CASE REPORT

A Case of Trisomy 18 : Twenty Five Weeks of Pregnancy With Multiple Congenital Anomalies

Farhana Rahman[1], Nasima Akhter[2], Sadia Hossain[3], Md. Sanowar Hossain[4]

Introduction:

Congenital anomalies are characterized by structural deformities due to defects in or damage to a developing fetus. A congenital disorder may be the result of genetic abnormalities, the intrauterine environment, errors of morphogenesis, infection, or a chromosomal abnormality. Fetal chromosomal abnormalities usually present with a variety of structural abnormalities detectable in prenatal ultrasonography. A greater number of malformations is associated with a greater risk of chromosomal abnormalities and increased occurrence of ultrasonographic soft markers[1,2]. A common type of chromosomal abnormality is called a 'trisomy'. Most common trisomies are trisomy 21(Down's syndrome), trisomy 18 (Edward's syndrome) and trisomy 13 (Patau's syndrome). Most fetuses with major chromosomal abnormalities have either external or internal defects that can be recognized by detailed ultrasonographic examination. These are defined as ultrasound markers for fetal chromosomal defects. In case of trisomy 13, 18, Turner's syndrome and triploidy, ultrasound markers are often major fetal abnormalities. In contrast, in Down's syndrome fetuses the structural defects are subtle and often isolated[2,3]. Based on the detection of growth restriction or fetal anomaly, antenatal suspicion of aneuploidy was present in 73% of fetuses with trisomy 21, in 85% of fetuses with trisomy 18 and 100% of fetuses with trisomy 13[4]. Here a case of 26 weeks pregnancy with multiple congenital anomalies is presented, the syndromal pattern of ultrasound findings are consistent with fetal abnormalities detectable in trisomy 18.

1. Senior Medical Officer, Center for Nuclear Medicine and Ultrasound, Bangladesh Atomic Energy Commission, Dhaka Medical College Hospital, Dhaka.
2. Senior Medical Officer, Center for Nuclear Medicine and Ultrasound, Bangladesh Atomic Energy Commission, Dhaka Medical College Hospital, Dhaka.
3. Medical Officer, Center for Nuclear Medicine and Ultrasound, Bangladesh Atomic Energy Commission, Dhaka Medical College Hospital, Dhaka.
4. Dirctor, Center for Nuclear Medicine and Ultrasound, Bangladesh Atomic Energy Commission, Dhaka Medical College Hospital, Dhaka.

Case report:

A 20 yrs old primi gravida was admitted in DMCH with a history of 8 months amenorrheoa with 1 day per vaginal blood stained discharge and mild lower abdominal pain. She was a Rh-negative mother with no family history of congenital anomaly or no history of consanguineous marriage. She was referred to our center (CNMU, Dhaka) for anomaly scan. Trans-abdominal ultrasound was done by TOSHIBA nemio-30 (Japan) real time ultrasound with 2-5 MHz curvilinear transducer. Ultrasound examination showed

that uterus was gravid, containing a single fetus with well visualized cardiac pulsation & fetal movement. Fetal bi-parietal diameter (BPD) was 62 mm, which corresponds to 25 weeks 3 days of gestational size & femoral length (FL) was 29 mm, which corresponds to 19 weeks 2 days of gestational size. But the gestational size did not correspond to the patients stated period of amenorrhoea. Amniotic fluid volume was normal. Fetal skull and brain were normal, intracranial ventricles were not dilated. Normal spine curvature was lost and the sacro-coccygeal part was open with a small (3.93X2.16 cm) cystic structure over the terminal part representing a small meningocele (Fig. 1A). Fetal chest cavity was narrow with downward displacement of the heart. Fetal abdomen was protruded outwards with a thin covering membrane containing the liver, bowel loops and fetal urinary bladder (Fig. 1B). Fetal kidneys could not be identified separately. Bony parts of upper limbs were normal, but both feet seem to be medially curved (Talipes varus) (Fig.1C). The ultrasonographic diagnosis was single live pregnancy of 25+ wks gestational size with asymmetrical IUGR and multiple fetal anomalies. Termination of pregnancy was done in Dhaka Medical College Hospital (DMCH). The attending physician stated that, the fetus was died after birth and there was a large omphalocele, a small sacro-coccygeal meningocele and clubbed feet (talipes varus) corresponding to the ultrasonographic findings. As karyotyping was not done, the confirmatory diagnosis was not possible.

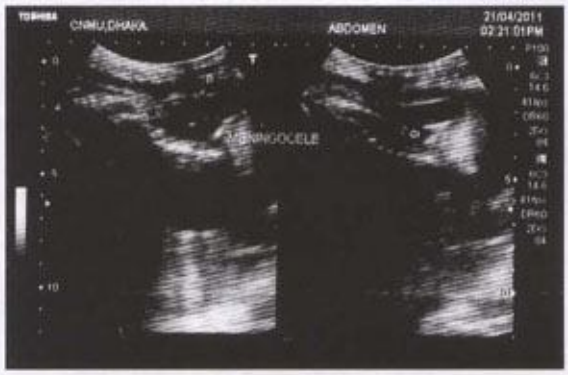

Figure-1A: Meningocele (Lt.) and Spina bifida (Rt.)

