

Tetra-Amelia syndrome with congenital diaphragmatic hernia - A rare entity

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ABSTRACT

Tetra-Amelia syndrome is a very rare disorder characterized by the absence of all four limbs. “Tetra” is the Greek word for “four” and “Amelia” refers to the failure of an arm or leg to develop before birth. This syndrome can also cause severe malformations of other parts of the body, including the face and head, heart, nervous system, skeleton, and genitalia. Tetra-Amelia syndrome with diaphragmatic defects (pulmonary hypoplasia) in a newborn is extremely rare entity. We report a very rare case of Tetra-Amelia associated with congenital diaphragmatic hernia.

Key words: Diaphragmatic hernia, Malformation, Pulmonary hypoplasia, Tetra-Amelia syndrome

Tetra-Amelia defined as the complete absence of the skeletal parts of all four limbs that occur when the limb formation process is either prevented or interrupted very early in the developing embryo between 24 and 36 days following fertilization [1-4]. Tetra-Amelia is a very rare congenital anomaly, with an incidence of 1.5-4/100,000 births [5]. Till date, only 2-3 stillborn cases were reported as Amelia from India [6,7]. Although thought to be a sporadic anomaly, <50% of the cases, it is associated with major malformations in other organ systems. The malformations commonly seen with Amelia include cleft lip and/or palate, body wall defect (omphalocele), malformed head, defects of the neural tube, kidneys, and diaphragm. The diaphragm may be herniated or absent [8-10]. Amelia etiology and the mode of inheritance are still not clear. Karyotype analysis and genetic counseling should be recommended. Here, we are reporting a case of female baby born live but unfortunately expired at 24 h of life.

CASE REPORT

We report a female, preterm baby (32 weeks), 1.7 kg, appropriate for gestational age born to a 26-year-old multigravida (gravida 3, para 2), unbooked but immunized mother. She was delivered by emergency cesarean delivery in view of previous cesarean section and fetal tachycardia. The baby cried immediately after birth. Apgar score was 7, 8, and 8 at 0, 1, and 5 min. Pediatrician noted the absence of all four limbs at birth. Risk factors for sepsis and maternal morbidity were absent. The baby was shifted to nursery for prematurity, mild respiratory distress (Silverman score 3/10), and tetra-Amelia for detailed evaluation.

In nursery, she was started on oxygen (FiO₂-40%) and other supportive treatment in view of prematurity and respiratory

distress. We reviewed detailed a history of pregnancy, but there was no known teratogenic exposure or any problem during pregnancy. There was no consanguinity or any other relevant family history. Previous live issues were healthy. There was an only single visit to obstetrician in the 3rd trimester, and ultrasound was done at 30 weeks which showed absence of both the upper and lower limbs (tetra-Amelia).

On detailed examination, the baby had complete absence of all four limbs, but no other visible malformation was noticed (Fig. 1a, b, and c). However, heart sounds were heard on the right side of the chest. Head circumference and length were 29 cm and 46 cm, respectively. Baby's respiratory distress increased (Silverman score 5/10) further at 3 h of life, and X-ray of chest and arterial blood gas (ABG) analysis were done. X-ray of the chest showed diaphragmatic hernia with pulmonary hypoplasia of the left side (Fig. 2). ABG showed metabolic acidosis. Simultaneously, infantogram, ultrasound whole abdomen and skull, and echocardiography were also planned to rule out the other associated congenital anomalies. However, we could not do these investigations as baby had severe pulmonary hemorrhage at 24 h of life and expired on the same day. An autopsy was planned but was refused by the parents. Parents were advised for karyotype analysis and genetic counseling.

DISCUSSION

Tetra-Amelia is a very rare congenital anomaly, with an incidence of 1.5-4/100,000 births. It may be associated with other anomalies. The clinical delineation of the different entities associated with tetra-Amelia is not yet clear [5]. The specific association of tetra-Amelia, lung hypoplasia or aplasia, and cleft lip or palate was first reported in 1991 by Rosenak et al. [11]. It has been shown that



Figure 1: (a-c) Tetra-Amelia (complete absence of all four limbs)



Figure 2: X-ray chest Diaphragmatic hernia (right side) with pulmonary hypoplasia

the cause of tetra-Amelia is probably a defect in the WNT3 gene in Roberts syndrome. WNT3 gene, located at 17q21, regulates the development of the limbs and other organs [4,12]. In the literature, six tetra-Amelia cases in the same family were reported by Zimmer et al. [13]. Since all tetra-Amelia patients were male, it was called tetra-Amelia syndrome due to X-chromosome [14].

