

Case Report

A Stillborn Baby with Tetra-amelia Syndrome in Jember: A Case Report

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Abstract

Tetra-amelia syndrome is a rare congenital disorder characterized by the absence of all four extremities. This extremity disorder occurs in 1 in 1,300 to 2,000 births. This condition is caused by genetic mutations in the WNT3 and RSPO2 genes. Specific risk factors for tetra-amelia syndrome remain unclear. This is also due to the lack of studies that discuss specific risk factors for tetra-amelia syndrome. In this case report, we discuss a stillborn baby with tetra-amelia syndrome to a mother with various pregnancy risk factors in Jember. This case report aims to examine the presence of several risk factors in the mother and their relationship with congenital disorders, especially tetra-amelia syndrome.

Keywords : congenital disorders, genetic disorders, malformations, still born, tetra-amelia syndrome

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INTRODUCTION

Tetra-amelia syndrome (TAS) is a rare congenital disorder characterized by the absence of all four extremities. “Tetra” in Greek means four and “amelia” means failure of development of arms or legs that occurs before birth. This condition can be accompanied by abnormalities in other parts of the body, such as the central nervous system, craniofacial, cardiopulmonary, digestive system, and urogenital system (Horn et al., 2018). The diagnosis of this disorder can be made clinically, but the majority of cases are identified by ultrasonography during routine antenatal examinations (Loughnan & Milan, 2020).

This extremity abnormality occurs in 1 in 1,300 to 2,000 births (Diarra N et al., 2020). This condition is caused by genetic mutations in the WNT3 and RSPO2 genes. Mutations in the WNT3 gene can cause tetra-amelia type 1 syndrome, while mutations in the RSPO2 gene are the cause of TAS type 2. Genetic mutations can be caused by viral infections, environmental factors, such as UV radiation from sun exposure, or a combination of all of these things (Diarra N et al., 2020).

Discussions regarding tetra-amelia syndrome are still rarely reported. The reason is that most babies with this syndrome are stillborn or die not long after birth (Horn et al., 2018). Therefore, this case report describes a stillborn baby with tetra-amelia syndrome in Jember.

CASE REPORT

A stillborn male baby was born through normal delivery in a lifeless state with incomplete extremities (lacking the antebrachial region (dextra et sinistra), humerus (dextra et sinistra), and cruris (dextra et sinistra)) as in Figure 1. This baby was born with eyes closed. The baby weighed 1,100 grams, body length 31 cm with an APGAR score of 0-0. No further internal surgical examination of the baby was carried out. The condition of the patient's delivery was an incident of preterm premature rupture of membranes (PPROM) with a gestational age of 30-31 weeks and accompanied by antepartum bleeding (APB).

The patient was a 28-year-old primigravida and a housewife. She had no recorded history of contraceptive use, including birth control pills, during her marriage. She was diagnosed with systemic lupus erythematosus (SLE) in 2021 and underwent long-term corticosteroid therapy, i.e. dexamethasone. She also opted to consume herbal medicines regularly, formulated by her family, while managing her condition. It is known that the patient lives at home with the patient's parents, while her husband, a 29-year-old, who works as a skipper, has not returned during pregnancy. The patient's parents and the patient's husband are active smokers. Conception was achieved after three years of attempting

pregnancy. During her pregnancy, it was found that there were abnormalities in the fetus at three months of gestation through ultrasonography evaluation, documented and performed by gynecologist. The patient experienced cough and flu for one week before giving birth. The patient is also known to have consumed herbal medicine containing turmeric, ginger, and saffron for 1.5 months at the start of pregnancy as requested by her in-laws due to frequent complaints of dizziness and nausea during her pregnancy also her SLE condition. The patient denied that there were any other ingredients in the herbal medicine and that she had ever taken medication during pregnancy. The patient did not know relevant family history of the disease and there was no further examination regarding this matter.



Figure 1 clinical features of the stillborn baby.

DISCUSSION

Tetra-amelia syndrome is a congenital abnormality characterized by the absence of all four extremities in newborn babies. This syndrome occurs due to disturbances during the baby's growth in the womb. Tetra-amelia syndrome can occur independently or in association with other anomalies or other syndromes (Diarra N et al., 2020). The presence of other congenital abnormalities in tetra-amelia also influences why tetra-amelia babies

usually die at birth or sometime after birth. However, tetra-amelia syndrome alone also has a high mortality rate at birth or sometime after birth (Dutta, 2012).

Growth of the extremities, both upper and lower extremities, is known to occur starting at the end of the fourth week. The upper extremities grow around day 26, followed by the lower extremities 1-2 days later or on day 28 (Bermejo-Sánchez et al., 2011; Eghbalian, Sharif, & Monsef, 2015). At the end of week 6, the embryo begins to acquire a human shape and at the end of week 14, all the extremities are formed, followed by muscle and nerve development at week 20 (Magdariaga et al., 2020).

