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اولین برنامه سمینار یکروزه

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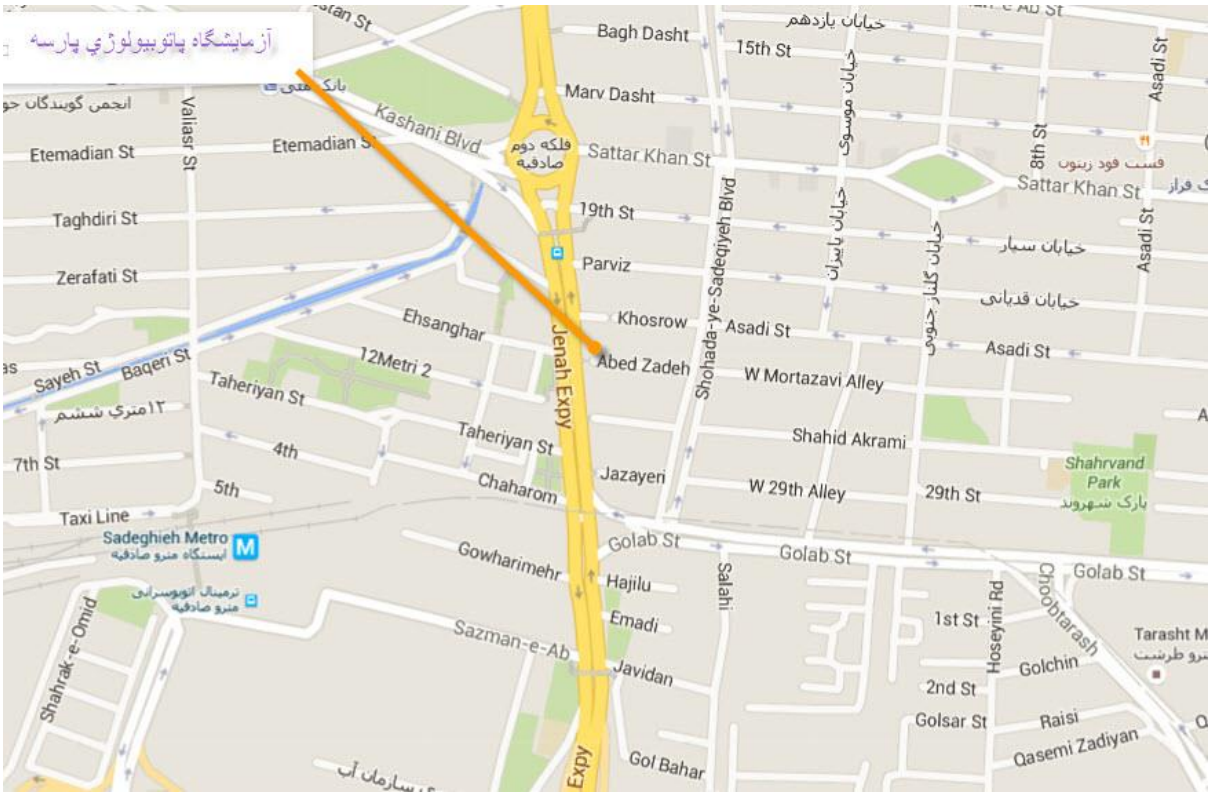

زمانبندی برنامه سمینار

۹:۴۵- ۹:۱۵ پذیرایی

۹:۵۵- ۹:۴۵ ← سخنرانی دکتر مصلایی (خوش آمدگویی و تبیین اهداف سمینار)

۱۰:۳۰-۹:۵۵← دکتر جواد کریم زاد حق (متخصص ژنتیک پزشکی)

Prental diagnosis of mosaic tetrasomy 18p in a case without songraphic abnormalities (Abstract 1)

۱۱:۰۰ – ۱۰:۳۰← دکتر داود زارع عبدالهی (متخصص ژنتیک پزشکی)

Prediction of a triploid conception based on the first trimester maternal serum screening (Abstract 2)

