ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
Index Copernicus Value: 49. 23
PubMed - National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 3, Issue – 5, September - 2018, Page No. :186 – 188

Echogenic Fetal Bowel as Indication for Prenatal Diagnosis of Cystic Fibrosis

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Type of Publication: Case Report

Conflicts of Interest: Nil

Abstract: The sonographic finding of hyperechoic or dilated fetal bowel raises suspicion of a number of prenatal disorders including meconium ileus (MI), meconium peritonitis, congenital infection, neoplasm, cystic fibrosis (CF), or chromosomal trisomy. The following case report, emphasizes on importance of looking for echogenic bowel and if found, mutation study for cystic fibrosis need to be carried out. The risk of cystic fibrosis in every pregnancy is 25%, but it may occur in repeated pregnancies. Therefore, proper evaluation should be done when echogenic bowel is noted on antenatal sonography and mutation study for cystic fibrosis should be considered. Earlier fetal diagnosis may help in providing more precise genetic counselling and parents can exercise their choice; also to anticipate postnatal problems associated with MI / CF, and therefore provide more optimal clinical management of the affected fetus.

***Key words*:** Cystic fibrosis, Echogenic bowel, Meconium ileus, Prenatal diagnosis.

Introduction : Cystic fibrosis (CF) is the commonest severe autosomal recessive disease that affects children in white populations, with an incidence varying from 1/2500 to 1/5000.[1] The disease, which is characterized by chronic pulmonary obstruction and infections, and by digestive disorders such as pancreatic insufficiency, is caused by mutations in a gene which encodes a protein called CFTR (cystic fibrosis transmembrane conductance regulator). Prenatal testing for CF by direct mutation study is possible.

More recently, the medical assessment of pregnancy performed in some countries has allowed, through systematic ultrasound examinations, the prenatal diagnosis of bowel echogenicity, an abnormality suggestive of CF. Other prenatal US signs suggestive of CF are hyperechogenic bowel, echogenic masses or pseudocysts, ascites and intraperitoneal calcifications. Fetal echogenic bowel, defined as bowel with sonographic density greater than that of the surrounding bone, is diagnosed in 0.2-1.8% of fetuses during routine ultrasound examination, especially in the second trimester of pregnancy.[2]

Case Report: A 23 year old female, G2P1 was referred for genetic analysis. The couple had non-consanguineous marriage. She was 32 weeks pregnant and her antenatal

ultrasound showed echogenic bowel loops [Figure – 1]. The bowel loops were dilated and were seen in right lower abdomen. She was advised for karyotyping and mutation study for CF. Karyotype was normal and mutation study could not be carried out as parents denied the test for financial constraints. The female child was born at term and on 6th day of her life, USG showed proximal ileal atresia. After a month she was operated but died after two months due to septicemia. They had a previous pregnancy with similar history where the child was operated for intestinal obstruction a month after delivery and then died in a couple of days due to infection.

The couple now wanted to get mutation study done for this child and since we had preserved the DNA, we could do the test. The mutation study showed a homozygous three base pair deletion in exon 11 of the CFTR gene that results in an in-frame deletion of an amino acid Phenylalanine at codon 508. The in-frame Phenylalanine at 508 amino acid is the most common pathogenic variant observed in CF patients.[3] Parents were counselled about the risk of having affected fetus in future pregnancy. Therefore, prenatal diagnosis was advised in subsequent pregnancies.

She again presented to us during her third pregnancy at 11 weeks gestational age. Prenatal diagnosis was carried out by chorionic villus sampling and mutation study of CF was done. The result was again positive for the same mutation in CFTR gene in homozygous form. The couple opted for termination of pregnancy. On autopsy, bowel loops were dilated, total occlusion of terminal ileum with meconium [Figure – 2].

Discussion : The risk for CF in fetuses with echogenic bowel has been extensively studied and is shown to vary from 0-33%.[4] This wide range could be the result of differences in ascertainment, CF prevalence, and mutation detection rate.

