INCIDENTAL DIAGNOSIS OF A PARENTAL BALANCED RECIPROCAL REARRANGEMENT IN COUPLES UNDERGOING ROUTINE ANEUPLOIDY SCREENING BY TARGETED NEXT GENERATION SEQUENCING (TNGS)

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OBJECTIVE: Next generation sequencing-based aneuploidy screening now allows for the detection and reporting of segmental aneuploidies with high accuracy. During the process of testing thousands of embryo biopsies we observed that several patients had embryo biopsies with segmental aneuploidy patterns suggestive of being unbalanced products of parental chromosome rearrangements. This study sought to confirm those findings and determine the frequency of this occurrence in our tested patient cohort.

DESIGN: Retrospective cohort data analysis

MATERIALS AND METHODS: A review of the patients with at least one embryo biopsy submitted for aneuploidy screening by tNGS over a five month span (10/1/16-3/1/17) was performed. If a balanced rearrangement was suspected in a couple, then the clinical teams were notified that parental karyotypes were required before a final diagnosis could be completed on the embryo biopsies.

RESULTS: For 1986 patients, at least one embryo biopsy was submitted for CCS testing by tNGS in this time period. Of this group, data from 12/1986 (0.6%) patients was consistent with a suspected parental chromosome rearrangement and 83.3% (10/12) of cases were confirmed positive for an apparently balanced reciprocal rearrangement in the patient or partner. Upon the review of these findings, the clinical reports categorized all embryos with segmental abnormalities related to the chromosome rearrangements as abnormal. Interestingly, to our knowledge none of the patients reported a history of recurrent pregnancy loss (RPL) or chromosomally abnormal offspring to their clinical teams.

CONCLUSIONS: tNGS can accurately detect unbalanced products of some reciprocal chromosome rearrangements. While routine work up for RPL includes karyotype analysis, there are patients without a history of RPL that also carry balanced rearrangements. In this cohort, the frequency of those patients (0.5%, 10/1986) is greater than the general population (~1/500). While there are various testing methodologies that are best suited in cases of known parental rearrangements, tNGS offers enhanced identification of balanced rearrangement carriers compared to previous testing methodologies. Further, it provides an additional opportunity for diagnosis in patients that may be missed in the clinical setting.