SEVEN CASES OF CHROMOSOMAL MOSAICISM PERSISTING THROUGH GESTATION: CLINICAL IMPLICATIONS AND RECOMMENDATIONS FOR PRENATAL TESTING

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Background:
Chromosomal mosaicism, or the co-existence of euploid and aneuploid cells, is a well-documented phenomenon that can affect a significant proportion of human embryos. Although current PGT-A technologies have the ability to detect mosaicism, the appropriate clinical management of mosaic embryos is a subject of ongoing research and debate. It has been reported that mosaic embryos may lead to apparently healthy babies [1,2], but the understanding of what occurs within the aneuploid cell portion during these pregnancies is still in the process of being clarified. Experimental models have presented indications of a self-correction process, wherein euploid cells demonstrate a competitive advantage over aneuploid cells due to differential proliferation [3]. However, whether this phenomenon occurs in human pregnancies has yet to be conclusively demonstrated. Furthermore, the guidelines for prenatal testing following the transfer of mosaic embryos differ significantly among various professional societies. and are predominantly grounded in theoretical concepts rather than concrete empirical evidence.

Objective:
To understand the implications of mosaicism detected by PGT-A persisting to later stages of pregnancy, and using clinical data to generate guidelines for prenatal testing.

Materials and Methods:
Data on mosaic embryo transfers was contributed by participating centers and was assembled by the International Registry of Mosaic Embryo Transfers (IRMET). Cases with evidence of mosaicism persisting through pregnancy as evidenced by prenatal and/or postnatal chromosomal testing were identified and profiled.

Results:
The dataset contained 610 pregnancies from mosaic embryo transfers with prenatal and/or postnatal testing results (64 CVS, 326 NIPT, 280 Amniocentesis, 24 POC, and 30 Postnatal testing). Seven pregnancies (1.2%) revealed the same mosaicism that was originally identified

with PGT-A in at least one pre- or postnatal test, indicating persistence of mosaicism. One case of mosaicism (low level +17) presented abnormalities by ultrasound and spontaneously aborted. Three cases of mosaicism (low level +1q,-7,-8,+9,-19,-20,+21; low level +21; and high level +15) were terminated after non-viable abnormalities were detected by ultrasound, and one mosaic segmental case (low level -1p36.33p31.1) was terminated due to the known risks of the abnormality. Two cases (low -2; low +4q32.3q34.3,-Xq27.3q28) resulted in birth of babies that were seemingly healthy.

Conclusions:
These findings suggest that mosaicism does not always become resolved during a pregnancy. Self-correction by differential competency of euploid and aneuploid cells appears to convert most mosaic embryos into euploid pregnancies, but the process is not 100% efficient. Cases with persistence of mosaicism can occasionally have negative clinical consequences, including non-viable abnormalities and spontaneous abortion. This small but real risk to the pregnancy of persistence of mosaicism must be considered when considering the transfer of a mosaic embryo. The data presented in this study suggests that prenatal testing, especially a combined program of 24-chromosome NIPT and amniocentesis by microarray, should be the recommended strategy to monitor the pregnancy resulting from a mosaic embryo transfer.

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References:

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