۱۱:۳۰ – ۱۱ ← دکتر حمید قائدی (متخصص ژنتیک پزشکی)

QF-PCR has power to detect partial trisomy (Abstract 3)

۱۲:۰۰ – ۱۱:۳۰۰ ← خانم محبوبه رجحان نژاد (فوق لیسانس مهندسی ژنتیک)

Running a heterozygote mutation of M694V mutation in a family with Familial Mediterranean fever (Abstract 4)

۱۲:۳۰- ۱۲:۰۰ ← خانم صدف سرابی(فوق لیسانس بیوتکنولوژی)

Characterization of a rare mosaicism in autosomal translocation of t(5;21) using conventional cytogenetics and FISH methods (Abstract 5)

۱۲:۴۵- ۱۲:۳۰ ← استراحت و پذیرایی

۱۳:۱۵- ۱۲:۴۵ ← بحث آزاد (برنامه برای سمینار بعدی در ۶ ماه آینده، مشکلات صنفی ژنتیک پزشکی، بیمه، متدها و استانداردسازی)

۱۳:۴۵-۱۳:۱۵ سخنرانی دکتر کرامتی پور (متخصص ژنتیک پزشکی)

NGS in clinical practice: case presentation (Abstract 6)

Abstract 1

Prental diagnosis of mosaic tetrasomy 18p in a case without songraphic abnormalities

Background:

Small supernumerary marker chromosomes (sSMC) are still a major problem in clinicalcytogenetics as they cannot be identified or characterized unambiguously by conventional banding cytogenetics alone. On the other hand, and perhaps more importantly in prenatal settings, there is a challenging situation for counseling how to predict the risk for an abnormal phenotype, especially in *de novo* cases with a sSMC.

Case:

Here we report on the prenatal diagnosis of a mosaic tetrasomy 18p due to presence ofa sSMC in a fetus without sonographic signs. For a 26-year-old, gravida 2 (para 1) amniocentesis was done due consanguineous marriage and concern for Down syndrome based on borderline risk assessment. Parental karyotypes were normal, indicating a *de novo* chromosome aberration of the fetus. FISH analysis as well as molecular karyotyping identified the sSMC as a i(18)(pter->q10::q10->pter), compatiblewith tetrasomy for the mentioned region. Cordocentesis was done due to normalsonography and the results from amniocentesis were confirmed. The parents opt forpregnancy termination and post mortem examination now noted, low anterior hairline,large philtrum, low-set posteriorly rotated malformed ears with prominent antihelix, lowerlimbs joint contracture and digital anomalies, including long and narrow toes withclinodactyly of the 1th and 5th toes and postaxial polydactyly of one hand.

Conclusion:

Our case emphasizes the need to determine the nature of euchromatic*de novo* markerchromosomes in an amniocentesis with normal ultrasound result, and supports thesuitability of a cordocentesis in order to better predicting the pregnancy outcome andparental counseling.

Keywords: tetrasomy; 18p; marker; sSMC; polydactyly

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Prenatal diagnosis of mosaic tetrasomy 18p in a case without sonographic abnormalities

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Keywords:	tetrasomy, 18p, marker, sSMC, polydactyly

Results

Karyotype of amniocentesis:

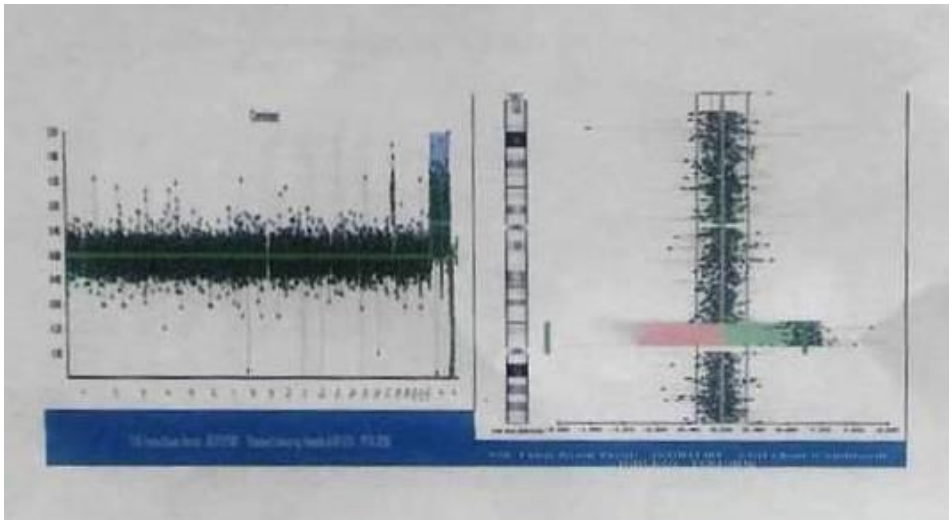
47,XX,+mar dn[36]/46,XX[4]

