



## **Ectopia Cordis in a Fetus with Mosaic Trisomy 16.**

Christos Arnaoutoglou, Soultana Meditskou, Anastasia Keivanidou, Marilena Manthou, Nikolaos Anesidis, Apostolos Athanasiadis, Efstratios Assimakopoulos, Sailesh Kumar

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## Ectopia Cordis in a Fetus with Mosaic Trisomy 16.

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**TITLE:**

Ectopia Cordis in a Fetus with Mosaic Trisomy 16.

**SHORT TITLE/ RUNNING HEAD:**

Ectopia Cordis with Trisomy 16 Mosaic.

For Peer Review

**ABSTRACT:**

Ectopia cordis is a rare congenital cardiac malformation which occurs sporadically. Mosaic Trisomy 16 is an extremely rare chromosomal disorder. An association between these two anomalies has never previously been reported. We report a case of an isolated ectopia cordis at 11<sup>+3</sup> weeks. Subsequent embryological examination confirmed thoracic ectopia cordis with normal heart structure and array comparative genomic hybridization of fetal tissue detected trisomy 16 mosaicism.

**KEYWORDS:**

extrathoracic heart; exocardia; ultrasound diagnosis; congenital heart defects; chromosome anomalies

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**INTRODUCTION**

Ectopia cordis (EC) is a sporadic congenital heart defect occurring in 5.5 to 7.9 per 10<sup>6</sup> live births [1]. It is defined as a complete or partial displacement of the heart outside the thoracic cavity [1]. EC may occur either as an isolated malformation or be associated with a ventral body wall defect that affects the thorax, and/or the abdomen. Five types are recognized: cervical, cervicothoracic, thoracic, abdominal, and thoracoabdominal [2]. Thoracic and thoracoabdominal types are the commonest followed by the abdominal and cervical malformations.

Mosaic trisomy 16 (mosaic T16) is an extremely rare chromosomal disorder in which an extra chromosome 16 is present in some of the cells of the affected.

Co-occurrence of EC and mosaic T16 has never previously been reported. We present a prenatally diagnosed case.

## CASE REPORT

A 20-year-old primigravida woman had an early viability scan (7<sup>+1</sup> weeks), performed with a Voluson 730 Expert scanner (GE Healthcare, Kretztechnik, Zipf, Austria) using a RIC 5-9 micro-convex endovaginal probe (5-9MHz). The examination showed a normal intrauterine pregnancy consistent with the gestational age by the last menstrual period (CRL: 9,2mm) and a normal heart rhythm without any obvious abnormal cardiac findings.

Subsequent nuchal translucency (NT) scan at 11<sup>+3</sup> weeks of gestation (CRL: 49mm) detected an extrathoracic heart and a raised NT measurement (5.5mm). The pulsating fetal heart was completely protruding from the thorax into the amniotic fluid (Figure 1). No other malformations were identified. Both scans were performed by a fetal medicine specialist.

After being counselled about the severity of the malformation and its dismal prognosis the patient decided to proceed to medical termination of the pregnancy. This was done at 13<sup>+3</sup> weeks gestation. The patient consented to a post mortem of the fetus. The post mortem showed a 13 week male fetus, with thoracic ectopia cordis. The heart was completely exposed without any associated intracardiac and great vessels abnormalities. Additional extracardiac malformations included low set ears, micrognathia, microstomia, a soft and discrete swelling in the area of the neck and a hypoplastic sternum (Figure 2). Myocardial calcification was also found on histology.

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Array comparative genomic hybridization (CGH) analysis (Spectral Chip, Perkin Elmer Life and Analytical Science, Courtaboeuf; France) revealed a) mosaic trisomy 16, b) gain at 22q12.1-22q12.2 and c) deletion at 22q13.1-22q13.2. The results were confirmed by fluorescent in situ hybridization (FISH) analysis. The gains and losses of genetic material of chromosome 22 were confirmed as true imbalances by controlling for putative polymorphisms. Single FISH experiments on the nuclei of the ectopic cardiac tissue and normal peripheral blood as controls were performed. A panel of FISH probes were derived by nick translation from BAC clones, tilling the regions 22q12.1-22.12.2 (RP11-76E8, RP11-89A2, RP11-91K24, RP11-79G21, RP11-79G6) and 22q13.1-22q13.2 (RP3-37OM22, RP5-979N1, RP1-185D5, RP4.695020). The list of BAC/PAC clones and the details of each can be found at National Center for Biotechnology Information.