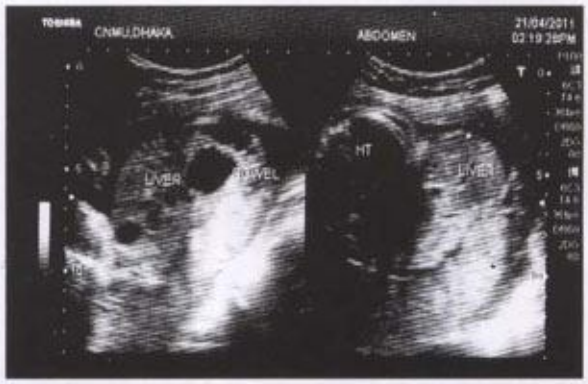

Figure-1B: Omphalocele (liver and bowel loops inside)

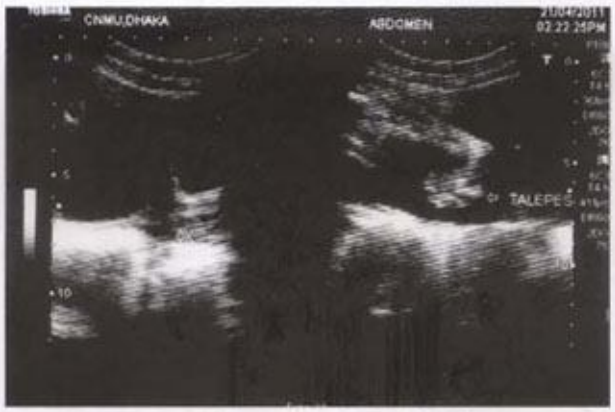

Figure-1C: Clubbed foot

Figure-1: Ultrasonographic images of spina bifida with meningocele (Fig.1A), omphalocele (Fig.1B), and clubbed foot (Fig.1C) in a 26 weeks fetus; the syndromal pattern consistent with trisomy 18.

Discussion:

Chromosomal abnormalities occur in 0.1% to 0.2% of live births. The most common clinically significant aneuploidy among live-born infants is Down syndrome or trisomy 21 (1 per 800 live births).[5-7] Other sonographically detectable aneuploidies include trisomy 13, 18, monosomy X, and triploidy. Second-trimester ultrasound scan detects two types of sonographic markers suggestive of aneuploidy. Markers for major fetal structural abnormalities comprise the first type; the second type of markers is known as "soft markers" of aneuploidy. The most commonly studied soft markers of aneuploidy include a thickened nuchal fold, limb shortening, mild fetal pyelectasis, echogenic bowel, and echogenic intracardiac focus (EIF) and choroid plexus cyst. There is a great deal of interest in the ultrasound detection of aneuploidy, as evidenced by the large number of publications in the literature on this topic[8,9]. Benacerraf and colleagues[4,7,10] have popularized a simple approach termed as the index scoring system (ISS), where a score of 2 is assigned for structural defects and nuchal thickening (≥ 6 mm) and a score of 1 is assigned for the ultrasound markers EIF, echogenic bowel, pyelectasis, short femur, and short humerus. A score of 2 or more is considered positive for aneuploidy. Using this method, the authors reported a sensitivity of 81% (26 of 32 fetuses) for detecting trisomy 21 and 100% for trisomies 18 (9/9) and 13(2/2) respectively with a false-positive rate of only 4.4% (26 of 588 fetuses)[7]. With this scoring system, there is a total score of 7 in our case (omphalocele=2, spina bifida with a meningocele=2, clubbed feet=2, short femur=1), which is highly predictive for aneuploidy. Sonography cannot be used to diagnose or exclude aneuploidy. Diagnosis of fetal chromosomal abnormalities requires invasive testing. Chorionic villous sampling (CVS) or amniocentesis is necessary to confirm the diagnosis by karyotyping[8].

Trisomy 18 and Trisomy 13 are the two live born trisomies apart from trisomy 21. These trisomy disorders tend to have much more severe clinical manifestations than trisomy 21, and only rarely do affected infants survive to one year of life[11,12]. A characteristic group of

sonographic abnormalities that suggest a specific diagnosis exist for common chromosomal defects. Since some of these patients may be mosaics for the trisomy cell line, a variety of phenotypic expression is possible. So, fetus with multiple anomalies would likely to carry chromosomal or structural defects[13]. In our case, multiple anomalies were detected in ultrasnography, such as spina bifida with meningocele, omphelocele, chest deformity, clubbed feet (Figure 1), short femur, but no investigation was done to screen for chromosomal defect. Considering the sonographic pattern of multiple structural abnormalities, the suspicion is high for Trisomy 18 or trisomy 13.