18

Karyotype of parents:

Normal

Array CGH of CVS:

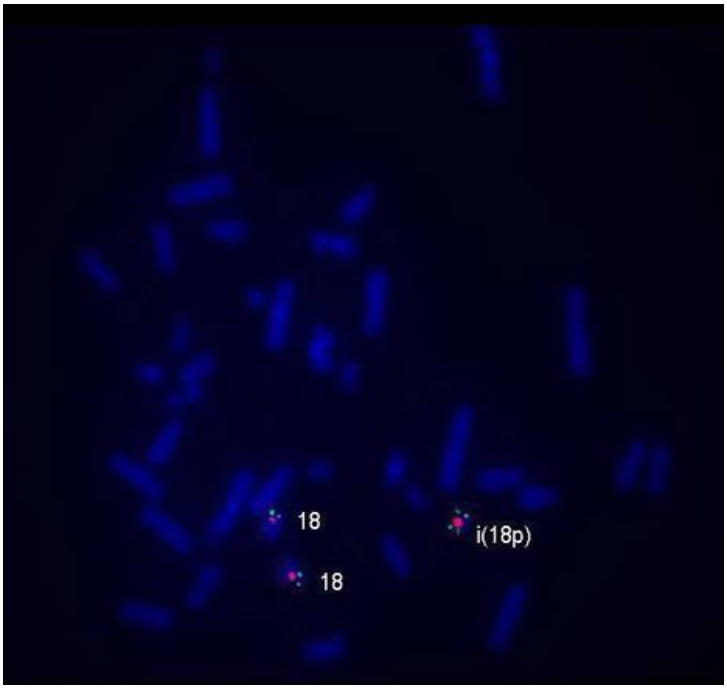


arr[GRCh37] 18p11.32q11.1(148,993-18,542,104)x3 18,393,112

Conclusion: **Fetus is female**
18.4Mb pathogenic gain on chromosome 18p11.32q11.1
from nucleotide 148,993 to 18,542,104
compatible with trisomy 18p11.32q11.1 or tetrasomy 18p11.32q11.1

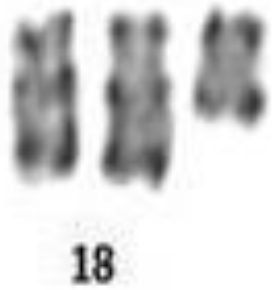
FISH Analysis:

i(18)(pter->q11.1::q11.1->pter)

