

CASE REPORT

Open Access



Multiple site neural tube defects at Zewuditu Memorial Hospital, Addis Ababa, Ethiopia: a case report

Mestet Yibeltal Shiferaw^{*}, Atalel Fentahun Awedew, Tsegazeab Laeke T/Mariam, Abenezer Tirsit Aklilu, Yemisirach Bizuneh Akililu and Aemiro Mazengia Andualem

Abstract

Background: Neural tube defects are common group of central nervous system anomalies of complex etiology and major public health importance worldwide. The occurrence of multiple neural tube defects, however, is an extremely rare event and has never been reported in Ethiopia so far. This study gives an insight into how the embryogenesis, management, and postoperative complications of multiple neural tube defects differ from the ordinary single neural tube defects on the basis of up-to-date existing literature.

Case presentation: This paper highlights a case of an 8 days old female black race Ethiopian neonate who was brought by her mother with the chief complaint of lower back and lower neck swelling since birth. The findings were a 5 × 4 × 5 cm sized ulcerated placode at the mid-lumbosacral area and a 1.5 × 1.5 × 1 cm sized fluctuant, nontender, transilluminating mass with overlying unruptured defect dysplastic skin at the cervicothoracic junction. With a diagnosis of multiple neural tube defects secondary to unruptured cervicothoracic meningocele and ruptured lumbosacral myelomeningocele, single-stage repair of the defects was done with good outcome.

Conclusion: There is insufficient evidence as to the exact mechanism of development of multiple neural tube defects. Similarly, whether patients with multiple neural tube defects had increased risk of post repair hydrocephalus compared with patients who have single neural tube defect is unknown. Hence, more research on the embryogenesis, management, and long-term outcome of multiple neural tube defects in particular and single neural tube defects in general should be done to better help patients with this costly and crippling problem. Lastly, the practice of folic acid supplementation is very low in resource-limited countries such as Ethiopia and, hence, should be improved.

Keywords: Case report, Ethiopia, Multiple neural tube defects, Neurulation, Re-zipping initiation model

Background

Neural tube defects (NTDs) are common group of central nervous system anomalies that occur from multifactorial perturbation of normal neural development [1]. They are a major public health problem with significant morbidity, mortality, disability, and economic costs worldwide [2, 3]. The prevalence of NTDs varies across regions worldwide.

According to a systemic review done in 2016, the median prevalence of NTDs was 11.7 per 10,000 births in Africa, 9 per 10,000 births in Europe, 11.5 per 10,000 births in America, and 21.9 per 10,000 births in Eastern Mediterranean [2]. A study conducted in the Addis Ababa and Amhara region, Ethiopia, revealed that NTDs were the leading cause of congenital anomalies and accounted for 40.3% of all congenital anomalies [4]. The prevalence of NTDs in Addis Ababa was 63.4 per 10,000 births and 126 per 10,000 births after 28 weeks and 12 weeks of gestation, respectively [5].

*Correspondence: jininuyibelt@gmail.com
Neurosurgery Division, Department of Surgery, School of Medicine, Addis Ababa University, Addis Ababa, Ethiopia



Multiple neural tube defects (MNTDs) are extremely rare congenital anomalies that are defined by the simultaneous occurrence of more than one NTD in a single case with “normal” neural tissue in between. It is mainly reported from developing African countries and India. It is a severe disorder that is thought to result from complex interaction of genetics and environmental factors, with folic acid deficiency being the most important environmental risk factor. There are different theories that explain how MNTDs and single NTDs develop, though the precise embryologic mechanism is still unknown [6].

Case report

History

An 8 days old female black race Ethiopian neonate born from a 28 years old para 1 abortion 1 mother by spontaneous vaginal delivery (SVD) at a gestational age of 40 + 1 week was brought by her mother to the pediatrics neurosurgical unit of Zewuditu Memorial Hospital with a complaint of lower back and lower neck swelling since birth. She had clear watery discharge from her lower back 1 day prior to her presentation. She was also not able to move her lower extremities since birth. Otherwise, she could suckle breast well and had no fever, abnormal body movements, or vomiting. Her mother lives in Addis Ababa and had unremarkable antenatal follow-up during her pregnancy. She, however, was not supplemented with folic acid before and during her pregnancy.

Physical examination

On physical examination, the baby was alert with normal vital signs. The baby had a 5 × 4 × 5 cm sized ruptured, shrunken and ulcerated placode at the mid-lumbosacral area. She also had a 1.5 × 1.5 × 1 cm sized fluctuant, nontender, transilluminating mass with overlying unruptured dysplastic skin at the mid-cervicothoracic junction area. She had lower limb paralysis. The head circumference was 31 cm, which lies within the normal range for her age (Fig. 1).

