5. CONCLUSIONES

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5.1. Respecto a las características de nuestra serie vemos que las **indicaciones diagnósticas** más frecuentes han sido la ansiedad materna y la edad materna avanzada, ambas representan un 40% de los casos analizados.

5.2. El estudio del posible efecto de la metodología de extracción de vellosidades coriales en la **evolución perinatal,** ha mostrado una frecuencia de un 2% de pérdidas fetales. Es de destacar que en las semanas en las que se realizaron estos estudios, la edad materna avanzada presenta, de forma espontanea, una elevada incidencia de abortos. Por otra parte, la frecuencia de pérdidas fetales mediante extracción de vellosidades coriales es algo mayor a la observada en amniocentesis (1%).

5.3. Se ha conseguido una **optimización de la técnica** citogenética teniendo en cuenta los siguientes aspectos:

- visualización de la muestra bajo lupa con el fin de procesar una muestra adecuada (todavía con la paciente en posición ginecológica)

- medio de transporte con antibióticos (medio completo).

- procesado de la muestra lo antes posible, siempre antes de las 24 horas post-extracción.

- separación de vellosidades coriales y decidua con el fin de evitar la contaminación materna.

- técnica secuencial uniforme-bandas G, que permite iniciar la detección de anomalías cromosómicas inmediatamente después de realizar una extensión (aumento de la rapidez diagnóstica), dichas anomalías serán posteriormente identificadas mediante la técnica de bandas. La tinción Wright asegura la obtención de bandas y con ello el diagnóstico citogenético, reduciendo el riesgo por pérdida de divisiones analizables debido a un tratamiento enzimático.

5.4. Nuestra técnica nos ha permitido conseguir un diagnóstico citogenético en un 94,3% de los casos en la primera extracción. Entre los factores que contribuyen decisivamente al **éxito diagnóstico** hemos comprobado que:

- la cantidad de muestra ha de ser superior a 5mg.

- se ha de seleccionar las vellosidades con la calidad morfológica óptima (aspecto digitiforme, capilar central y numerosos brotes irrigados).

- las semanas de gestación idóneas para efectuar el diagnóstico prenatal con éxito están entre la 10-14 semana (96,4%).

- el medio de cultivo más adecuado ha sido el Chang sin incorporación de suero (98,6%) seguido del RPMI-1640 con 5% de suero (93,8%).

- la incorporación del laboratorio en el lugar de la extracción permite un incremento de éxito diagnóstico ya que minimiza el tiempo de transporte de la muestra así como valorar la cantidad y calidad de la misma.

5.5. Para la **obtención de un diagnóstico citogenético,** en los casos de no conseguirlo en un primer intento, mediante la obtención de una nueva muestra de vellosidad corial, líquido amniótico o cordocentesis, ha llegado a ser de un 100%, lo que nos da un éxito diagnóstico global en la serie de un 98,5%.

5.6. En el presente estudio *se* ha detectado un 4% de **cromosomopatías.** La frecuencia de anomalías cromosómicas en mujeres es superior a la de los varones (2,8% y 1,2% respectivamente). La distribución de las mismas ha sido de 2.2% anomalías numéricas, 0.8% estructurales y 1.1% mosaicos. Estos resultados se corresponden con los valores obtenidos en otras series.

5.7. Al analizar las frecuencias de anomalías coriales **respecto a otros tejidos,** correspondientes a distintos estados del proceso reproductivo, desde células germinales, abortos espontáneos, amniocitos y recién nacidos, se observa una disminución progresiva de las mismas, sugiriendo que a lo largo de la gestación se produce una cierta "selección natural" de embriones.

5.8. Dentro de las **aneuploidías** autosómicas la más frecuente ha sido la trisomía 21 y la 18 (0.5% y 0.3% respectivamente) y en el grupo de las gonosómicas la 45,X y 47,XXY (0.4% en ambos casos).

