

# Craniorachischisis in a 33-week-old Female Fetus: A Case Report

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## ABSTRACT

We report the case of a 33-week-old female fetus born with craniorachischisis to a gravida 5, para 4 (3104) mother with no previous history of conceiving a child with a neural tube defect. Craniorachischisis is characterized by anencephaly and an open defect extending from the brain to the spine and is the most severe and fatal type of neural tube defect. Although the cause of neural tube defects is hypothesized to be multifactorial and is usually sporadic, the risk is increased in neonates born to mothers with a family history or a previous pregnancy with neural tube defect, both of which are not present in the index case. This case is unique in that only during the fifth pregnancy did the couple conceive a child with a neural tube defect, emphasizing that folic acid supplementation, the sole preventive measure proven to decrease the risk of neural tube defects, remains to be important in the periconceptual period for all women of childbearing age.

*Keywords: autopsy, case report, congenital abnormalities, craniorachischisis, neural tube defects*

## INTRODUCTION

Neural tube defects (NTD) are one of the most common congenital anomalies among live births, occurring in 1.9 to 66.2 per 10,000 births in Southeast Asia.<sup>1</sup> Studies on NTDs have hypothesized that these conditions are caused by many factors, genetic and non-genetic, that disrupt the normal closure of the neural tube during embryogenesis.<sup>2,3</sup> Craniorachischisis is the most severe of the NTDs and is characterized by an open defect extending from the skull to the spine and is usually associated with anencephaly.<sup>2</sup> The condition is uniformly fatal. Although most cases are conceived in the first pregnancy, the case to be presented is notable in that it was the mother's fifth conception, stressing that neural tube defects can occur at any time. We aim to report a case of craniorachischisis and present what is currently known about neural tube defects and their prevention. As of this writing, there also have been no reported cases in the Philippines after utilizing web-based search engines and electronic databases such as PubMed and SCOPUS. Preventive factors that decrease the risk of conceiving a child with NTDs include folic acid supplementation during the periconceptual period.<sup>4</sup>

## CASE PRESENTATION

We report a case of a preterm female neonate with multiple lethal congenital anomalies, delivered via repeat cesarean section to a then 37-year-old gravida 5, para 4 (3104) mother with no known family history of genetic



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disorders. All previous pregnancies were conceived with the same partner. The first three pregnancies were full-term, delivered via spontaneous vaginal delivery without fetomaternal complications. The fourth pregnancy was a twin gestation, delivered preterm via cesarean section. Twin 2 was born with ambiguous genitalia and expired on the 10<sup>th</sup> day of life. None of the previous pregnancies were born with neural tube defects. For the current pregnancy, folic acid supplementation was started at 26 weeks of gestation.

A congenital anomaly scan done at 28 weeks showed polyhydramnios, acrania, cardiomegaly, hypotelorism, abnormal spine curvature, pulmonary hypoplasia with a bell-shaped thorax, and absence of gastric bubble.

Termination of the pregnancy was done via repeat cesarean section at 33 weeks of gestation. At birth, the patient was born with multiple congenital anomalies, of which anencephaly was most prominent. The neonate was limp, apneic, and cyanotic with a heart rate in the 90s (APGAR 2, 2). At 33 minutes of life, the patient was declared asystolic and referred for autopsy.

## AUTOPSY FINDINGS

An autopsy was performed 30 hours postmortem. The decedent was appropriate for gestational age weighing 1468 grams with a foot length of 5.2 cm.

External examination showed the following physical findings: absence of the fetal skull with a contiguous defect extending to the cervical spine exposing the underlying neural tissue, a short neck, hyperextension of the cervicothoracic spine, lack of breast buds, and a sacral dimple (Figures 1A to 1D). On closer inspection of the head, there was facial edema, low-set ears, and hypotelorism. No cleft lip or cleft palate was appreciated. The decedent was phenotypically female with labial edema and a patent anus. No amniotic bands were noted.

A post-mortem babygram was done with a final clinical impression as follows: acrania-anencephaly, vertebral segmentation defects, caudal neuropore defects, and chondrodysplasia punctata. Of note, the neurocranium, lungs, bowel loops, and normal cervical vertebrae were not visualized. The thoracolumbar spine is markedly kyphotic and there was marked swelling throughout the visualized soft tissues (Figures 2A and 2B).

Opening of the thoracoabdominal cavity revealed bilateral pleural effusion with approximately 10 mL and 5 mL of serosanguinous fluid on the right and left pleural cavities, respectively. Both lungs were hypoplastic with a combined weight of 2 grams. The heart exhibited normal inflow and outflow tracts with a patent foramen ovale and ductus arteriosus. The larynx, thyroid, and adrenal glands were not identified, likely due to incomplete harvesting of the organ block. No abnormalities were seen in the other internal organs.