Investigations

Her laboratory results were all in the normal range but did not include imaging because of an affordability issue.

Diagnosis

Based on the clinical examination findings, the patient was clearly diagnosed to have multiple neural tube defects secondary to ruptured lumbosacral myelomeningocele and unruptured cervicothoracic meningocele.

Surgical procedure

After informed written consent was obtained, the patient was taken to operation room. The patient was intubated



Fig. 1 Cervicothoracic meningocele and lumbosacral ruptured myelomeningocele swellings (photo was taken after getting informed consent from the mother)

supine and repositioned to prone position. The surgical field was then cleaned with antiseptics (both alcohol and providone) and draped properly. Lidocaine with adrenaline was administered at the defect sites to minimize intraoperative bleeding and decrease postoperation pain. First, incision was made at the junction of the dysplastic and normal skin of the lumbosacral defect to free the placode. There was fibrinous material but no gush of cerebrospinal fluid in doing so. The fibrinous material was removed gently. The placode was then tubularized to facilitate optimal skin closure and decrease postoperation retethering. Nerve roots were freed from the arachnoids and dura circumferentially dissected. Hemostasis was secured with bipolar cautery and dura closed with proline (6, 0) in watertight fashion. Absence of cerebrospinal fluid (CSF) leak was checked using Valsalva maneuver. Repair of cervicothoracic meningocele was done using a similar technique. There was gush of clear CSF upon opening of the dysplastic skin, and the sac had communication with subdural space of the spinal cord. Part of the meninges sac was then excised and closed with proline (6, 0) in watertight fashion. Subcutaneous tissue and skin was also closed using vicryl (3, 0) at both sites. Patient was extubated and transferred to postanesthesia care unit with stable vital signs. Single-stage repair of the defects was completed safely.

Postoperative course and follow-up

Postoperatively, the patient's clinical status including serial head circumference was followed. Accordingly, she had no repair site CSF leak, wound failure, meningitis, or postrepair hydrocephalus. She took antibiotics for the ruptured myelomeningocele for 7 days. On her seventh postoperative day, she was discharged with

no complication. Currently, the patient is on her 11th smooth postoperative month on our follow-up, requiring no shunt so far.

Discussion

Among the 57 MNTDs that existed in published literatures, only 3 were MNTDs that consisted of cervicothoracic and lumbosacral myelomeningocele [6], ours being the fourth case (6.9% of MNTDs were cervicothoracic and lumbosacral myelomeningocele). Multiple site neural tube defects (MNTDs) were never reported in Ethiopia, probably because of poor documentation and reporting, despite single-site NTD being the most common congenital anomaly in Ethiopia [4, 5]. Proper documentation of this case was possible as initial evaluation of the patient's clinical presentation, therapeutic interventions, and postoperative follow-up were given by authors, while delayed presentation to our neurosurgical unit was the pitfall in the management of this patient.

The exact embryologic mechanism of how single- and multiple-site NTDs occur continues to be an area of controversy. To date, there exist three major hypotheses in this regard. These are the “single site” closure theory also known as zipper-like closure theory, the multisite closure theory, and re-zipping initiation model [7, 8].

The more widely accepted zipper-like closure (“single site” closure) theory explains the occurrence of single neural tube defect, and it states that the neural tube closure begins in the mid-cervical region and then progresses to close the caudal and cranial neuropores (on days 24 and 26, respectively) in a zipper-like fashion. According to this theory, the most caudal or the most rostral end should have been the most common site of an myelomeningocele (MMC) [6]. It, however, fails to explain how MNTDs and cranial NTDs do occur and why some types of NTDs are more common in some regions of the craniospinal axis. The areas caudal to S-2 form through secondary neurulation due to the neural tube forming above S-2, a concept that the three theories agree on.

The “Multiple initiation sites of closure model,” which was initially proposed by Van Allen *et al.*, hypothesizes that there are five closure sites and that closure proceeds in an orderly fashion. Initially, it begins at site 4, followed by sites 2 and 3 and then sites 1 and 5. This theory tries to explain how the development of MNTDs occurs. However, it is subject to criticism because of the rarity of MNTDs and continuous debate on the exact number of multiple sites of neural tube closure [7] (Fig. 2).

