Introduction

A 23-year-old, gravida 2, presented at 9 weeks. An anatomy scan (ultrasound most likely) at 27 weeks, demonstrated abnormal arterial echogenicity and elasticity, suspicious for IIAC. In one study of IIAC patients, 8/11 cases involved a mutation in the ectonucleotide pyrophosphatase/phosphodiesterase 1 (ENPP1) (Rutsch, 2003; Ramjan 2009). IIAC is lethal due to the increased risk of myocardial infarction or congestive heart failure, secondary to hypertension (Rutsch, 2008). ENPP1 is involved in the breakdown of adenosine triphosphate, into adenosine monophosphate and pyrophosphate, specifically outside the cell. More than 40 mutations in ENPP1 gene have been associated with IIAC. These mutations inactivate ENPP1 causing a decrease in the availability of pyrophosphate, a physiologically inhibitor of calcification.

Materials and Methods

Amniocentesis and capillary sequencing analysis were performed using primer sets that make up the whole ENPP1 gene. The PCR products were sent for cleanup and sequencing: 2669bp-4797bp and 5707bp-6197bp. After delivery, placenta was evaluated by placental histopathology with calcium staining.

Objective

To evaluate DNA from amniocytes using primers for ENPP1, to determine the causative mutation.

Results

Figure 2: DNA sequence comparison between reference and primer. Whole Blood From Mother:

Mutations in exon 25

Figure 3: Capillary Sequence from amniocyte and whole blood from mother-derived DNA amplified with primer sets 2669bp-4797bp.

Discussion

Pathology related to ENPP1 mutation: Ossification of the posterior longitudinal ligament of the spine, arterial calcification of infancy, Diabetes mellitus, non-insulin dependent, hypophosphatemic rickets, Cole disease, and obesity.

Conclusion

We were able to demonstrate, using SNP Microarray, multiple contiguous regions of allele homozygosity across many chromosomes which confirmed our suspicions of a rare case of IIAC. In the regions of ENPP1 which we have sequenced: 2669bp-4797bp and 5707bp-6197bp. The sequence shows a deletion of a T at 4849bp in Exon 25.

References