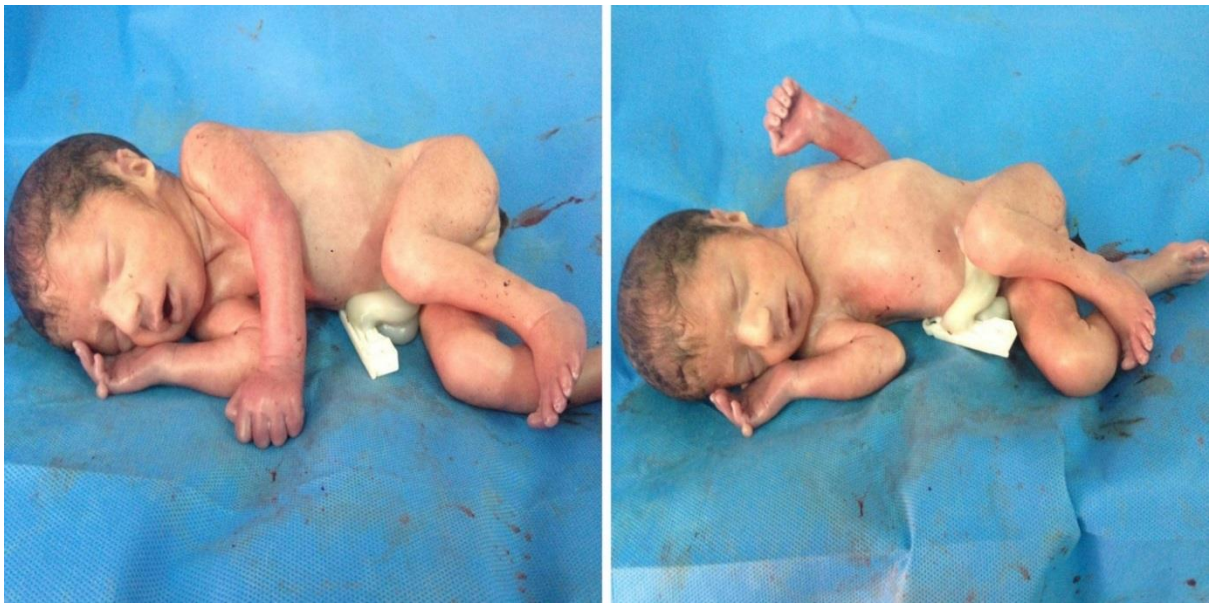


Karyotype of cordocentesis:

47,XX,+mar dn[18]/46,XX[22]



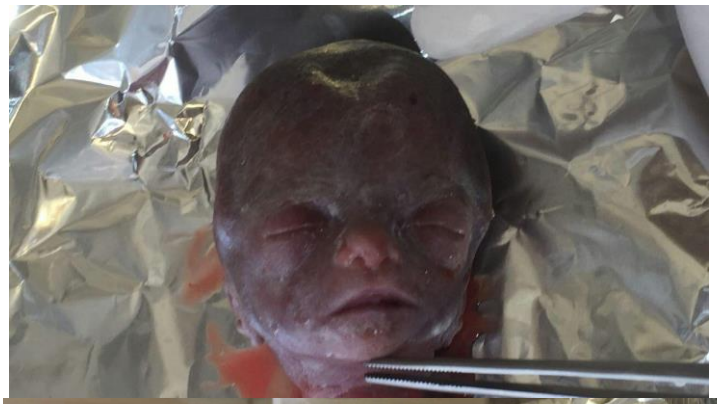
Two photos of the index patient after abortion:

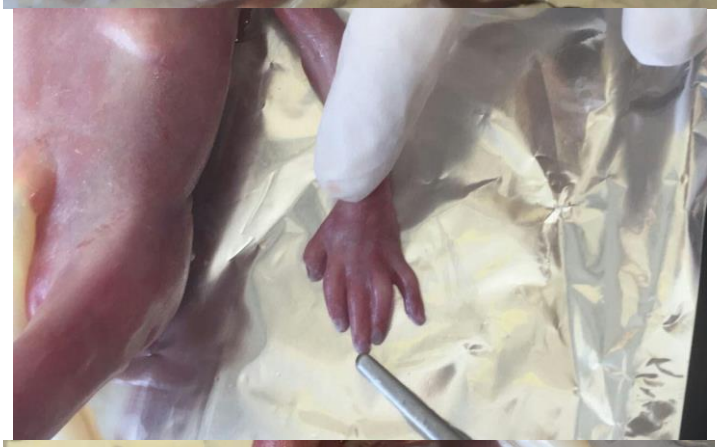


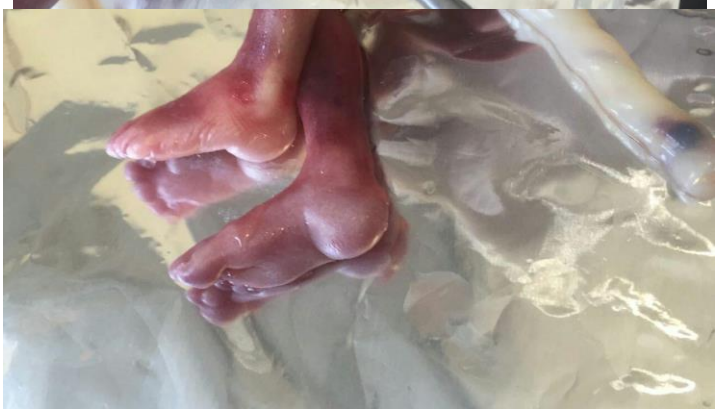
Abstract 2

Prediction of a triploid conception based on the first trimester maternal serum screening

Triploidy, a rare chromosomal abnormality, occurs in approximately 1% of conceptions. Many triploid conceptions are aborted spontaneously in the first trimester; triploidy was present in 20% of spontaneous abortions in one series. Triploidy associated with fetal development and survival beyond the first trimester is rare. The prevalence of triploidy at 16 to 20 weeks of pregnancy has been estimated to be 1 in 5,000.The aim of our presentation is to describe the distribution of fetal NT thickness and maternal serum free ß-hCG and PAPP-A at 11 weeks to 13 weeks and 6 days in two fetuses with triploidy and the effectiveness of maternal serum biochemistry screening for this chromosomal abnormality by the combined use of the risk algorithms for trisomies 21, 18 and 13.The large deviations in of fetuses with triploidy are the basis for their identification during the first trimester screening with the algorithms for trisomies 21, 18 and 13. The risk for triploidy is not related to maternal age and the sonographic markers of fetal NT is not substantially different from values in euploid fetuses. In about one-fourth of the cases of triploidy, the condition is diandric in which the associated very high maternal serum free ß-hCG results in the pregnancies being given a high risk for trisomy 21. In the other three-fourths of the cases, the triploidy is digynic in which the associated very low levels of free ß-hCG and PAPP-A result in the pregnancies being given a high risk for trisomies 13 and 18. Given these premises, beneficial consequence of first trimester screening for trisomies 21, 18 and 13 using specific algorithms for each of these trisomies is the identification of a high proportion of fetuses with triploidy. In a case of mosaic triploidy presented here, it has been shown that in some triploid pregnancy fetal NT is normal and both free β-hCG and PAPP-A are decreased but in a range that the pregnancy does not considered high risk for trisomies 13 and 18. Based on our experience with this case and literature review, we suggest that in the face of normal NT and decreased free β-hCG and PAPP-A, but yet still low risk for trisomies 13 and 18, the risk of a triploid pregnancy should be raised, and follow up effort like second trimester maternal serum screening and anomaly scan should be taken in to account.







Abstract 3

QF-PCR has power to detect partial trisomy

Prenatal diagnoses of chromosome abnormalities are performed by conventional cytogenetic analysis using in vitro culture of fetal nucleated cells retrieved by amniocentesis, chorion biopsy or fetal blood sampling. During the past 10 years, the Quantitative Fluorescent Polymerase Chain Reaction (QF-PCR) has been introduced to perform rapid prenatal diagnoses of common chromosome aneuploidies.

The clinical utility of this assay has repeatedly been confirmed together with its high sensitivity and specificity in detecting major chromosome abnormalities. The use of several highly polymorphic and chromosome specific STRs also makes it possible to detect partial trisomies. When a trisomic pattern is detected in only one marker, parents should be tested to detect the presence of such aberration, thus ruling out the possibility of partial trisomy.

Here, we present a fetus with 46,XX,der (5) t(5;21)(q35.3;q22.1)mat karyotype, which was detected initially by QF-PCR. The QF-PCR showed a tri-allelic pattern for a distal marker D21S1444, while other chromosome 21 markers were normal bi allele. Fine mapping the region showed a pattern consisted with partial trisomy for chromosome 21. Further analysis revealed that the fetus mother is a balanced translocation carrier 46,XX,t(5;21)(q35.3;q22.1).