Teratogens such as thalidomide and alcohol, vascular compromise by amniotic bands or other causes, and maternal diabetes have been reported to cause this severe limb deficiency. Head malformation is variable; it may be minor to severe with a near absence of the brain. The diaphragm may be herniated or

absent, and one or both kidneys may be of small size or absent. In our case, bowel was herniated into the left thoracic cavity through malformed hemidiaphragm, and due to this, there was pulmonary hypoplasia. Tetra-Amelia could be seen as a syndrome or as an isolated case. Its etiology and the mode of inheritance are still not clear. Karyotype analysis and genetic counseling should be recommended for next pregnancy.

CONCLUSION

Early prenatal diagnosis including detailed ultrasonography and amniocentesis (for karyotype analysis and genetic) examination plays a major role in counseling parents with fetal anomalies including Amelia and termination of pregnancy may be considered if indicated.

REFERENCES

- Gupta P, Kumar A. Amelia-meromelia sequence with atrial septal defect - A rare occurrence. *Fetal Pediatr Pathol.* 2014;33(2):92-7.
- Klaassen Z, Choi M, Musselman R, Eapen D, Tubbs RS, Loukas M. A review of supernumerary and absent limbs and digits of the upper limb. *Surg Radiol Anat.* 2012;34(2):101-6.
- Bianca S, Bartoloni G, Libertini C, Boemi G, Barrano B, Cataliotti A, et al. Fetal upper limb Amelia with increased nuchal translucency. *Congenit Anom (Kyoto).* 2009;49(3):121-2.
- Lenz W. Genetics and limb deficiencies. *Clin Orthop Relat Res.* 1980;148:9-17.
- Sousa SB, Pina R, Ramos L, Pereira N, Krahn M, Borozdin W, et al. Tetra-Amelia and lung hypo/aplasia syndrome: New case report and review. *Am J Med Genet A.* 2008;146A(21):2799-803.
- Dutta R, Phukon MJ. Tetra Amelia syndrome. *Int J Biol Med Res.* 2012;3(2):1835-6.
- Shukla AK, Sanjay SC, Krishna L, Krishnappa N. Tetra-phocomelia: A rarest of rare case. *J Clin Diagn Res.* 2015;9(3):TD03-4.
- Froster-Iskenius UG, Baird PA. Amelia: Incidence and associated defects in a large population. *Teratology.* 1990;41(1):23-31.
- Evans JA, Vitez M, Czeizel A. Patterns of acrorenal malformation associations. *Am J Med Genet.* 1992;44(4):413-9.
- Mastroiacovo P, Kallen B, Knudsen LB, Lancaster PA, Castilla EE, Mutchinick O, et al. Absence of limbs and gross body wall defects: An epidemiological study of related rare malformation conditions. *Teratology.* 1992;46(5):455-64.
- Rosenak D, Ariel I, Arnon J, Diamant YZ, Ben Chetrit A, Nadjari M, et al. Recurrent tetraamelia and pulmonary hypoplasia with multiple malformations in sibs. *Am J Med Genet.* 1991;38(1):25-8.
- Niemann S, Zhao C, Pascu F, Stahl U, Aulepp U, Niswander L, et al. Homozygous NT3 mutation causes tetra-Amelia in a large consanguineous family. *Am J Hum Genet.* 2004;74(3):558-63.
- Zimmer EZ, Taub E, Sova Y, Divon MY, Pery M, Peretz BA. Tetra-Amelia with multiple malformations in six male fetuses of one kindred. *Eur J Pediatr.* 1985;144(4):412-4.
- Eskicioglu F, Ülkümen BA, Pala HG, Koyuncu FM. Familial tetra-Amelia syndrome. *Int J Womens Health Reprod Sci.* 2014;2(4):263-4.

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