After these results were available the parents were advised that parental karyotyping was necessary. However they declined any further investigations.

## DISCUSSION

Ectopia cordis develops secondary to failure of maturation and fusion of the midline mesodermal components of the chest and abdomen. The sternum originates from two longitudinal mesenchymal bands, which start fusing in a cephalocaudal direction from the 7-10<sup>th</sup> week of gestation. The earliest prenatal sonographic EC diagnosis has been reported at 8<sup>+5</sup> weeks of gestation [3]. However, very early diagnosis before the 9<sup>th</sup> embryonic week may be extremely difficult because midline fusion and formation of the thoracic cavity is only completed after that gestation. In this particular case, images from the early viability scan were reviewed retrospectively and it was concluded that the EC was not apparent at 7<sup>+1</sup> weeks.

Increased nuchal translucency has previously been reported in a fetus with EC [4]. It is likely that the nuchal edema arises as a consequence of cardiac dysfunction or coexistence of a chromosomal abnormality. This is the likely explanation in our case.

In our case, cytogenetics of the fetus were explored using CGH array analysis followed by FISH confirmation as this is a detailed and effective technique for fetal karyotyping [5]. There is relative sparse evidence associating EC with chromosomal anomalies or specific genetic mutations. Reported cases include an association with triploidy [6], trisomy 18 [7], Turner syndrome [8] and 46,XX,17q+ [9]. A mosaic trisomy 16 pregnancy originates from a trisomy 16 zygote as a consequence of non disjunction in meiosis I. Some mosaics are products of "trisomic rescue", the loss of a 3<sup>rd</sup> chromosome, resulting in a euploid cell line, where the two remaining chromosomes may come from one parent (uniparental disomy).



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Trisomy 16 is the most frequently encountered trisomy in early abortion specimens representing an occurrence of ~1.5% of all clinically recognized conceptions. Most of these embryos undergo spontaneous abortion or developmental arrest between 8-15 weeks of gestation [10]. Micrognathia and microstomia (present in our case) has previously been reported in mosaic trisomy 16 fetuses. Although cardiac anomalies are commonly seen with mosaic trisomy 16, EC has never previously been reported. Furthermore, most reported EC cases (95%) have associated intracardiac malformations [11]. In contrast, this is one of very few reported cases with normal cardiac structure [12]. Body stalk defects have been reported in a case of uniparental disomy of chromosome 16 [13]. In our case the ventral body wall failure was indeed associated with an abnormality of chromosome 16.

In general, mosaic T16 is characterized by variable anatomic findings and pregnancy outcomes. A specific trisomy 16 mosaic syndrome has not been defined yet. It has been suggested that the phenotype and the genetic aberration have a complex relationship [14] and make precise genotype-phenotype correlation somewhat difficult.

It was not possible to ascertain if the abnormalities in chromosome 22 seen in this fetus were inherited from either parent (as they declined karyotyping). There have been no reported fetal abnormalities associated with chromosomal gains of 22q12.1-22q12.2 or losses of 22q13.1-22q13.2. Although the validity of gains and losses on chromosome 22 was confirmed as real imbalances and not mere polymorphisms, further parental testing would have been desirable in order to address the significance of the finding in more detail.

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3 In conclusion, this case demonstrates that 1<sup>st</sup> trimester diagnosis is possible for EC.  
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5 Our case also suggest that karyotyping should be performed in all cases as rare  
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7 chromosome abnormalities are sometime present, which may be of importance in  
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9 counselling parents about future pregnancies.  
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**REFERENCES:**

1. Khoury MJ, Cordero JF, Rasmussen S. Ectopia cordis, midline defects and chromosome abnormalities: an epidemiologic perspective. *Am J Med Genet* 1988;30(3):811-7.

2. Skandalakis JE, Gray SW, Ricketts R, et al. Anterior Wall Defects; in Skandalakis LJ, Gray SW (ed.) *Embryology for surgeons*. Baltimore, Lippincott Williams & Wilkins, 1994, p 552.

