disease revealed multiple involvements in the bone and lungs. Treatment with Vincristine, doxorubicin, cyclophosphamide, and dexamethasone was initiated, resulting in a significant regression of the masses and an improvement in the cytopenia picture. **Conclusion:** The presence of RMS in the bone marrow can complicate both the diagnosis and treatment of the disease. It may require additional diagnostic procedures, such as bone marrow biopsy, to confirm the presence of RMS cells. Treatment may also need to be more aggressive, approaches. Bone marrow involvement in RMS is considered a more advanced stage of the disease and may be associated with a more challenging prognosis. Early detection and tailored treatment are crucial for managing RMS with bone marrow infiltration.

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OP 15

NEW MOLECULAR TARGETS IN CANCER CELL BIOENERGETIC PATHWAYS

Tyumin Ivan [1]

[1] *A. F. Tsyba MRSC, a branch of the Federal State Budgetary Institution "NMRC of Radiology" of the Ministry of Health of the Russian Federation*

Research Supervisor: L.Y. Grivtsova, PhD in medical science, PhD in biology science, Head of Laboratory Medicine Department, Head of Clinical Immunology Laboratory of A.F. Tsyba MRSC, a branch of the Federal State Budgetary Institution "NMRC of Radiology" of the Ministry of Health of the Russian Federation Over the last ten years, the ideas of molecular oncology about the energy metabolism of malignant cells have changed dramatically, and new molecular mechanisms in the cascade pathways of cancer bioenergetics are being searched for. Numerous data show that the emergence and development of tumors are closely related to the metabolism of iron ions (Fe). Inorganic substrates, namely iron ions involved in the metabolic processes of the tumor cell, have received limited attention in the world literature to date. Our research group has put forward and is developing the concept of «Energy metaplasia of cancer cells», i.e. acquisition of an additional autotrophic way of energy production (respiratory reactions involving iron ions) in the process of oncogenesis. Proof of the hypothesis opens prospects for explaining some issues of oncogenesis and a new approach to the treatment of cancer. The aim of the study: to investigate and obtain evidence for the existence of respiratory (chemosynthetic) reactions involving iron ions as a way to obtain energy in cancer cells. The studies were conducted on the basis of the «Center of Cell Technologies», Samara city, Russia, under the guidance of specialists from A.F. Tsyba MRSC, Obninsk city, Russia. All experiments were conducted in vitro using HeLa cell line (cervical carcinoma) and human mesenchymal stromal cell line (MSC) culture as a control. The proof-of-concept study was carried out in 3 stages. The 1st stage was analytical review, the 2nd stage - study of energy metabolism by extracellular flux analysis on the SeaHorseXFp apparatus (USA), the 3rd stage - bioinformatic study on search in the human genome for homolog genes responsible for chemosynthetic reactions using blastp and exonerate programs. As a result of the analytical review of works on the evolution of the way of energy production by plant and animal cells, a possible chemosynthetic reaction in cancer cells - oxidation of iron ions (Fe^{+2} - Fe^{+3}+E) was revealed. As a result of 50 performed protocols on SeaHorseXFp cell metabolism analyzer we found suppression of two classical pathways of energy production - oxidative phosphorylation (by 54,2%) and glycolysis (by 85,4%) in malignant HeLa culture in contrast to normal index in MSC cell culture. As a result of bioinformatic study, 6 proteins and 11 domains related to iron metabolism were found in the human genome, which are highly similar in sequence to the genes responsible for chemosynthetic reactions involving iron ions in iron bacteria. Thus, respiratory chemosynthetic reactions involving iron ions are possible in malignant cells, which allows the cancer cell to change its energy phenotype and acquire an additional autotrophic way of energy production, allowing it to acquire the properties of uncontrolled growth and metastatic spread. This molecular cascade requires additional study and is of interest as a target for the development of targeted antitumor drugs.

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Pediatric Hematology Abstract Categories Coagulation and Fibrinolysis Disorders
OP 16

THE COEXİSTENCE OF NOVEL MUTATİONS OF FX, DİMETHYLGLYCİNE DEHYDROGENASE GENES WİTH FAMİLİAL EPİSODİC PAİN SYNDROME: A CASE REPORT

Hatice Mine Çakmak [1]

[1] *Duzce Unıversıty*

Objective: Congenital Factor X (FX) deficiency is an autosomal recessive disorder with variable clinical severity associated with heterozygosis or homozygosis inheritance. Genetic mutations are located on the glutamic acid domain on exon two and the catalytic site of FX on exons 7, 8. Missense mutations of specific patients or families are reported. Severe forms of the disease result from homozygosis or compound heterozygosis genetic mutations. In this case report, we aim to write a rare cause of epistaxis and novel mutations of FX and DMDGH (**Dimethylglycine Dehydrogenase)** deficiencies, and he and his family are the second with TRAP1-related FEPS1 (familial episodic pain syndrome) in the World. **Case report:** A 6-year-old boy, born in Turkey, with no known