Intestinal echogenicity was initially described as a normal variant, which usually disappeared at 20 weeks of gestation. In our case, it is probably the result of the malfunctioning of the CFTR protein leading to the dehydration of mucus secretions, which becomes viscous, obstructs the bowel lumen, and cause meconium ileus.[5]

The discovery of more than 1000 different mutations in the CFTR gene makes it impossible to detect all mutations by simple routine screening. Consequently, in general, prenatal testing consists of analysis of a limited number of known mutations, and the mutation detection rate varies according to the molecular technique used, the proportion of the gene screened, and the ethnic origin of the population tested.

Estroff et al. reviewed US images and medical records of 15 fetuses with bowel dilated loops and found that 5 of them (33%) had CF.[6] There were no major US differences between fetuses with or without CF. Prenatal diagnosis is also essential to anticipate postnatal problems and provide optimal clinical management of the affected infant. The knowledge of the couple CFTR mutations will be important for future prenatal counselling.[7]

Conclusion: The finding of isolated echogenic bowel in the second trimester should prompt genetic counseling and consideration of karyotypic analysis and mutation study. The importance of testing for CFTR mutation, in cases of prenatal diagnosis of echogenic bowel, as well as the importance of preserving DNA in any affected fetus (unknown cause) should be stressed upon.

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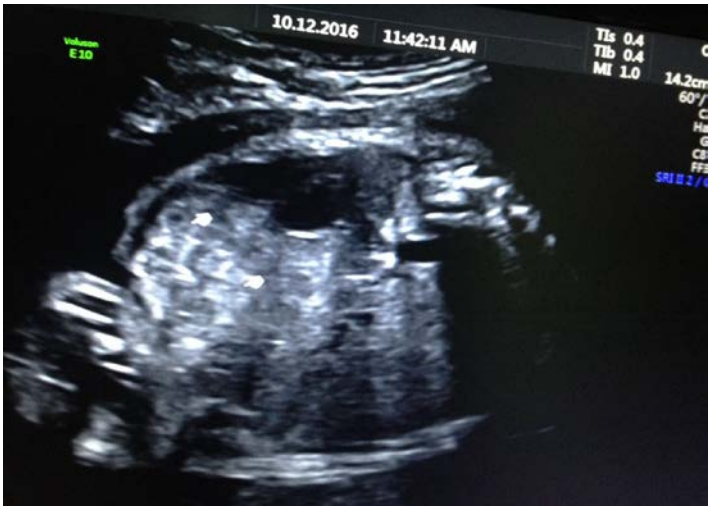

Figure 1: Sonography image showing echogenic bowel

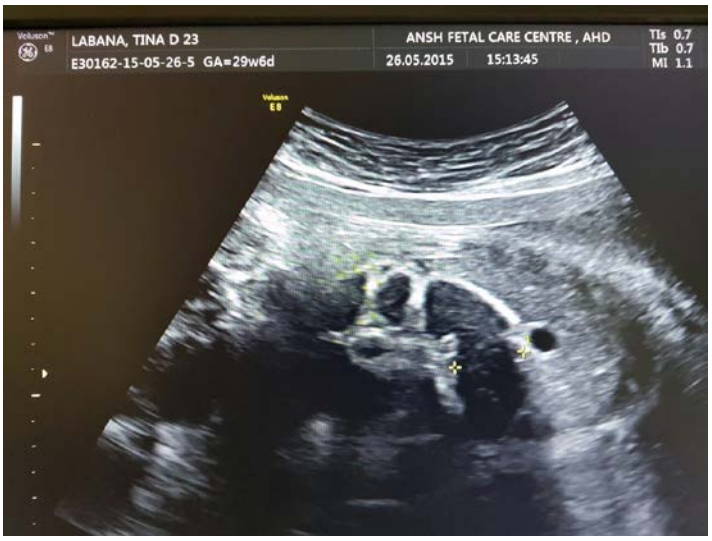

Figure 2: Sonography image showing dilated bowel