3. Donald SH. First-Trimester Ectopia Cordis in a Twin Gestation, Using 3D Surface Rendering and Reconstruction. *Journal of Diagnostic Medical Sonography* 2005;21(5):420-23.

4. Staboulidou I, Wustemann M, Schmidt P, et al. Increased fetal nuchal translucency as a predictor of Cantrell's pentology - case report. *Z Geburtshilfe Neonatol* 2005;209(6):231-4.

5. Benkhalifa M, Kasakyan S, Clement P, et al. Array comparative genomic hybridization profiling of first-trimester spontaneous abortions that fail to grow in vitro. *Prenat Diagn* 2005;25(10):894-900.

6. Sepulveda W, Weiner E, Bower S, et al. Ectopia cordis in a triploid fetus: first-trimester diagnosis using transvaginal color Doppler ultrasonography and chorionic villus sampling. *J Clin Ultrasound* 1994;22(9):573-5.

7. Shaw SW, Cheng PJ, Chueh HY, et al. Ectopia cordis in a fetus with trisomy 18. *J Clin Ultrasound* 2006;34(2):95-98.
8. Garson A, Hawkins EP, Mullins CE, et al. Thoracoabdominal ectopia cordis with mosaic Turner's syndrome: Report of a case. *Pediatrics* 1978;62(2):218-21
9. Say B, Wilsey CE. Chromosome aberration in ectopia cordis (46,XX,17q+). *Am Heart J* 1978;95(2):274-5.
10. Yong PJ, Barrett IJ, Kalousek DK, et al. Clinical aspects, prenatal diagnosis, and pathogenesis of trisomy 16 mosaicism. *J Med Genet* 2003;40(3):175-82.
11. Cabrera A, Rodrigo D, Luis MT, et al. Ectopia cordis and cardiac anomalies. *Rev Esp Cardiol* 2002;55(11):1209-12.
12. Goncalves FD, Novaes FR, Maia MA, et al. Thoracic ectopia cordis with anatomically normal heart. *Rev Bras Cir Cardiovasc* 2007;22(2):245-7.
13. Chan Y, Silverman N, Jackson L, et al. Maternal uniparental disomy of chromosome 16 and body stalk anomaly. *Am J Med Genet* 2000;94(4):284-6.
14. Moradkhani K, Puechberty J, Blanchet P, et al. Mosaic trisomy 16 in a fetus: the complex relationship between phenotype and genetic mechanisms. *Prenat Diagn* 2006;26(12):1179-82.

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**FIGURE LEGENDS:**

**Figure 1:** Sonographic detection of EC at 11+3 weeks of gestation (arrow shows protruding heart).

**Figure 2:** Photograph of the same fetus at 13 weeks of gestation.

For Peer Review

**TITLE:**

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**SHORT TITLE/ RUNNING HEAD:**

Ectopia Cordis with Trisomy 16 Mosaic.

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**ABSTRACT:**

Ectopia cordis is a ~~sporadic~~ rare congenital cardiac malformation which occurs sporadically. ~~and mosaic~~ Mosaic Trisomy 16 is an extremely rare chromosomal disorder. An association between these two anomalies has never previously been reported. We report a ~~prenatal diagnosis~~ case of an isolated ectopia cordis at 11<sup>+3</sup> weeks ~~associated with increased nuchal translucency~~. Subsequent embryological examination ~~displayed~~ confirmed thoracic ectopia cordis with normal heart structure. ~~Array~~ and array comparative genomic hybridization of fetal tissue detected trisomy 16 mosaicism.

**KEYWORDS:**

extrathoracic heart; exocardia; ultrasound diagnosis; congenital heart defects; chromosome anomalies

## INTRODUCTION

Ectopia cordis (EC) is a sporadic congenital heart defect occurring in 5.5 to 7.9 per 10<sup>6</sup> live births [1]. It is defined as a complete or partial displacement of the heart outside the thoracic cavity [1]. EC may occur either as an isolated malformation or be associated with a ventral body wall defect that affects the thorax, and/or the abdomen. ~~or both, thus being classified in five types:~~ Five types are recognized: cervical, cervicothoracic, thoracic, abdominal, and thoracoabdominal [2]. Thoracic and thoracoabdominal types are ~~commonly~~ the commonest followed by the abdominal and cervical malformations types.

