Prenatal Phenotype of Down Syndrome Using Three-Dimensional Virtual Reality

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Abstract

Background: Down syndrome is a chromosomal abnormality characterized by an additional acrocentric chromosome, resulting in an aneuploid number of 47 chromosomes (trisomy 21). Fetal face phenotype of Down syndrome is typical in the second trimester and characterized by plane face and a big and protruding tongue.

Case: We present a case of Down syndrome at 29 weeks of gestation in which the fetal face was created using 3-D virtual reality model from 3-D ultrasound scan data.

Conclusion: A 3-D virtual model from 3-D ultrasound or magnetic resonance imaging scan data allowed an immersive real environment, improving the understanding of fetal congenital anomalies by the parents and the medical team.

Résumé

Contexte : Le syndrome de Down est une aberration chromosomique caractérisée par la présence d'un chromosome acrocentrique excédentaire, ce qui conduit à un nombre aneuploïde de chromosomes, soit 47 (trisomie 21). Le phénotype facial du syndrome de Down, caractérisé par un visage aplati et une langue hypertrophiée et proéminente, est habituellement présent chez le fœtus au cours du deuxième trimestre de la grossesse.

Cas : Nous présentons un cas de syndrome de Down détecté à 29 semaines de grossesse, où un modèle virtuel en 3D du faciès fœtal a été créé à partir de données venant d'une échographie 3D.

Conclusion : La réalisation d'un modèle virtuel en 3D à partir de données venant d'une échographie ou d'une imagerie par résonance magnétique 3D a permis la création d'un environnement immersif et réel qui, à son tour, a permis aux parents et à l'équipe médicale de mieux comprendre les anomalies congénitales fœtales.

Key Words: Prenatal diagnosis, Down syndrome, three-dimensional ultrasound, three-dimensional virtual reality

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INTRODUCTION

In 1866, Langdon Down described people with the following phenotype: plane face, rounded cheeks, hypertelorism, narrow eyelid fissure, transversely pleated forehead, thick lips, small nose, long tongue, and excessive skin on the body.[1] The association between Down syndrome and advanced maternal age was described by Shuttleworth.[2] Lejeune et al.[3] and Jacobs et al.[4] described that an additional acrocentric chromosome was found in people with Down syndrome, resulting in an aneuploid number of 47 chromosomes (trisomy 21).

The screening of Down syndrome was introduced in the beginning of 1990, and it was based on the advanced maternal age as well as nuchal translucency thickness measurement between 11 and 14 weeks of gestation.[5] Posteriorly, other biochemical and biophysical markers, such as free-beta human chorionic gonadotrophin, pregnancy-associated plasma protein A, and nasal bone length measurement, were incorporated in the first trimester screening. The identification rate of trisomy 21 is 91%, which includes a false-positive rate of 0.5%.[6] In the second trimester, several soft ultrasound markers for trisomy 21, such as intracardiac echogenic foci, hyperechogenic bowel, structural defects, nuchal-fold thickness, femur length, humerus length, renal pelvis diameter, and prenasal thickness can increase the detection rate of Down syndrome combined with the first trimester screening.[7]

The phenotype of Down syndrome by 2-D ultrasound is very characteristic in terms of the face, neck, heart, and

hands. These are the main anatomical areas with high likelihood of trisomy 21 as observed using visual analysis.[8] Phenotypic characteristics of absent and hypoplastic nasal bones in fetuses with Down syndrome by 3-D ultrasound have been described in the literature.[9] Virtual 3-D and physical models from ultrasound and MRI to distinguish normal and malformed fetuses have allowed for a better understanding of fetal face features by the parents and the medical team.[10–13] Important clinical applications have been found in blind pregnant women.[14]

The objective of this article is to describe the technique to obtain a 3-D virtual phenotype model of a fetus with Down syndrome and its possible clinical applications.

THE CASE

A primigravid woman, 39 years old, was referred to our service for first trimester screening at 12 weeks of gestation. Ultrasound findings were as follows: nuchal translucency thickness measurement of 3.4 mm, ductus venosus Doppler with positive A-wave, non-visualized nasal bone, and absence of structural anomalies. Non-invasive prenatal testing at 11 weeks of gestation showed high risk for trisomy 21. Fetal karyotype by amniocentesis at 16 weeks of gestation confirmed the diagnosis of Down syndrome. Brazilian laws do not allow the termination of pregnancy in cases of fetal malformations; therefore, the pregnancy was followed after parental counselling.

The patient did not undergo second trimester screening, but she returned to the service at 29 weeks of gestation because the 2-D ultrasound examination revealed double bubble sign and atrioventricular septal defect (Figure 1). A 3-D ultrasound in the HDlive rendering mode using a Voluson E8 Expert apparatus (General Electric Healthcare, Milwaukee, WI, USA) equipped with a convex probe (RAB4-8L) clearly showed a phenotype of Down syndrome characterized by plane face and a big and protruding tongue (Figure 2, Video S1).

The 3-D volume datasets of fetal face were stored in the ultrasound apparatus and subsequently transferred to a compact disc for offline analysis. These datasets were transferred to a workstation in the Digital Imaging and Communications in Medicine format for manual, slice-by-slice segmentation using a digital high-definition screen tablet (Cintiq, Wacom, Tokyo, Japan). The 3-D fetal face structure was reconstructed by generating skinning surfaces that joined the resulting profiles. The software that converts medical images into numerical models (Mimics v. 12, Materialise, Leuven, Belgium) was used for 3-D virtual model reconstruction, and the model was exported into a standard triangular language format and converted into an "OBJ" extension for adjustment using 3-D modeling polygonal software (Autodesk Mudbox, San Francisco, CA, USA). Using this software, the volumetric surface was smoothed to be compared and analyzed later as a topographic construction. After this procedure, the 3-D model was again converted and exported as a standard triangular language extension. The model file was then opened in Mimics software to correlate the contours of the 3-D ultrasound with the generated 3-D virtual fetal face surface (Figure 3, Video S2).

The patient was followed up in prenatal care without complications and had spontaneous labour at 38+4 weeks of gestation, delivering a male newborn weighting 3120 g with Apgar scores of 9 and 10 at 1 and 5 min, respectively. The newborn died at age 2 months because of congestive heart insufficiency.

DISCUSSION

Virtual reality is a technology that uses software-generated realistic images enriched by other modes, such as sounds,

Figure 1. (A) Axial plane at the level of abdominal circumference measurement showing the double bubble sign. (B) Four-chamber view showing the atrioventricular septal defect.