Given the above findings, the primary consideration is craniorachischisis due to the presence of the contiguous open

defect from the skull to the cervical spine. Considering the presence of short neck and retroflexion, a close differential diagnosis would be iniencephaly, another type of neural tube defect. However, in contrast to craniorachischisis, iniencephaly presents with a skin-covered neural tube defect and is more associated with an occipital encephalocele instead of anencephaly.

The above findings were limited by the quality of the organ block harvested during evisceration which was difficult due to the anatomy of the decedent. Furthermore, genetic studies such as karyotyping were also considered as further work-up in this case but was not done due to the cost and lack of fresh tissue for culture.

## DISCUSSION

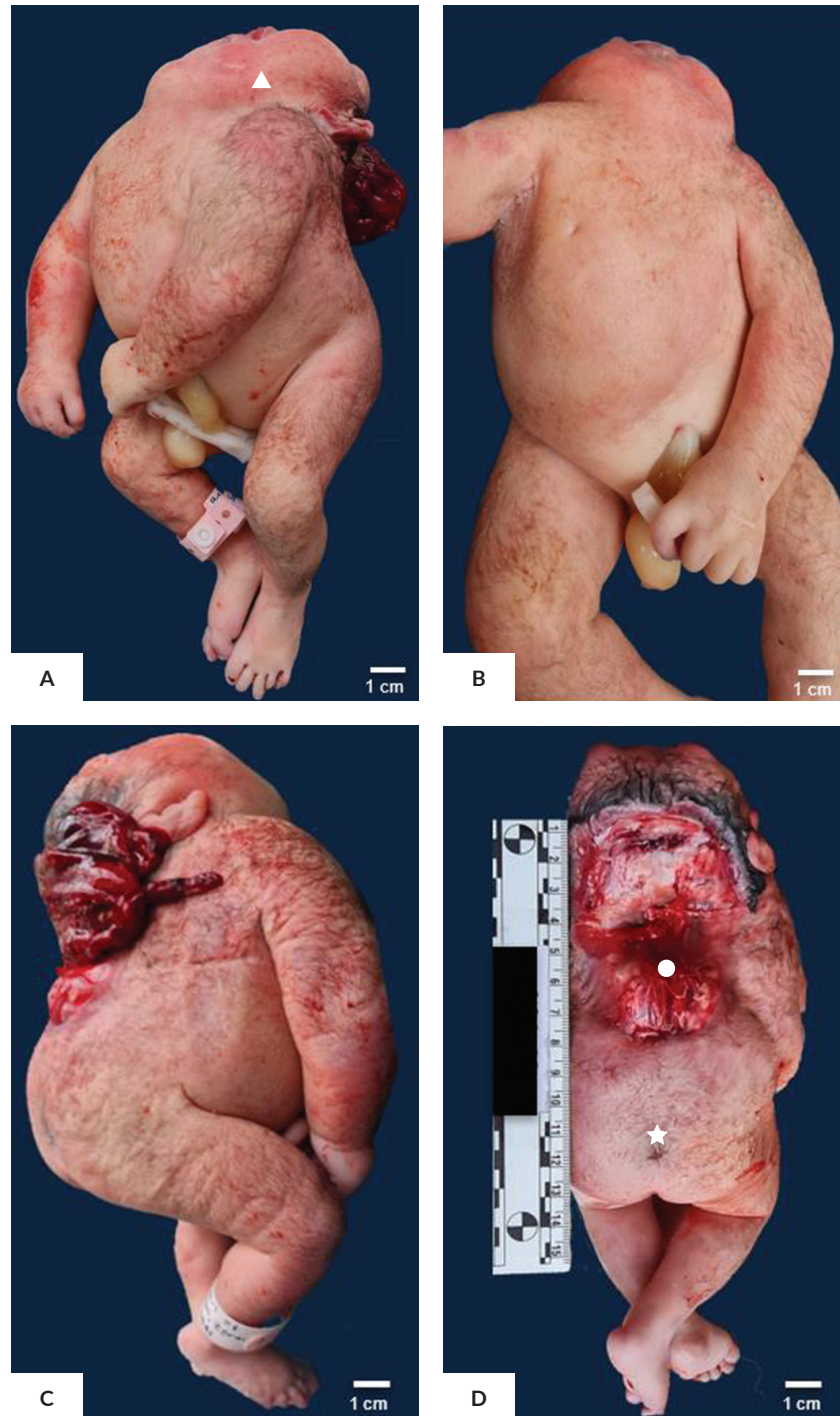
NTDs are a group of congenital birth defects that result from the incomplete closure of neural tube during embryogenesis. The incomplete closure results in an open or closed defect depending on the presence of an overlying membrane or skin, exposing underlying neural tissue.<sup>2</sup> This process normally occurs between the third to fourth week of gestation and is completed after the 28<sup>th</sup> day of conception.<sup>2,5,6</sup> Since this occurs early in embryogenesis, NTDs are detectable as early as 13 weeks of gestation by prenatal ultrasound and 22 weeks by magnetic resonance imaging.<sup>6</sup>