Mosaic trisomy ~~Trisomy~~ 16 (mosaic T16) is an extremely rare chromosomal disorder in which an extra chromosome 16 is present in some of the cells of the affected fetus. Co-occurrence of EC and mosaic T16 ~~concurrence is extremely rare and~~ has never previously been reported ~~before~~. We present a prenatally diagnosed case.



CASE REPORT

A 20-year-old primigravida woman had an early viability scan (7<sup>+1</sup> weeks), performed with a Voluson 730 Expert scanner (GE Healthcare, Kretztechnik, Zipf, Austria) using a RIC 5-9 micro-convex endovaginal probe (5-9MHz). The examination showed a normal intrauterine pregnancy consistent with ~~to~~ the gestational age by the last menstrual period ~~LMP~~ (CRL: 9,2mm) and a normal heart rhythm without any obvious abnormal cardiac findings.

~~Mother had a~~ Subsequent nuchal translucency (NT) scan at 11<sup>+3</sup> weeks of gestation (CRL: 49mm) detected an extrathoracic heart and a raised NT measurement (5.5mm) ~~performed with the same scanner using a RAB 2-5 abdominal convex probe (2-5MHz).~~ The pulsating ~~palpating~~ fetal heart was completely protruding from the thorax into ~~to~~ the amniotic fluid (Figure 1/A) ~~and the nuchal translucency was 5.5mm.~~ No other ~~further~~ malformations were identified. Both scans were performed by a fetal medicine specialist.

~~Two weeks later, after~~ After being counselled ~~informed~~ about the severity of the malformation and its dismal prognosis the patient ~~couple~~ decided to proceed to medical termination of the pregnancy, This was done at 13<sup>+3</sup> weeks gestation. The patient consented to a post mortem of the fetus. The autopsy post mortem showed a 13 week male fetus, with thoracic ectopia cordis. The heart was completely exposed without any associated intracardiac and great vessels abnormalities. ~~congenital heart or major vessel defects.~~ Additional extracardiac malformations ~~The findings of the autopsy (Figure 1/B)~~ included a low set ears, micrognathia, microstomia, a soft and

discrete swelling in the area of the neck and a hypoplastic sternum ([Figure 2](#)). Myocardial calcification was [also](#) found [on histology](#) ~~in the histological exam~~.

Array comparative genomic hybridization (CGH) analysis (Spectral Chip, Perkin Elmer Life and Analytical Science, Courtaboeuf; France) revealed a) mosaic trisomy ~~of chromosome~~ 16, b) gain at 22q12.1-22q12.2 and c) deletion at 22q13.1-22q13.2. The results were confirmed by fluorescent in situ hybridization (FISH) analysis. The gains and losses [of genetic material](#) of chromosome 22 were confirmed as true imbalances by controlling for putative polymorphisms. Single FISH experiments on ~~the~~ nuclei of [the ectopic cardiac](#) ~~ectopia cordis~~ tissue and normal peripheral blood as ~~control~~ [controls](#) were performed. A panel of FISH probes were derived by nick translation from BAC clones, tilling the regions 22q12.1-22.12.2 (RP11-76E8, RP11-89A2, RP11-91K24, RP11-79G21, RP11-79G6) and 22q13.1-22q13.2 (RP3-37OM22, RP5-979N1, RP1-185D5, RP4.695020). The list of BAC/PAC clones and the details of each can be found at National Center for Biotechnology Information.

After these results [were available](#) the parents were advised that ~~were counselled for~~ parental karyotyping [was necessary](#). ~~but they refused to be tested further~~. [However they declined any further investigations](#).

## DISCUSSION

Ectopia cordis EC develops secondary ~~due~~ to failure of maturation and fusion of the midline mesodermal components of the chest and abdomen. The sternum originates from two longitudinal mesenchymal bands, which start fusing in a cephalocaudal direction from the 7-10<sup>th</sup> week of gestation. The earliest prenatal sonographic EC diagnosis has been reported at 8<sup>+5</sup> weeks of gestation [3]. However, very early diagnosis before the 9<sup>th</sup> embryonic week may be extremely difficult because ~~be impossible since the~~ midline fusion and ~~the~~ formation of the thoracic cavity is only completed after that gestation time. In this particular case, ~~All saved~~ images from the early viability scan were reviewed retrospectively and it was ~~we~~ concluded that the EC was not apparent ~~visible~~ at 7<sup>+1</sup> weeks.

