Anencephaly and Sodium Valproate: Case Report and Lessons for the Future

Nana Njamen Theophile¹,², Paul Nkemtendong Tolefac³,⁴, Rita Frinue Tamambang³, Charlotte Nguefack Tchente¹,⁵, Kouam Siegning⁵, Eugene Vernuyu Yeika⁴, Pascal Foumane³

¹Service of obstetrics and gynaecology, Douala general hospital, Douala Cameroon
²Faculty of Health Sciences, University of Buea, Buea, Cameroon
³Faculty of Medicine and Biomedical Sciences, University of Yaounde I, Yaounde Cameroon
⁴Clinical Research Education Networking and Consultancy, Douala, Cameroon
⁵Faculty of Medicine and Pharmaceutical Sciences, University of Douala, Douala, Cameroon

Corresponding Author: Dr. Nana Njamen Theophile
njanathee@yahoo.fr

ABSTRACT

Background: Anencephaly is a common variant of neural tube defects that results from complex interaction between the gene and the environment. Case presentation: We report the case of a 25-year-old female Cameroonian gravida 1 para 0 epileptic and routine daily sodium valproate referred after a routine ultrasound at 20 weeks showed anencephaly. Medical termination of pregnancy was done after counselling and the recovery uneventful. Conclusion: This case highlights the importance of stopping drugs preconception and after the first missed period as well as the importance of preconceptional and periconceptional folic acid. Together with evidence from previous studies, the author recommends fortification of regular food products such as salts before selling.

Keywords: Anencephaly, Neural tube defect, Valproate, Case report

1. INTRODUCTION

Anencephaly is congenital absence of a major portion of the brain, skull and scalp. It results due to the defective neurulation process, which is defined as the process of neural tissue formation from the ectoderm(1). In anencephaly, the abnormality occurs in neurulation of the cranial part, Due to this, the neural tissue is exposed and is not covered with the skull. The development of the cerebral hemispheres is also absent. Numerous risk factors have been associated with development of Neural Tube Defects (NTD). These risk factors are multifactorials that combine an interaction between genetic, environmental, low socioeconomic status, member of racial or ethnic minority group or folic acid deficiency(1). The vast majority of patients suffering from seizures require daily antiepileptic drugs (AED) therapy, and in most instances, this is a lifelong treatment. Infants born to epileptic women have significantly higher risks of having one of the features of the embryopathy (i.e., major malformations, microcephaly, growth retardation, and hypoplasia of the midface and fingers) associated with in utero exposure to AED(2). A case control study published by the new England journal of medicine (NEJM) in 2010 showed that the use of sodium valproate monotherapy in the first trimester of pregnancy was associated with significantly increased risks of several congenital malformations amongst which are neural tube defects(3). The authors report the case of a 25-year-old female Cameroonian gravida 1 para 0 epileptic and routine daily sodium valproate referred after a routine ultrasound at 20 weeks showed anencephaly. Medical termination of pregnancy was done after counselling and the recovery uneventful.

2. CASE PRESENTATION

A 25-year-old female gravida 1 para 0 at 20 weeks of gestation was referred by her obstetrician to Douala general hospital (DGH) after a routine obstetric ultrasound showed anencephaly. The patient is a known epileptic for over seven years and has been taken sodium valproate 500mg twice daily for over seven years. The pregnancy was unplanned and she denied taking folic acid prior to conception and or after conception. On arrival, she was alert and anxious, the abdomen was distended with the uterus at the level of the umbilicus. The cervix was long, posterior and closed. After counselling, medical termination of pregnancy was decided with 400µg misoprostol in the posterior vaginal fornix. This was followed by an expulsion of an anencephalic living fetus which died after a few minutes (fig. 1). The early post abortum period was unremarkable. After counselling for family planning she chose levonorgestrel-containing intrauterine device.

3. DISCUSSION

Neural tube defects (NTDs) are congenital malformations that affects 1:1000 pregnancies. NTDs alongside congenital heart disorders and are ranked the commonest congenital anomalies⁴⁵. Reports of foetuses and infants with anencephaly, myelomeningocele and craniorachischisis extend back to Ancient Egyptian times⁶. Our index case describes the case of anencephaly. Both genetic and non-genetic factors have been implicated in the aetiology of NTDs, with up to 70% of the variance in NTD prevalence due to genetic factors⁷. Evidence for genetic component includes an increased recurrence risk for siblings of index cases (2.5%) compared with the 0.1% risk in the general population, together with a gradually decreasing frequency in more distant relatives. Women with two or more affected pregnancies have a higher risk (~10%) of further recurrence. NTD prevalence is greater in like-sex twins (assumed to include all monozygotic cases) compared with unlike-sex pairs, consistent with a significant genetic component. Nevertheless, NTDs rarely present as multiple cases in families; instead a sporadic pattern is usually observed. Taken together with the relatively high prevalence of NTDs across the world, this is consistent with a multifactorial polygenic or oligogenic pattern of inheritance, and an important role for non-genetic factors⁴¹. Neural tube defects (anencephaly and spina bifida) are more frequent in children born to mothers with low folic acid and B12 levels and high homocysteine levels⁸⁹. Antiepileptic drugs (AEDs) such as sodium valproate, carbamazepine interfere with the metabolism of folic acid decreasing serum folate. These drugs also induced hyper-homocysteinemia¹⁰. Strongest evidence indicates that valproate exposure is associated with a 1–2% risk of NTDs, a 10- to 20-fold increase over the general population and an increased risk of neurodevelopmental deficits¹¹¹². Our indexed case had no genetic predisposition but was on AEDs (valproate) for over seven years. The anencephaly could be explained by the complex interaction between genes and folate deficiency resulting from AEDs. Hard evidence is available to advise all women capable of becoming pregnant to have periconceptional (i.e. 2–3 month before and until 3 months after conception) folic acid supplementation to reduce the major part of NTDs. This periconceptional folic acid should be taken at a dose of 400µg (0.4mg) if no history of NTDs or 1mg if the woman has a history of NTDs¹³¹⁴. Nevertheless, this opportunity is frequently missed as in our indexed case. This is because more than 50% of pregnancies are unplanned and most women start antenatal care late¹⁵¹⁶ as in our case reported above that even though the pregnancy was unplanned she continues taking valproate for her...
Neural tube defects are the most common congenital abnormality after congenital heart disorders. These disorders result from a complex interaction between gene and the environment. This case highlights the importance of preconceptional counselling and prevention and periconception folic acid in all women of child bearing age as pregnancies are not always planned. Furthermore, it demonstrates the importance of stopping all drugs prior to conception and or after the first missed period as well as the need for early antenatal care booking.

4. CONCLUSION

Neural tube defects are the most common congenital abnormality after congenital heart disorders. These disorders result from a complex interaction between gene and the environment. This case highlights the importance of preconceptional counselling and prevention and periconception folic acid in all women of child bearing age as pregnancies are not always planned. Furthermore, it demonstrates the importance of stopping all drugs prior to conception and or after the first missed period as well as the need for early antenatal care booking.

REFERENCES