Worldwide, the incidence of NTDs varies by region but is thought to be higher in countries with lower socio-economic status and in females.<sup>7,8</sup> Most cases of NTDs are sporadic. However, studies have shown that the risk is increased for couples who have had a child with an NTD or for those with a family history of NTD compared to the general population.<sup>3</sup>

In the Philippines, congenital anomalies have consistently remained in the top ten causes of infant mortality in the past 50 years. In a recent study conducted in Philippine General Hospital, disorders of the nervous system were discovered to be the second most common birth defect, next to musculoskeletal system anomalies. A significant number of cases among the nervous system disorders were NTDs such as anencephaly, encephalocele, and spina bifida (50 out of 174 cases).<sup>9</sup>

Multiple attempts have been made to pinpoint the exact cause of NTDs, but no concrete evidence has been identified. Previous studies demonstrate that the cause is likely multifactorial and that both genetic and environmental factors contribute synergistically to impair neural tube closure. Genetic factors that could play a role include the planar cell polarity (PCP) signaling pathway and genes that encode enzymes related to folate metabolism such as 5,10-methylenetetrahydrofolate reductase.<sup>2,3</sup> In relation to the latter, folic acid deficiency during the periconceptional period may also increase the risk of NTDs.<sup>3</sup>

The sole preventive measure proven to decrease the risk of NTD is folic acid supplementation. Folic acid supplementation in women of reproductive age with 0.4-



**Figure 1.** (A) Antero-left side view (B) Anterior view (C) Right side view: The fetus showed hyperextension cervicothoracic spine (▲) with a short neck, kyphoscoliosis, and an absence of breast buds. (D) Posterior view: This view demonstrates absence of the brain and cranial vault with a contiguous defect extending to the cervical spine exposing the underlying neural tissue (●) and a sacral dimple (★).



**Figure 2.** (A) Anteroposterior view (B) Lateral view radiographs showing acrania-anencephaly, vertebral segmentation defects, caudal neuropore defects, chondrodysplasia punctata, severe kyphoscoliosis, and marked swelling of the soft tissues.

0.8 mg/day of folate should be initiated 5-6 months before conception and continued until the first month of pregnancy, when neural tube closure is completed. Higher doses (4 mg/day) are recommended for those at increased risk of NTD.<sup>4</sup> However, this does not eliminate the risk. In 2018, Rabarikoto reported a case of craniorachischisis wherein the mother had a prior pregnancy with anencephaly and high dose folic acid was given three months prior to conception of the second pregnancy.<sup>6</sup> This implies that factors other than nutritional folic acid deficiency are at play in the pathogenesis of neural tube defects.

Public health strategies such as food fortification can also be of benefit in areas where there is inadequate compliance to folic acid intake.<sup>4,10</sup> Couples at higher risk of conceiving a child with NTD (e.g., those with a family history of NTD or those who have a previous child with NTD) can undergo genetic counselling as another preventive measure.<sup>6</sup>

In other reported cases of craniorachischisis, folic acid supplementation was not given or were started later than recommended, such as in the case reported by Costa et al. and in the case presented.<sup>5,7,11</sup> Craniorachischisis is more commonly associated with anencephaly wherein exposed brain tissue is dissolved upon prolonged exposure to amniotic fluid, but it may also present occasionally with exencephaly.<sup>12</sup> However, there was no mention in the literature of whether anencephaly is primarily caused by the dissolution of brain tissue or an intrinsic developmental pathology. Another case reported calcifications in the liver, although its significance is not known.<sup>11</sup>

Anomalies or syndromes associated with craniorachischisis are variable. In a literature review by Coskun et al., several cases of craniorachischisis were associated with congenital malformations such as pentalogy of Cantrell and sirenomelia. Some cases also report craniorachischisis in association with genetic disorders such as trisomy 18 and trisomy 11.<sup>7</sup> On the other hand, it can also be an isolated finding such as in the case reported by Costa et al., where a karyotype of fetal skin was done and was unremarkable.<sup>5</sup> In retrospect, karyotyping and/or genetic testing would have also been beneficial for this case to determine if other genetic syndromes or anomalies are present but was not performed.

## CONCLUSION

Craniorachischisis is the result of failure of closure of the neural tube during embryogenesis and is considered the most severe form of NTD. It is characterized by an open, contiguous defect extending from the cranium to the spine. The etiology of this group of disorders has yet to be elucidated, however, recent research points to mutations in the PCP signaling pathway and defects in folate metabolism as possible causes. As of present, there is no effective treatment for patients born with craniorachischisis and the condition is uniformly fatal. Folic acid supplementation during the periconceptual period is the only known prophylactic measure to reduce the risk of occurrence. Genetic counselling can also inform, guide, and increase the couple's awareness

regarding the risk of conceiving another child with an NTD in subsequent pregnancies.

### Ethical Considerations

The mother of the decedent signed an autopsy consent form.

### Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

### Author Disclosure

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