Increased nuchal translucency has ~~been~~ previously been reported in a fetus with EC [4]. It is likely that the nuchal edema arises as a consequence of cardiac dysfunction or coexistence of a chromosomal abnormality. ~~The neck edema probably developed due to the cardiac dysfunction. Increased NT is also found to aneuploid fetuses due to alteration of the composition of extracellular matrix. The exact cause of this finding in our occasion is probably due to the coexistence of both causes.~~ This is the likely explanation in our case.

In our case, ~~the~~ cytogenetics of the fetus were explored using ~~with a~~ CGH array analysis followed by ~~a~~ FISH confirmation as this is a detailed and effective technique for fetal karyotyping ~~since previous use in investigating chromosomal anomalies has been proved to be more detailed and effective~~ [5]. There is little relative sparse evidence associating EC with specific chromosomal anomalies or specific genetic

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3 mutations. ~~Reported~~ ~~The reported~~ cases include an association ~~associate~~ ~~EC~~ with  
4 triploidy [6], trisomy 18 [7], Turner syndrome [8] and 46,XX,17q+ [9]. ~~A~~ ~~The~~ mosaic  
5 trisomy 16 pregnancy ~~pregnancies~~ originates from a trisomy 16 zygote as a  
6 consequence of non disjunction in meiosis I. ~~a maternal meiosis I non-disjunction~~.  
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8 Some mosaics are products of “trisomic rescue”, the loss of a 3<sup>rd</sup> chromosome,  
9 resulting in a euploid cell line, where the two remaining chromosomes may come  
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22 Trisomy 16 is the most frequently encountered trisomy in early abortion specimens  
23 representing ~~presenting~~ an occurrence of ~1.5% of all clinically recognized  
24 conceptions ~~gestations~~. Most of these embryos undergo spontaneous abortion or  
25 developmental arrest between 8-15 weeks of gestation ~~the 8th and 15<sup>th</sup> weeks~~ [10].  
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27 Micrognathia and microstomia ~~have been evidenced in our case~~ (present in our case)  
28 ~~and have been~~ has previously been reported in mosaic trisomy 16 fetuses ~~to be~~  
29 ~~associated with Trisomy 16 mosaicism~~. ~~Although~~ ~~Even though~~ cardiac anomalies are  
30 ~~most~~ commonly seen with mosaic trisomy 16, EC has never previously been reported  
31 ~~to be associated with it~~. ~~Furthermore, Moreover, most of EC~~ most reported EC cases  
32 (95%) ~~are~~ have associated ~~with further~~ intracardiac malformations [11]. In contrast,  
33 ~~On the contrary,~~ this is one of very few reported cases associated with normal  
34 cardiac structure ~~heart anatomy~~ [12]. Body stalk defects have been reported in a  
35 case of uniparental disomy of chromosome 16 [13]. In our case the ventral body wall  
36 failure was indeed associated with ~~a mosaic trisomy~~ an abnormality of chromosome  
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In general, mosaic T16 is characterized ~~from~~ by variable anatomic findings and pregnancy outcomes. ~~therefore, a~~ A specific trisomy 16 mosaic syndrome has not been defined yet. It has been suggested that ~~it's~~ the phenotype and the genetic aberration mechanism have a complex relationship [14] . ~~The fact that all these chromosomal abbreviations occurred simultaneously restrict us from a~~ and make precise genotype-phenotype correlation somewhat difficult.

~~The segmental abbreviations may represent a familial variant of chromosome 22 and parental testing was suggested as a means of future family planning and a way to identify any parental karyotypic abnormality. However, it was not feasible and consequently, conclusions for these imbalances are difficult to be drawn, since we cannot evaluate the link to the parents. No previous developmental defects have been attributed to the~~

It was not possible to ascertain if the abnormalities in chromosome 22 seen in this fetus were inherited from either parent (as they declined karyotyping). There have been no reported fetal abnormalities associated with chromosomal gains of 22q12.1-22q12.2 or losses of 22q13.1-22q13.2. Although the validity of gains and losses on chromosome 22 was confirmed as real imbalances and not mere polymorphisms, further parental testing would have been ~~be~~ desirable in order to address the significance of the finding in more detail. ~~Sadly, further testing was rejected by the parents, thus we were only able to present the findings in this case report.~~

~~Conclusively, EC can be diagnosed during the NT scan and an increased NT may be one of the early findings. On the contrary, detection of such malformation is not feasible before the 8<sup>th</sup> embryonic week. Also, investigation of cytogenetics should be~~

performed with the most detailed method since specific chromosomal abnormalities have not been totally associated with this condition.

