed that there was inflammation and destruction of the muscular architecture of the internal and external oblique muscles of the anterior abdominal wall with thrombosed blood vessels and infiltration with cells of inflammations.

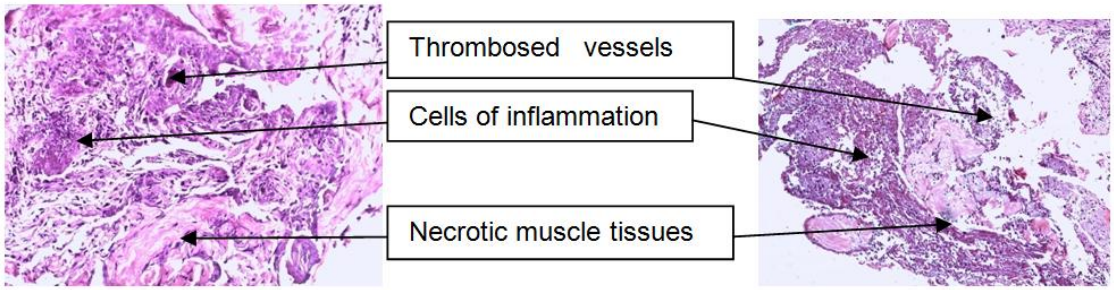

Fig. 1. Histology report of the muscle biopsy which shows destruction of the muscle architecture and thrombosis in the vessels (pyomyositis)

5. CONCLUSION

Nodding syndrome is an unknown neurological disorder affecting children whose nodding episodes are probably related to the high Anion Gap metabolic acidosis.

CONSENT

All authors declare that written informed consent was obtained from the parent of this child with NS.

ETHICAL APPROVAL

All authors hereby declare that the research have been examined and approved by Gulu University Faculty of Medicine Institutional Review Committee, which is the appropriate ethics committee and the approval have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. The Ethical clearance reference number is HS 922 and find attached the approval letter.

ACKNOWLEDGEMENTS

We acknowledge the roles played by members of the investigation team especially the staffs from Gulu Regional Hospital. We are greatly indebted to this pyomyositis patient with NS for accepting willingly to participate in this study.

This work was made possible by Gulu University and Medical Education for Equitable Services to All Ugandans (MESAU); a Medical Education Partnership Initiative (MEPI), grant number 5R24TW008886 from the Office of Global AIDS Coordinator and the U.S. Department of Health and Human Services, Health Resources and Services Administration and National Institutes of Health. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the government.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Lacey M. Nodding disease: Mystery of southern Sudan. Lancet Neurology. 2003;2(12):714. PubMed.
2. Richer M, Baba S, Kolaczinski J. Nodding disease/syndrome In: Neglected tropical diseases in Southern Sudan. Ministry of Health, Government of Southern Sudan. Southern Sudan; 2008.
3. Sejvar J, Foltz J, Dowell S. Nodding disease in Uganda: new clues, persistent enigma. Scientific Seminar Series Presentation, CDC. Washington; 2010.
4. Winkler AS, Friedrich K, König R. The head nodding syndrome-clinical classification and possible causes. Epilepsia. 2008;49(12). PubMed.
5. Kitara DL, Amone C. Perceptions of the population in Northern Uganda to Nodding syndrome. J Med Med Sci. 2012;3(7):464-470. PubMed.
6. David Lagoro Kitara, Amos Deogratius Mwaka, Henry R. Wabinga, Paul Okot Bwangamoi. Pyomyositis in Nodding Syndrome (NS) patient: A case report. Pan Afr Med J; 2013. PubMed.
7. Kitara DL, Mwaka AD, Anywar AD, Uwonda G, Abwang B, Kigonya E. Nodding Syndrome in Northern Uganda: A probable metabolic disorder. Br J Med Med Res. 2013; 3(4):2054-2068.

8. David Lagoro Kitara, Amos Deus Mwaka, Edward Kigonya. High anion gap metabolic acidosis in children with nodding syndrome in Northern Uganda. A Case Series. Br J Med Med Res. 2014;4(6):1301-1314.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history.php?iid=907&id=12&aid=7714