Abstract 4

Running a heterozygote mutation of M694V mutation in a family with Familial Mediterranean fever

Background: Familial Mediterranean fever (FMF) is an autoinflammatory disorder which is mostly inherited in an autosomal recessive manner. FMF is characterized by acute attacks of fever and serosal inflammation. This disorder occurs as a result of point mutations in Mediterranean fever gene (MEFV). This gene is located on the short arm of chromosome 16p13.3 consisting of 10 exons and encodes a protein called pyrin. Most of identified mutations occur in exon 10 including M680I, M694V, M694I, and V726A.

Clinical report: Here we report a 7 year old proband and his unt with typical FMF symptoms including recurrence fever and abdominal pain. Also probands̀ mother and uncle experienced severe abdominal pain and synoviositis. Treatment with colchicine, the most effective known drug for FMF, reduced the rate of attacks, thus it was clinically confirmed as FMF. DNA extraction, polymerase chain reaction and sequencing was done for point mutations known to be responsible for the disease. Sequencing results showed just one mutation (M694V) in exon 10.

Conclusion: Although the FMF mode of inheritance is autosomal recessive, here in our case we observed affected members of the same family with only one mutation. This could be due to simply non recognizable mutations, polymorphisms of other inflammatory related genes and also effect of environmental or epigenetic factors. Similar to our case some other studies report heterozygote individuals manifesting the disease.

Abstract 5

Characterization of a rare mosaicism in autosomal translocation of t(5;21) using conventional cytogenetics and FISH methods

Mosaicism for a normal cell line and an unbalanced autosomal structure is rarely seen. If the abnormal cell line is widespread and contributes to a substantial fraction of the soma, is likely to cause dysmorphism and malformation and if the brain is included, intellectual disability. Whether, if only a fraction of soma is abnormal, the phenotype is likely to be normal and will probably never be recognized.

We report a 29-years-old woman which had the chromosome constitution of apparently balanced translocation of 46,XX,t(5;21) on lymphocyte study with a 2-years-old affected girl, characterized by mental retardation, dystrophia, low weight, hearing impartment and dysphasia.

Conventional cytogenetic investigation revealed a low mosaic unbalanced translocation of 46,XX,t(5;21)/46,XX. This result also confirmed by FISH analysis, studying 200 metaphases and interphases of peripheral blood sample which revealed 70% partial monosomy and 30% of normal pattern.

In conclusion, translocations involving chromosome 21 may consequence a low level of mosaicism.

اسامی شرکت کنندگان

۱. **آزمایشگاه نیلوفر** (دکتر علی شجاعی)

۲. انتقال خون ایران (دکتر سبحانی)

۳. **آزمایشگاه نورا** (دکتر کلاهی)

۴. **مدیا طب ژن** (دکتر عارف نژاد)

۵. آزمایشگاه مهر هشتگرد (دکتر حامدی)

۶. **کانون هموفیلی** (دکتر میرآخوری)

۷. **بیمارستان شریعتی، مرکز تحقیقات غدد** (دکتر شهرآبی)

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۱۰. **متخصص زنان و زایمان** (دکتر کنی)

۱۱. **آزمایشگاه دکتر هوشمند** (سوره سليماني, محيا عطايي)

۱۲. آزمایشگاه ژنتیک واتسون (دکتر محمد کرامتی پور, مهدیه رجحان نژاد**)**

۱۳. **آزمایشگاه پاتوبیولوژی و ژنتیک پارسه** (دکتر میرمجید مصلایی, دکتر سید بهروز محسنی مقدم, دکتر جواد کریم زاد حق , دکتر داود زارع عبدالهی, دکتر حمید قائدی, نوشین مسعود زاده, معصومه رستمی,صدف سرابی, منصوره ایرج پور, محبوبه رجحان نژاد, زهرا بی آزار, زهرا معینی)