Trisomy 18 or Edwards Syndrome is the second most common trisomy behind Down syndrome. This syndrome has an incidence of between 1 in 3000 and 1 in 8000. Fetus with trisomy 18 may have some or all of the following sonographic abnormalities: kidney malformations, structural heart defects (VSD), omphalocele, esophageal atresia, diaphragmatic hernia, enlarged cistern megna, nuchal thickening, strawberry-shaped skull, choroid plexus cyst, spina bifida, clubfoot deformity, clenched hand, polyhydramnios, IUGR, abnormal DV waveform, etc. In experienced hands, the sensitivity of detecting fetal trisomy 18 on prenatal sonography is 100%, and all cases will have multiple anomalies visualized[14-16]. This case presented here may be considered as trisomy 18 as there were multiple such features (omphalocele, spina bifida, clubbed feet and short femur), non-visualized kidney and asymmetrical IUGR and was terminated after ultrasonographic diagnosis. Though it was not confirmed by karyotyping, the syndromal pattern consistent with the trisomy 18.

Detailed ultrasound at mid pregnancy would detect most of the chromosomal anomalies from the characteristic sonographic patterns. Early prenatal detection would help in timely management of pregnancy with anomalous fetus and reduce the live birth prevalence of congenital anomaly.

Reference:

1. Chen CH, Qiu YW, Chang QX, Yin AL. Correlation of fetal chromosomal abnormalities to prenatal ultrasound features. Nan Fang Yi Ke Da Xue Xue Bao 2011; 31: 347-9.
2. Singh K. Fetal anomalies in chromosomal aberrations. In: Singh K (editor). Ultrasound imaging of fetal anomalies. New Delhi: Jaypee Brothers Medical Publishers Ltd. 2007. pp-320-37.
3. Bilardo C. Second trimester ultrasound markers for fetal aneuploidy. Early Hum Dev 1996; 47: S31-3.
4. Benacerraf BR, Nadel A, Bromley B. Identification of second-trimester fetuses with autosomal trisomy by use of a sonographic scoring index. Radiology. 1994; 193: 135–140.
5. Shipp TD, Benacerraf BR. Second trimester ultrasound screening for chromosomal abnormalities. Prenat Diagn. 2002; 22: 296–307.
6. Nyberg DA, Resta RG, Luthy DA, Hickok DE, Mahony BS, Hirsch JH. Prenatal sonographic findings of Down syndrome: review of 94 cases. Obstet Gynecol. 1990; 76: 370–377.
7. Benacerraf BR, Neuberg D, Bromley B, Frigoletto FD., Jr Sonographic scoring index for prenatal detection of chromosomal abnormalities. J Ultrasound Med. 1992; 11: 449–458.

8. Raniga S, Desai PD, Parikh H. Ultrasonographic soft markers of aneuploidy in second trimester: are we lost? Med Gen Med 2006; 8: 9.
9. Chen CP. Prenatal sonographic features of fetuses in trisomy 13 pregnancies (I). Taiwan J Obstet Gynecol 2009; 48: 210-7.
10. Bromley B, Lieberman E, Benacerraf BR. The incorporation of maternal age into the sonographic scoring index for the detection at 14–20 weeks of fetuses with Down's syndrome. Ultrasound Obstet Gynecol 1997; 10: 321–324.
11. Rasmussen SA, Wong LYC, Yang Q, May KM, Friedman JM. Population-based analyses of mortality in trisomy 13 and trisomy 18. Pediatrics. 2003; 111
12. Duarte AC, Menezes AIC, Devens ES, Roth JM, Garcias GL, Martino-Roth MG. Patau syndrome with a long survival. A case report. Genetics and Molecular Research 2004; 3: 288-92.
13. Nyberg DA, Kramer D, Resta RG, Kapur R, Mahony BS, Luthy DA, Hickok D. Prenatal sonographic findings of trisomy 18: review of 47 cases. J Ultrasound Med 1993; 12: 103-13.
14. Tongsong T, Sirichotiyakul S, Wanapirak C, Chanprapaph P. Sonographic features of trisomy 18 at midpregnancy. J Obstet Gynaecol Res 2002; 28: 245-50.
15. Yeo L, Guzman ER, Day-Salvatore D, Walters C, Chavez D, Vintzileos AM. Prenatal detection of fetal trisomy 18 through abnormal sonographic features. J Ultrasound Med 2003; 22: 581-90.
16. Sepulveda W, Wong AE, Dezerega V. First-trimester sonographic findings in trisomy 18: a review of 53 cases. Prenat Diagn 2010; 30: 256-9.