chronic medical condition, was admitted to the pediatric hematology-oncology policlinic with epistaxis lasting for approximately 10 minutes and repeating daily. The family history revealed prolonged bleeding episodes in his father, uncle, aunt, and uncles' sister. The patient denied mucosal bleeding, spontaneous bruising, or prolonged bleeding after dental extraction. The physical examination included; weight: 22 kg (50-75 p), height: 127 cm (>95 p), and regular systemic features. In addition, prolonged PT (21.1s) and normal aPTT levels were found. In his family, prolonged PT was also detected in his father (16.9s) and sister (13.7s). Factor and coagulation levels and their normal ranges consistent with age are given in Table 1. In the clinic exom study, NM_000504.4:c. 785 G>A p.Gly262Asp heterozygosis mutation on the F10 gene has a nonsynonymous_SNV effect, causing Factor X deficiency (Table 1). This mutation is a new change undefined in the Clinvar database with a DANN score of 0.988. According to the ACMG rules (PP3, PM2, PP2), this mutation is pathogenic (Figure 1). Clinic exom study revealed other mutations (Table 2) associated with the case's clinic features. For example, the patient had a fish odor and muscle tiredness associated with dimethylglycine dehydrogenase deficiency. In addition, the patient suffered from episodic pain syndrome (upper body pain after cold, physical stress, and fasting) and frequent fevers that may be associated with Immunodeficiency and TNFRS13B mutation. Episodic pain syndrome was common in the patient's father's family (uncle, uncle's sister, aunt, grandfather, aunt, and aunt's three children) (Figure 2). However, the diagnosis of immune deficiency is not defined in his family. Family segregation mutation analyses are under study. **Results:** Factor X deficiency is a rare coagulation disorder. The clinic severity differs according to the genetic mutations generally localized to the glutamic domain exon 2 [(1)]. Gokcebay et al. represented an infant with a homogenous FX gene mutation in Exon2 (Gly51Arg) with an FX serum level of 0.03 U/ml. This infant had umbilical cord bleeding and cephalic hematoma and received fresh frozen plasma and activated prothrombin complex concentrate (aPCC). PT (INR) was elevated only[(5)]. Nagaya et al. reported Four heterozygous mutations [p.Gly154Arg, p.Val236Met, p.Gly263Val, and p.Arg387Cys] and a compound heterozygous FX gene mutation (p.Gly406Ser and p.Val424Phe) were identified [(6)]. Another case report showed that a heterozygous nonsense mutation in the F10 gene led to prolonged vaginal bleeding after polypectomy [(7)]. In neonates, FX levels <10% may cause severe bleeding like CNS, gastrointestinal, hematomas, and hemarthroses. In addition, severe deficiency may cause epistaxis and menorrhagia. The results of the EN-RBD study showed a variable target level of 10% to 20% up to 40% to prevent bleeding. In addition to fresh frozen plasma, Apcc, FIX/FX, and FX concentrates are available to treat FX deficiency. Doses of treatment and schedules differ according to the surgery preparation, prophylaxis, or bleeding. Tranexamic acid is preferred for menorrhagia, nosebleeds, presurgery, and surgery to prevent excessive factor administration (8,9). Our study showed mild FX deficiency with a nucleotide protein change of NM_000504.4:c.785 G>A p. Gly262Asp, and a novel mutation of FX deficiency. Recurrent epistaxis episodes were controlled with a nasal tampon. We plan to administer tranexamic acid for uncontrolled nasal bleeding. In trauma and surgery, fresh frozen plasma and concentrates are the treatment options. Familial non-inflammatory pain syndromes (FEPS) are divided into three groups; only one reported family has TRAP1-related FEPS1 syndrome. The predisposing factors for FEPS3 in children are cold, fatigue, hunger, and the rainy season. Pain mainly occurs in the afternoon or at night; paroxysmal pain lasts for tens of minutes, then relieves, and then starts again after a short interval. Unlike FEPS3(cardiac ion channel disease and congenital myotonia), caused by the SCN11A mutation with pain in the distal limbs, TRAP1-related FEPS1 syndrome has pain symptoms in the upper body with autonomic symptoms. Currently, there is no specific drug for treating familial paroxysmal pain syndromes. The primary treatment is to use analgesics, keep warm, and avoid cold environments. Here, we report the second family with TRAP1-related FEPS1 syndrome. The pain is in the upper body, similar to his family [(10)]. Dimethylglisin dehydrogenase deficiency, as fish odor syndrome, is a likely benign condition with mild muscle involvement [(11)]. We report a novel variant consistent with the clinical situation, a heterozygotic stop gain, NM_013391.3:c.972 G>A p.Trp324 mutation, defined as pathogenic/VUS/likely benign. **Conclusion:** This is the first report of F10, DMGDH novel mutations, and the coexistence of TRPA1 (clinic was compatible) and TNFRSF13B with a need for investigation for immunodeficiencies in a child. In conclusion, this is the first patient with two novel mutations for FX and DMDGH deficiencies, and his family is the second with TRAP1-related FEPS1 syndrome in the World.

Laboratory Values (normal ranges)	Patient	Father	Mother	Sister (7 years old)
PT (s)	21.1 (10.1-12.1)	16.9 (11-14)	13 (11-14)	13.7 (10-12.1)
APTT (s)	32.6 (26-36)	27.8 (27-40)	28.7 (27-40)	26.8 (26-36)
Factor VII (%)	75.3 (65-180)	97.7 (61-127)	97.7 (65-180)	69.4 (61-127)
Factor X (%)	**20.3** (88-94)	**65.9** (70-150)	78.5 (70-150)	**69.5** (88-94)

Gen	Nucleotide Protein Change	Zygosis	dbSNP	Effect	Variant	Classification
F10	NM_000504.4: c.785 G>A p. Gly262Asp	het	-	nonsynonymous-SNV	-	Disease (Dominance, OMIM#) Factor X Deficiency (OR; 227600)
DMGDH	NM_000504.4: c.785 G>A p. Gly262Asp	het	rs139044238	Stop gain	Pathogenic/ VUS/Likely benign	Dimethylglisin dehydrogenase deficiency (OR;605850)
TRPA1	NM_007332.3: c.2564 A>G p.Asn855Ser	het	rs398123010	nonsynonymous-SNV	Pathogenic	Familial episodic pain syndrome (OD;615040)
TNFRSF13B	NM_012452.3: c.198 C>A p. Cys66	het	rs144718007	Stop gain	Pathogenic	Tumor Necrosis Factor Receptor Superfamily Member 13B;604907

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