

# A rare association of major congenital malformations : a case report

**Charles B R Ibingira** MMed  
Surgeon and Lecturer,  
Department of Anatomy,  
Makerere Medical School,  
P O Box 7072 Kampala.

**Key words:** congenital anomalies, foetus, amelia, ectopia cordis, gastroschisis, syndactyly.

## Introduction

Congenital abnormalities may be structural, behavioral, functional or metabolic disorders that are present at birth. In most developed countries, statistics indicate that major structural anomalies are present in 2%-3% of live-borne infants<sup>1</sup>. Congenital anomalies account for 21% of infant mortality.

There are major congenital anomalies that frequently occur together. From review of the literature, however, no case of congenital anomalies including amelia, sternal cleft, ectopic hypoplastic lung, ectopic heart, diaphragmatic hernia, gastroschisis and syndactyly has been described as occurring together in one baby.

## Case report

A full-term baby was born to a 17-year-old schoolgirl on 17th November, 1997 at a rural hospital. The mother could not recall the date of her last normal menstrual period but remembered that, following the period, she developed intense headache, nausea, morning sickness and anorexia. She was advised by a friend to use "*Hedex*" and this relieved her of all the symptoms. She took as many tablets as necessary to relieve the symptoms each day. On some occasions, she took 16 tablets or more a day and this went on regularly during the first trimester.

She never attended an antenatal clinic and was never immunised. She denied use of any other drugs and she had no other illness. She neither took alcohol

nor smoked. There was no history of congenital anomalies in her family. The foetus seemed to grow normally and she felt fetal movements from 18 weeks until onset of labour.

She delivered a full-term male baby who did not breathe immediately. The midwife noted that the baby had gross congenital malformations. It weighed 3.2kg. When I examined the baby an hour later it had cyanosis of the face and neck but other body parts were of normal colour. The baby had a number of major congenital abnormalities involving the musculoskeletal, cardiothoracic, and gastro-intestinal systems. All the anomalies were on the right side of the body.

The anomalies (Fig 1) included:

- 1 right upper limb amelia,
- 2 sternal cleft extending from the manubrium to above the umbilicus on the anterior abdominal wall,
- 3 right ectopic hypoplastic lung,
- 4 ectopia cordis with actively contracting heart,
- 5 right anterior diaphragmatic hernia, with the oesophagus mobile and externalised
- 6 gastroschisis with the entire stomach, liver, spleen and three quarters of the mid gut herniating through the defect but not covered by a membrane, and
- 7 syndactyly of the toes of the right foot, the adhesions involving the skin only.

The baby was unconscious but had reasonable air entry into the left side of the chest. The peripheral pulses were palpable but poor. I derotated the intestines and liver to avoid strangulation but the baby died eight hours later.

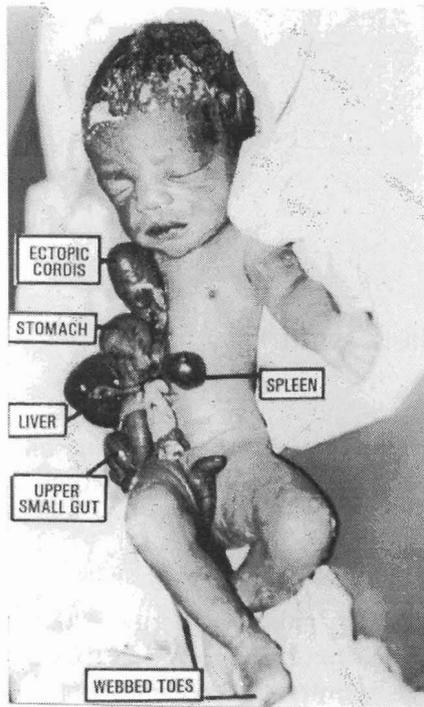


FIG 1  
The foetus soon after delivery

## Discussion

The aetiology of congenital anomalies is not known<sup>2</sup> but genetic and environmental factors both play roles. Congenital anomalies, apart from causing abortions, stillbirths or birth defects, are among the five leading causes of years of potential life lost before the age of 65 years in the USA. In developing countries, the figure is difficult to compute because of a number of factors among which are inadequate health facilities and services (poor record keeping, poor referral systems, poor prenatal diagnostic facilities and inadequate health education) and social stigma.

How either genetic or environmental factors cause congenital malformations is not well understood<sup>3</sup>. It may depend upon the susceptibility of the foetus to teratogens (which again depends upon the genotype of the conceptus)<sup>1,12,13</sup>.

The most sensitive period for inducing congenital malformations is during the period of organogenesis, the third to eighth week of gestation<sup>1,2,3</sup>. Each organ system has its period of peak susceptibility to teratogens but deformation and disruptions may occur at any time.

Although such a collection of major congenital anomalies has not been reported in one individual before, the separate entities are common<sup>4,6,9,10,14</sup> and other abnormalities would probably have come to light had a postmortem examination been conducted.

Association of these anomalies diverges from the recorded patterns. For instance, amelia commonly occurs with dextrocardia, asplenia, congenial short bowel and patent ductus arteriosus<sup>11</sup>, all following deleted ring chromosome 4.