The “re-zipping initiation model” from interrupted site of closure, proposed by Mahalik *et al.*, hypothesizes that it is the interplay of *Shh* (Sonic hedgehog) and its antagonist *Wnt* that mediates the initiation and

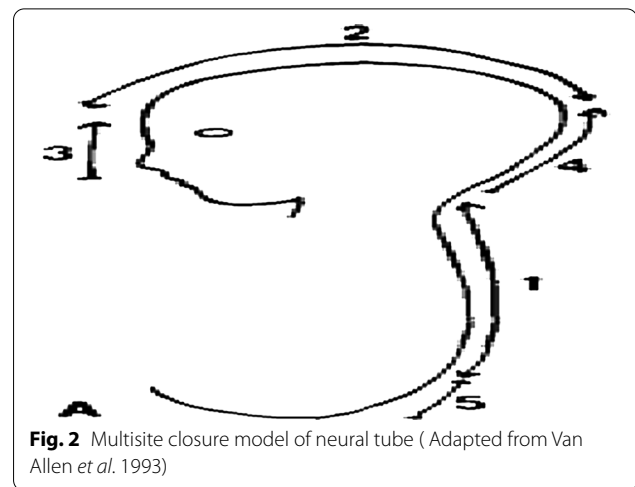
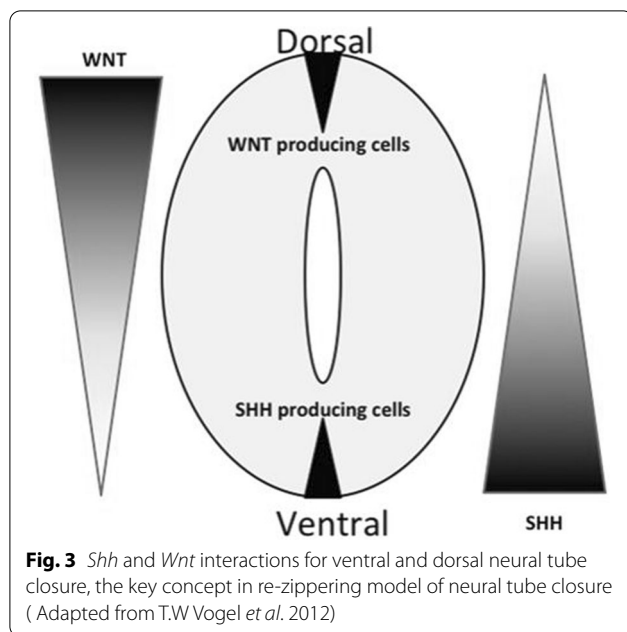


Fig. 2 Multisite closure model of neural tube (Adapted from Van Allen *et al.* 1993)

sustenance of neural tube closure. Normally, the antagonistic interactions between canonical *Wnt*, promoting dorsal identities, and *Shh* pathways, inducing ventral ones, would define the dorsoventral patterning of the developing central nervous system. In other words, *Shh* inhibits dorsolateral hinge point formation, and *Wnt* represses *Shh* activity. Mahalik *et al.* have stated that the focal alterations in the magnitude of *Shh* signaling lead to focal disruption of neural tube closure, while the normal neural tube closes normally in the adjacent segments. Thus, each segment will have an independent potential to close. Any local environmental insult to these regulatory pathways can affect the ability of succeeding segments to close, while the duration and local extent of the insult determine the extent of NTD. Once the causative insult subsides, the subsequent segments close because of their innate potential (Fig. 3).

The author gives emphasis to this theory as it better explains how any of the neural tube defects including MNTDs come into existence by taking the strong sides of previous theories and addressing their limitations. It also uses the results of many developmental neurobiology studies that explain the neural tube closure much better than the previous theories [8].

The MNTDs can be repaired with a single- or multiple-staged procedure. Whether to repair the MNTDs as a single- versus multiple-staged procedure is mainly a function of patient's tolerance to the duration of anesthesia and the anticipated blood loss for patient's age. Accordingly, single stage repair of defects is safe and not associated with increased postoperative complications. The repair for our case was done as a single-staged procedure with smooth postoperative course, which is consistent with other case reports [9]. However, whether patients with MNTD had increased risk of post-defect-repair



hydrocephalus compared with single NTD patients is unknown. Hence, further study is needed to guide clinicians' decision in management.

Prevention of neural tube defects

Folic acid deficiency among women of reproductive age is > 20% in most low-income countries while < 5% in high-income countries according to a systematic review done to assess global folic acid deficiency in women of reproductive age [10]. A public health importance of folic acid is defined by folic acid deficiency prevalence of > 5% among women of reproductive age. In Ethiopia, only one-third (32.7%) of reproductive women had normal (> 6.6 ng/mL) serum folic acid level, while nearly half (46.1%) of them had severe (< 4 ng/mL) deficiency [11].

Evidence from randomized control trials (RCT) clearly revealed that supplementation of folic acid could have decreased NTD recurrence rate by 72% [12, 13]. The practice of folic acid supplementation should be emphasized in resource-limited countries, including Ethiopia, as only 13.5% of mothers having kids with NTD get folic acid supplementation compared with 30.6% of mothers who deliver normal babies [5].

