Editoral : Chromosomal microarray : A boon or boom

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Technology in genetic testing has advanced dramatically. Care during pregnancy is completely transformed in realm of fetal medicine. Various tests are available but judicial and appropriate application is very important. Chromosomal Microarray (CMA) is one of these newer technique. It is a method to find gain or loss in human genome . CMA can identify not only large change in structure of chromosome and aneuploidies butsubmicroscopic chromosomal abnormalities too,whichcan not be identified by traditional modalities like karyotyping. It can be boon in detection of certain , conditions .and can offer options exceeding just karyotype. Yet appropriate indication and interpretation of results is very important as at times it may create lot of dilemma to doctor and distress to patient if not properly dealt with.

Cases where one should do CMA test

1 Fetus with one or more major structural malformation on ultrasoundand prenatal invasive testing is required.

2. In fetal death or still birth.

3, in productof conception in recurrent pregnancy loss.

It can be offered after normal karyotyping if high suspicion of chromosomal anomalies. Unlike aneuploidies these chrosomal abnormalities are not considered related to maternal age. Hence maternag age per se is not an indication to do CMA testing.

Benefits of CMA

It gives higher diagnogticyield . It can identify very small 1-2 lac (0.2mb) base pairs whereas conventional karyotyping read 3-10 million base pairs. CMA can give additional information about chromosomal problems in 6% cases where conventional karyotyping report in normal. In abnormal aneuploidy screening it adds abnormal findings in chromosome in 1.7% more cases.

As no dividing cells are required for CMA test , it can give report after IUD or still born tissues or can say any cells from product of conception .

No culture of tissues is required as it does not require dividing cells, it yields a quicker report, in 4-7 days rather 10-14 days in conventional karyotyping.

There is possibility of detection of consanguinity .incest or non-paternitity. It can identify maternal contamination quickly.

Limitations

Whereas it has ability to detect even submicroscopic unbalanced translocations ,it can not detect balanced translocations or inversion as there is no loss or gain in copies numbers

It can notdifferenciate between aneuploidy trisomy21 or 21/22 robertsoniantranslosation so determination of recurrence risk is difficult, as in unbalanced translocations parental karyotyping is required for assessing the risk of recurrence.

Secondary findings are possible which may be associated with asymptomativ adult onset disease. But policies for incidental findings are not yet established.

Detection of VUS:Whole CMA intead of targeted CMA may result indetection of variant of uncertain significance (VUS) where management may be challenging. Chances of copy no variants of uncertain significance may be in 1-2% of cases. At times it becomes a difficult decision to continue pregnancy.**Example of VUS**: patient presented in early pregnancy with previous baby having autism. VUS detected in whole CMA of effected baby . Same was found in amniotic fluid of current pregnancy. On parent's CMA testing ,mother was carrying same variant and she was phenotypically normal,so pregnancy was continued in this pretext and that baby is growing as a normal baby now.

Copy no. variants (CNvs) may be pathogenic or benign .Pathogenecitydepends on size of variant.As high as 15% is usually pathogenic and associated withstructural fetal anomalies. Problem of VUS exists as there is limited dataon variable phenotypes of these VUS, incomplete penetrations and variable expressions also.

As knowledge on human genome will continue to grow, we would be able to interpretateCMA reports better. India also requires to establish our population genome so we can have better informations in future to manage genetic conditions. I suggest and expect more funding agencies to supportfor research in this field.