Congenital abnormalities affecting the extremities such as meromelia or amelia usually occur in the 5th to 6th week (Magdariaga et al., 2020). Tetra-amelia can be diagnosed prenatally using prenatal ultrasound (Eghbalian et al., 2015). The cause of Tetra-amelia is the presence of genetic mutations in the WNT3 and RSPO genes which play a role in the process of limb development. Congenital abnormalities are also influenced by several factors, although they are not specific to Tetra-amelia.

The patient, diagnosed with systemic lupus erythematosus (SLE) prior to pregnancy. SLE is a chronic autoimmune disorder characterized by the body's immune system mistakenly attacking its own tissues. While the precise etiology remains elusive, evidence suggests a complex interplay between genetic predisposition and environmental factors in triggering aberrant immune responses. These responses culminate in the overproduction of pathogenic autoantibodies by B cells and dysregulation of cytokines, leading to tissue damage. SLE can significantly impact pregnancy, often resulting in adverse outcomes for both mother and fetus. A study by Liu et al (2013) corroborates this association, demonstrating a heightened risk of poor fetal and maternal outcomes among women with SLE (Ameer et al., 2022). Pregnancy exacerbates the symptoms of the disease, often leading to adverse maternal and fetal outcomes. In severe cases, these complications can result in maternal or fetal mortality, or impaired fetal development (Rajaei et al., 2019). SLE is associated with a heightened risk of adverse fetal outcomes, including fetal mortality, preterm birth, small for gestational age (SGA) newborns, intrauterine growth restriction (IUGR), congenital heart block, and myocardial dysfunction. A prospective cohort study of 1,000 SLE pregnancies by Cervera et al. (2015) revealed a significant rate of early pregnancy loss, affecting 16.5% of cases, underscoring the substantial maternal morbidity associated with SLE during pregnancy. Compared to healthy pregnant individuals, women with SLE experience a greater likelihood of unfavorable perinatal outcomes (Sangah et al., 2023).

The patient received dexamethasone therapy and was frequently administered herbal supplements. Pregnancy-related problems, such as nausea, vomiting, constipation, and heartburn, usually cause pregnant women to try to self-medicate using over-the-counter

medications or using herbal remedies. Herbal products are more commonly used because they are considered safer for the fetus. Herbal medicines have been defined as medicinal product based on herbs, herbal materials, herbal preparations and finished herbal products that contain as active ingredients parts of plants, other plant materials, or combinations. Herbal extracts contain many active molecules that may cause adverse effects including teratogenicity (Bruno et al, 2018; John & Shantakumari, 2015). It is well-established that numerous medications and other substances can act as teratogens, inducing congenital malformations (Salemn & Suliman, 2024).

The use of medicines and herbs during pregnancy should be treated with extreme caution as they may have adverse effects on the mother and fetus. If prescribed correctly, traditional Chinese medicines are safe and rarely cause life-threatening events. However, if herbal medicines are used incorrectly or used in combination with regular medications, interactions and side effects between herbal medicines and prescribed drugs may occur. Interactions between herbal medicines and prescribed drugs may have unknown effects on the pregnancy or cause serious complications to the fetus. The first trimester in particular is the most critical period of pregnancy when fetal organ formation occurs, and utmost care should be taken to reduce the risk of fetal morbidity and mortality (Bruno et al., 2018; John & Shantakumari, 2015). A case of tetra-amelia syndrome was reported that a baby was born without all four extremities and the baby's mother had previously consumed herbal medicines in the first trimester of pregnancy in an attempt to abort the baby (Dutta, 2012).

In this case report it is known that the patient and the patient's family are active smokers. It is known that smoking can be a factor in the occurrence of genetic mutations in humans. Cigarettes are also known to be associated with an increased risk of congenital defects such as cleft lip, intrauterine growth retardation, or another congenital defect (Delcroix-Gomez et al., 2022; McGrath-Morrow et al., 2020).

Specific risk factors for tetra-amelia syndrome remain unclear. This is because there are still few studies discussing specific risk factors for tetra-amelia syndrome (Bermejo-Sánchez et al., 2011). However, known risk factors for congenital abnormalities such as lifestyle, environment, genetics, and teratogenic are believed to contribute as risk factors for tetra-amelia syndrome.

CONCLUSION

Specific risk factors for tetra-amelia syndrome remain unclear because of the limitation of these studies which discuss the various risk factors for tetra-amelia syndrome. However, known risk factors for congenital abnormalities such as lifestyle, environment, genetics, and teratogenic are believed to contribute as risk factors for tetra-amelia syndrome.

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