In conclusion, this case demonstrates that 1<sup>st</sup> trimester diagnosis is possible for EC. Our case also suggest that karyotyping should be performed in all cases as rare chromosome abnormalities are sometime present, which may be of importance in counselling parents about future pregnancies.

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**REFERENCES:**

1. Khoury MJ, Cordero JF, Rasmussen S. Ectopia cordis, midline defects and chromosome abnormalities: an epidemiologic perspective. *Am J Med Genet* 1988;30(3):811-7.

2. Skandalakis JE, Gray SW, Ricketts R, et al. Anterior Wall Defects; in Skandalakis LJ, Gray SW (ed.) *Embryology for surgeons*. Baltimore, Lippincott Williams & Wilkins, 1994, p 552.

3. Donald SH. First-Trimester Ectopia Cordis in a Twin Gestation, Using 3D Surface Rendering and Reconstruction. *Journal of Diagnostic Medical Sonography* 2005;21(5):420-23.

4. Staboulidou I, Wustemann M, Schmidt P, et al. Increased fetal nuchal translucency as a predictor of Cantrell's pentology - case report. *Z Geburtshilfe Neonatol* 2005;209(6):231-4.

5. Benkhalifa M, Kasakyan S, Clement P, et al. Array comparative genomic hybridization profiling of first-trimester spontaneous abortions that fail to grow in vitro. *Prenat Diagn* 2005;25(10):894-900.

6. Sepulveda W, Weiner E, Bower S, et al. Ectopia cordis in a triploid fetus: first-trimester diagnosis using transvaginal color Doppler ultrasonography and chorionic villus sampling. *J Clin Ultrasound* 1994;22(9):573-5.

7. Shaw SW, Cheng PJ, Chueh HY, et al. Ectopia cordis in a fetus with trisomy 18. *J Clin Ultrasound* 2006;34(2):95-98.
8. Garson A, Hawkins EP, Mullins CE, et al. Thoracoabdominal ectopia cordis with mosaic Turner's syndrome: Report of a case. *Pediatrics* 1978;62(2):218-21
9. Say B, Wilsey CE. Chromosome aberration in ectopia cordis (46,XX,17q+). *Am Heart J* 1978;95(2):274-5.
10. Yong PJ, Barrett IJ, Kalousek DK, et al. Clinical aspects, prenatal diagnosis, and pathogenesis of trisomy 16 mosaicism. *J Med Genet* 2003;40(3):175-82.
11. Cabrera A, Rodrigo D, Luis MT, et al. Ectopia cordis and cardiac anomalies. *Rev Esp Cardiol* 2002;55(11):1209-12.
12. Goncalves FD, Novaes FR, Maia MA, et al. Thoracic ectopia cordis with anatomically normal heart. *Rev Bras Cir Cardiovasc* 2007;22(2):245-7.
13. Chan Y, Silverman N, Jackson L, et al. Maternal uniparental disomy of chromosome 16 and body stalk anomaly. *Am J Med Genet* 2000;94(4):284-6.
14. Moradkhani K, Puechberty J, Blanchet P, et al. Mosaic trisomy 16 in a fetus: the complex relationship between phenotype and genetic mechanisms. *Prenat Diagn* 2006;26(12):1179-82.



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**FIGURE LEGENDS:**

**Figure 1:** Sonographic detection of EC at 11+3 weeks of gestation (arrow shows protruding heart).

**Figure 2:** Autopsy Photograph of the same fetus at 13 weeks of gestation.

For Peer Review



Figure 1: Sonographic detection of EC at 11<sup>+3</sup> weeks of gestation (arrow shows protruding heart).  
90x99mm (72 x 72 DPI)



Figure 2: Photograph of the same fetus at 13 weeks of gestation.  
99x99mm (72 x 72 DPI)