5.9. Dentro de las anomalías cromosómicas **estructurales,** las más frecuentes han sido las equilibradas (0.5%), cuando uno de los progenitores era portador de la misma. En la mayoría de los casos se ha observado herencia vía materna.

5.10. En el presente trabajo, el porcentaje de **mosaicismo** ha sido de un 1,1% del total de muestras, superior al observado en líquido amniótico (0,3%). Las anomalías cromosómicas más frecuentes en nuestra serie han sido las trisomías 21 y 7 y la monosomía X.

5.11. La frecuencia de **discrepancias** en cuanto a falsos positivos, entre vellosidades coriales y tejido fetal ha sido de un 0,7%, muy superior al detectado en líquido amniótico (0,6%). La principal fuente de discrepancias ha sido el mosaicismo confinado a la placenta (71,4%). Los cromosomas más implicados han sido el X, 2, 7 y un cromosoma mar. Es necesario avanzar en los estudios para determinar si los mosaicos confinados a la placenta afectan al feto ya que gestaciones con la misma anomalía cromosómica pueden tener consecuencias distintas durante el desarrollo embrionario.

5.12. Entre los **factores que influyen en la aparición de anomalías cromosómicas** hemos analizado:

-la indicación diagnóstica. El porcentaje más elevado de cromosomopatías ha correspondido a la indicación de progenitores portadores de anomalías cromosómicas (40%), seguido de la anomalía ecográfica previa (19%) y de la edad materna avanzada (4,3%).

-la edad de gestación. Hemos detectado una ligera disminución de las anomalías cromosómicas a medida que avanza la gestación (4% en las semanas 8-11 a un 3.5% en las semanas 12-15).

-el medio de cultivo. La frecuencia de cromosomopatías es similar en los dos medios utilizados moyoritariamente (3,6% en Chang y 4,1% en RPMI-1640), lo que pone de manifiesto que las anomalías cromosómicas halladas no dependen del medio utilizado. El único problema atribuible al medio sería la presencia de células anómalas "individuales" (pseudomosaicismo).

5.13. Hemos observado la aparición espontanea de **lesiones cromosómicas** en vellosidades coriales, pero la frecuencia de lesiones no varía ni con el medio de cultivo utilizado (9% en RPMI-1640 y 9,3% en Chang) ni con la semana gestacional. Estas lesiones coinciden en un 76,2% con la localización de bandas donde se han descrito lugares frágiles. El 47,5% de las lesiones se han localizado en ocho bandas cromosómicas, siendo la región 1q12-q21 la más implicada (15,8%).

5.14. Se ha observado una **descondensación espontánea de la heterocromatina constitutiva** de las regiones de los cromosomas 1,9,16 e Y en el 46,6% de las muestras de vellosidades coriales; siendo la más frecuente la descondesación de la heterocromatina 9qh (42,4%) seguida de la del 1qh (22,2%). El medio de cultivo no influye en la aparición de dicha descondensación. Respecto a la semana gestacional se ha observado un incremento de descondensación de la heterocromatina del 41,7% (en las semanas 8-14) a un 85,7% (a partir de la 20 semana). Esto último parece indicar que en estas etapas de desarrollo embrionario temprano dichas regiones podrían, al descondensarse, dejar de transcribir determinados genes próximos a ellas.

5.15. Entre las limitaciones para la obtención de un **diagnóstico prenatal citogenético a** partir de vellosidades coriónicas, indicaríamos: la contaminación materna, los mosaicos y las discrepancias. En cuanto al primer problema podemos reducirlo con la experiencia del citogenetista, en los otros dos casos se necesita un buen estudio ecográfico paralelo y la realización de una amniocentesis. Sin embargo, la posibilidad de obtener un diagnóstico fiable, en un corto periodo de tiempo (2-3- días frente a las 2-3 semanas de la amniocentesis) hace que dicha técnica citogenética sea valiosísima en el diagnóstico prenatal actual.

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