318. GENETIC MECHANISMS OF DRUG RESISTANCE IN CANCER CHEMOTHERAPY

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Introduction. One of the major problems in cancer chemotherapy is the development of drug resistance during treatment. Currently, 90% of failures in chemotherapy are during the invasion and metastasis of cancers related to drug resistance that can develop in different mechanisms.
Aim of the study. To study genetic mechanisms of drug resistance in cancer chemotherapy.
Materials and methods.: This paper is a descriptive research, based on retrospective analysis. Analysis of statistical data, current management documents, reports, studies, bibliographic and digital sources have been carried out with reference to the topic.
Results. The study of the genetic mechanisms of drug resistance in the treatment of cancer has identified the presence of different extracellular and intracellular mechanisms: tumor heterogeneity, tumor microenvironment, cancer stem cells, inhibition of cell death, inactivation of anticancer drugs, multi-drug resistance (MDR), changing drug metabolism, changing chemotherapeutic agents targets, enhancing DNA repair, gene amplification, epigenetic changes, microRNA. Responsible for multiplication, growth and metastasis have been shown to be some genes that encode for kinases. According to the latest studies, use of kinase inhibitor preparations is effective in both stopping progression of cancer and increasing the intracellular concentration of the preparation in MDR cells.
Conclusions. Cancer drug resistance is a complex phenomenon determined by numerous mechanisms and some genes. Gaining knowledge about these particularities and performing genetic tests make it possible to avoid the misuse of the preparations, in order to prevent the chemotoxicity on the organism and affect the systems with a high division rate.
Key words: Cancer, multi-drug resistance, epigenetic changes, kinases.

319. DEFECTS IN SPERMATOGENESIS OF MEN WITH Y CHROMOSOME MICRODELETIONS

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Introduction. Male infertility has multiple etiology, most commonly caused by spermatogenesis disorders, clinically manifested by oligo/azoospermia. Until recently, Y microdeletion had little clinical significance since men with a deletion were considered unable to reproduce. However, by utilizing of Intracytoplasmic sperm injection (ICSI) and Testicular sperm extraction (TESE) it is now possible for oligo/azoospermic men with Y microdeletion to father children.
Aim of the study. To analyze the type of defect in spermatogenesis associated with specific Y deletions found in our IVF program, for prevention the transmission of these deletions through ICSI to offspring.

Materials and methods. A group of 46 infertile men were investigated during genetic counseling among infertile couples referred for ART treatment. Criteria for including patients were fulfilled if they presented with oligo/azoospermia, raised or normal levels of FSH, LH and testosterone. Genomic DNA was isolated and used to analyze AZF microdeletions by PCR. The regions and sequence-tagged sites of AZFa (SY86, SY84), AZFb (SY127, SY134), and AZFc (SY254, SY255) were sequenced by multiplex PCR. Five non-obstructive azoospermic men had Y chromosomal microdeletions. All five Y-microdeleted men underwent microsurgical observation of testicular architecture and quantitative histology of spermatogenesis in a strip of testicular tissue. The results were compared with the different type of Y microdeletion.
Results. Deletions of Y chromosome were seen in the AZFc regions of 2 patients, deleted markers were sY254 and sY255. In both men with AZFc deletions, the histological defects were variable, but no sperm were found. In only one case the defect of Sertoli cell-only syndrome (SCOS) in patient with microdeletions in each region of AZFa-sY84, sY86; AZFb-sY127, sY134; AZFc-sY254, sY255 was present. One patient with deletion of AZFb (SY127, SY134) had spermatogenetic maturation arrest. In all men with AZF microdeletions of the Y chromosome, we found severe spermatogenic defects: however, we also did not find, in all of them, mature sperm sufficient for ICSI. The patients were advised to use sperm from the donor for ICSI and IVF.
Conclusions. This study highlights for all couples with the diagnosis of male infertility with oligo/azoospermia the need of genetic testing and counseling prior to employment of assisted reproduction techniques. This is important for providing a firm diagnosis and fertility treatment to couples with infertility and for prevention of the transmission of AZFc deletions through ICSI to offspring.
Key words: male infertility, PCR, deletion, AZF region

320. GENETIC ASPECTS OF VON WILLEBRAND DISEASE

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Introduction. Von Willebrand disease (VWD), the most common inherited bleeding disorder in humans, is a heterogeneous disorder caused by a partial quantitative (type 1 VWD), qualitative (type 2 VWD) or severe quantitative (type 3 VWD) deficiency of von Willebrand factor protein (VWF). It is characterised clinically by mucocutaneous bleeding, such as epistaxis and menorrhagia, and prolonged bleeding after surgery or trauma. VWF is a large, multimeric protein that plays a role in platelet adhesion and serves as a carrier for the thrombotic protein factor VIII. The VWF gene is located at the short arm of chromosome 12 (12p13.31). Depending on its type, VWD can either have an autosomal dominant inheritance pattern (type 1, type 2A, 2B, 2M) or an autosomal recessive inheritance pattern (type 2N and type 3).
Aim of the study. Expanding the understanding of the genetic basis of different types of VWD.
Materials and methods. This study is based on a review of different articles from the open access data bases: PubMed, OMIM, SpringerLink.