Conclusion

There is insufficient evidence as to the exact mechanism of MNTD development. Similarly, whether patients with MNTD had increased risk of postrepair hydrocephalus compared with single neural tube defect remains unknown. Hence, more research on the embryogenesis, management, and long-term outcome of MNTDs in

particular and single NTDs in general should be done to better help patients with this costly and crippling problem. Lastly, the practice of folic acid supplementation is very low in resource-limited countries such as Ethiopia and should be improved.

Abbreviations

CSF: Cerebrospinal fluid; MNTD: Multiple neural tube defects; NTDs: Neural tube defects; RCT: Randomized control trial; SVD: Spontaneous vaginal delivery.

Acknowledgements

We would like to give our sincere thanks to the goodwill of the patient's legal guardian for this work to get published.

Patient perspective

Initially, the baby's mother was depressed of the multiple sites swelling that her baby was born with. Following proper advice and surgical closure of defects, the mother has got better satisfaction and is adherent to our follow-up.

Authors' contributions

Conceptualization: MY, AF, TL, AT, YB, and AM. Case narration: MY. Manuscript draft: MY, AF, TL, AT, YB, and AM. Manuscript review and editing: MY, AF, TL, AT, YB, and AM. All authors read and approved the final manuscript.

Funding

No funding needed for this study.

Availability of data and materials

Availability of supporting data: besides the patient's picture, the photo of the patient's chart is available from corresponding author and can be shared when needed.

Declaration

Ethics approval and consent for participation

The case report was not submitted for ethical approval.

Consent for publication

Written informed consent was obtained from patient's legal guardian for publication of this case report and use of any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

All authors declare that they have no competing interests.

Received: 30 September 2020 Accepted: 18 May 2021

Published online: 17 August 2021

References

- Vogel TW, Carter CS, Abode-Iyamah K, Zhang Q, Robinson S. The role of primary cilia in the pathophysiology of neural tube defects. *Neurosurg Focus*. 2012;33(4):E2.
- Blencowe H, Kanacherla V, Moorthie S, Darlison MW, Modell B. Estimates of global and regional prevalence of neural tube defects for 2015: a systematic analysis. *Ann New York Acad Sci*. 2018;1414(1):31–46.
- Zaganjor I, Sekkarie A, Tsang BL, Williams J, Razzaghi H, Mulinare J, et al. Describing the prevalence of neural tube defects worldwide: a systematic literature review. *PLoS ONE*. 2016;11(4):e0151586. <https://doi.org/10.1371/journal.pone.0151586>.
- Taye M, Afework M, Fantaye W, Diro E, Worku A. Congenital anomalies prevalence in Addis Ababa and the Amhara region, Ethiopia: a descriptive cross-sectional study. *BMC Pediatr*. 2019;19(1):1–1. <https://doi.org/10.1186/s12887-019-1596-2>.

5. Tadesse BT. Magnitude of neural tube defects and associated risk factors at three teaching hospitals in Addis Ababa Ethiopia. *BioMed Res Int*. 2018. <https://doi.org/10.1155/2018/4829023>.
6. Deora H, Srinivas D, Shukla D, *et al*. Multiple-site neural tube defects: embryogenesis with complete review of existing literature. *Neurosurg Focus*. 2019;47(4):E18.
7. Van Allen MI, Kalousek DK, Chernoff GF, Juriloff D, Harris M, McGillivray BC, *et al*. Evidence for multi-site closure of the neural tube in humans. *Am J Med Genet*. 1993;47:723–43.
8. Mahalik SK, Vaze D, Kanojia RP, Narasimhan KL, Rao KLN. Multiple neural tube defects may not be very rare. *Childs Nerv Syst*. 2013;29:609–19.
9. Ahmad FU, Dwarakanath S, Sharma BS, Mahapatra AK. Multiple neural tube defects: a clinical series of seven cases and their embryological basis. *Pediatr Neurosurg*. 2008;44(4):280–7. <https://doi.org/10.1159/000131676>.
10. Rogers LM, Cordero AM, Pfeiffer CM, *et al*. Global folate status in women of reproductive age: a systematic review with emphasis on methodological issues. *Ann NY Acad Sci*. 2018;1431(1):35–57. <https://doi.org/10.1111/nyas.13963>.
11. Haidar J, Melaku U, Pobocik RS. Folate deficiency in women of reproductive age in nine administrative regions of Ethiopia: an emerging public health problem. *S Afr J Clin Nutr*. 2010;23(3):132–7.
12. American College of Obstetricians and Gynecologists. Neural tube defects. Practice Bulletin No. 187. *Obstet Gynecol* 2017; 130: e279–90
13. Wilson RD, Audibert F, Brock JA, *et al*. Pre-conception folic acid and multivitamin supplementation for the primary and secondary prevention of neural tube defects and other folic acid-sensitive congenital anomalies. *J Obstet Gynaecol Can*. 2015;37(6):534–49.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