The most notorious cause of amelia and phocomelia followed use of thalidomide by pregnant mothers in 1957-1960<sup>1</sup>. Other causes of amelia and phocomelia with genetic and chromosomal linkages are, for instance, Zimmer's Phocomelia, characterised by 46XX. Children are still-born with absence of ears, severe nasal hypoplasia, cleft palate, pulmonary hypoplasia, imperforate anus and defects of the caudal extremities<sup>10</sup>.

This woman used very high doses of *Hedex* in the first trimester to relieve headache and the symptoms of early pregnancy. *Hedex* is a mixture of paracetamol, caffeine and aspirin. The manufacturers recommend use of not more than eight tablets a day. Paracetamol has been reported to be non-teratogenic but caffeine in high doses was found to be teratogenic in rodents and other animal models because of its zero order kinetics<sup>15</sup>. Aspirin can be teratogenic. It produces malformations of the skeletal and vascular systems of embryos of experimental animals and also in humans, especially in babies of mothers who have taken overdoses in early pregnancy in an attempt to commit suicide<sup>16</sup>. Furthermore a low dose of aspirin taken in the first trimester may interact with alcohol to induce arched palate, cleft palate, digital deformities, congenital dislocation of the hips and haematomas<sup>17</sup>. In other experiments<sup>1</sup>, embryotoxicity and fetal malformations were induced by treatment with aspirin before implantation in a dose dependent manner<sup>18</sup>. Since the period of high susceptibility of the limbs to teratogens is between 4th and 5th weeks, it could possibly be adduced that *Hedex* was the likely teratogen. The most likely period for the action of the teratogen in this case was from the 3rd to 8th weeks, since most of these organs have their peak susceptibility then. Overdose of *Hedex* by this

mother during the organogenesis could have caused these anomalies. Studies on the possible teratogenic effects of *Hedex* and other similar drugs should be carried out, since these drugs are sold on the open market and yet the literature does not mention teratogenic effects.

## References

- 1 Sedler TW. Congenital malformations in *Langman's Medical Embryology* 7th edition 1994; pp 122-141 William Wilkins.
- 2 Williams PL, Roger W, Mary D, Lawrence HR. Congenital abnormalities; Teratology in *Gray's Anatomy* pp 156-158 1989; London and Edinburgh, Churchill Livingstone.
- 3 Mugisa D. Bochdalek hernia in a patient with asymmetry of the face, breasts and fingers *Med Rev J* Nov-Dec 1997; 18-19.
- 4 Schwartz MZ, Ramachandran P. Congenital malformation of the lung and mediastinum: a quarter century experience from a single institution *J Paed Surg* 1997; 32:44-47.
- 5 Vajda G, Pal A. Intrauterine ultrasonic diagnosis of ectopia cordis associated with exencephaly *Orv hetil* 1996; 137:187-189.
- 6 Grisar D, Achiron R, Lipitz S, Yahav J, Hegesa J, Rotsteins D. Ultra Antenatal ultrasonographic findings associated with scimitar syndrome *Ultrasound Obstetr Gynecol* 1996; 8:131-3.
- 7 Cregg N, Casey W. Primary congenital pulmonary hypoplasia *Paediatr Anaesth* 1997; 4:329-33.
- 8 Martinez-Frias ML. Epidemiological analysis of the association of congenital diaphragmatic hernia with upper limb deficiencies, : a primary polytopic developmental field defect *Am J Med Genet* 1996; 62:68-70.
- 9 Song S Y, Chi JG. Triamelia and phocomelia with multiple malformations resembling Robert's syndrome in a foetus: is it a variant or new syndrome? *Clin Genet* 1996; 50:502.
- 10 Kosakik J, Staybolt MC. Zimmer phocoelia: delineation by principle coordinate analysis. *Am J Med Genet* 1996; 66:55-9.
- 11 Hon JW, Wang TR. Amelia, dextrocardia, asplenia and congenital short bowel in deleted ring chromosome 4 *J Med Genet* 1996; 33:879-89.
- 12 Skandalakis A. *Embryology for surgeons* Williams Wilkins 1994.
- 13 Gormak P. *J Pediatr Surg* 1984 35:29.
- 14 Nwako FA. The umbilicus and disorders of the hand (pp 141-143 and 323-324) in *Paediatric surgery in the tropics* 1980, Macmillan Press.
- 15 Bowman WC, Rand MJ. Teratology in *Textbook of Pharmacology* 2nd edition pp 20.43-20.53, 1990, Blackwell Scientific Publications.
- 16 Gilles HC, Rogers HJ, Spector RG, Trounce JR. Drug dependence and drug overdose: caffeine dependence and adverse effects in *Textbook of clinical pharmacology* 2nd edition p 861 1986 Macmillan India Ltd for Edward Arnold Athenaeum Press Ltd.
- 17 Padmanabhan R, Pallot DJ. Aspirin/alcohol interaction in production of and limb deformations in the mouse *Teratology* 1995; 51:404-17.
- 18 Loy YJ, Ding GS, Tu ZH. Toxicity to transferred rat embryos after aspirin treatment during the pre-implantation stage in vivo. *Chung-Kuo-Yao-Li-Hsue-Pao* 1996; 17:52-4.