

Hematology and Oncology Congress

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Accepted Abstracts



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Management of orbital plasmacytoma with concurrent plasma cell leukemia: A case report

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Solitary plasmacytoma of the orbit is very rare, occurring in <1% of plasma cell neoplasm. We present a 49-year-old female with 2-months history of hip pain, associated with visual changes, headache, diplopia and minimal proptosis. Work up revealed anemia, hypercalcemia, azotemia and lytic lesions on skeletal X-ray. Bone marrow aspiration and biopsy was done which confirmed presence of plasma cell neoplasm. Improvement of symptoms was noted within 21 days of chemotherapy with Bortezomib, Melphalan and Dexamethasone. Bortezomib used was not according to the recommended dose (1.3 mg/m²); instead, we utilized the dose available at that time, due to financial constraints. Despite the discrepancy in the dosing of Bortezomib, her symptoms improved as confirmed by cranial MRI, showing decrease orbital mass size. Other laboratory parameters also showed improvement. Patient was discharged stable and advised regular out-patient follow-up for chemotherapy and radiation therapy. Plasma cell neoplasms are a group of disorders associated with proliferation of immunoglobulin-secreting cells derived from B-cells. Involvement of the orbital in plasma cell leukemia (PCL) is very rare and serious condition. In our literature review, most ocular manifestations present in plasma cell neoplasm occur in concurrence with multiple myeloma. There were very rare reports of orbital plasmacytoma occurring simultaneously with PCL. Diagnosis of PCL needs to be made in a timely manner and immediate therapy should be initiated. Strategies to improve long-term survival include incorporation of high-dose therapy with autologous Stem Cell Transplant (SCT). In patients who are not candidates for SCT, a Bortezomib-based induction regimen appears to be the best choice. Our case, with its dramatic presentation and quick resolution of the symptoms after initiation of induction chemotherapy with Bortezomib, Dexamethasone and Melphalan, showcases the importance of prompt recognition of disease and immediate referral to a hematologist for evaluation and management, so as to institute chemotherapy as soon as possible.

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Access to health-breast cancer awareness and screening camps in rural India

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Breast cancer is the most common cancer of urban Indian women and the second most common in rural women. Owing to lack of awareness of the disease in India and in absence of breast cancer screening programs, majority of breast cancers are diagnosed at a relatively advanced stage. Government agencies, NGOs and charity organizations have put great emphasis on improved breast cancer awareness among masses for promotion of early detection, providing comprehensive treatment module, providing support for breast cancer management and for screening and rehabilitation. In rural areas, there is still a lack of good health care and awareness among masses regarding the importance of early breast cancer screening and thus cases of late diagnosis are more prevalent. The other common factors that lead to late diagnosis include delays on the part of womenfolk of rural areas to seek advice for a recognized health problem which is mainly due to financial reasons, social/cultural reasons such as general inhibition of women to see the doctor for breast ailments, general scare of people towards cancer like disorders and a general indifference of women towards their health. In rural areas Illiteracy is widespread and also people are inhibited and not motivated to come to the hospitals for screening/checkup. Considering various factors of cancer incidence rate, to address the most common barriers such as lower cancer literacy, lesser availability and accessibility of proper medical facilities, three Indian states were shortlisted to initiate the project ECHO by organizing breast cancer awareness and screening programs for rural and semi-urban Indian population. In addition to being a CSR approach, project ECHO also increased the cancer literacy amongst the rural population and emphasized on health education, early diagnosis of breast cancers and more public facilities for breast cancer treatments.

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The epidemiology and presenting clinical characteristics of myeloproliferative neoplasms in Malaysia

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Background: The evolution of molecular studies in Myeloproliferative Neoplasms (MPN) has enlightened us the understanding of this complex disease consisting of Polycythemia Vera (PV), Essential Thrombocythemia (ET) and Primary Myelofibrosis (PMF). The epidemiology is well described in the western world but not in Asian countries like Malaysia.

Method: This retrospective national registry of MPN was conducted from year 2009 to 2015 in Malaysia.

Result: A total of 1010 patients were registered over a period of 5 years. The mean age was 54 years with male predominance. The ethnic distribution revealed that Chinese had a relatively high weighted incidence proportion (43.2%), followed by Indian (23.8%), Malay (15.8%) and other ethnic groups (17.2%). The types of MPN reported were 40.4% of ET (n=408), 38.1% of PV (n=385), 9.2% of PMF (n=93), 3.1% of Hypereosinophilic Syndrome (HES) (n=31) and 7.9% of unclassifiable MPN (MPN-U) (n=80). Splenomegaly was only palpable clinically in 32.2% of patients. The positive JAK2 V617F mutation was present in 644 patients with 46.6% in PV, 36.0% in ET, 9.0% in PMF and 7.4% in MPN-U and had significantly lower hemoglobin ($p<0.001$), hematocrit ($p<0.001$) and White Blood Cells (WBC; $p<0.001$) than those with negative mutation. Significant differences in platelet and WBC count were detected in ethnic groups and MPN sub-types. There were more arterial thrombosis events seen in those with JAK2 V617F mutation as compared to venous thrombosis events (23.1% vs. 4.4%). The bleeding rate was only 6.6%. Among the risk factors, previous thrombosis, old age (≥ 60 years) and hypertension were significantly correlated to positive JAK2 V617F mutation. The arterial thrombosis event is associated with higher presenting HB, HCT and PLT while the bleeding event is associated with lower presenting HB, HCT but higher PLT. The presence of JAK2 V617F mutation is associated with higher risk of arterial thrombosis.

Conclusion: Chinese ethnicity is associated with higher rates of MPN. The history of thrombosis, age ≥ 60 years and hypertension are risk factors that can be correlated to JAK2 V617F mutation. This study is instrumental for policy makers to ensure preventive strategies that can be implemented in future.

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Frequencies of human platelet antigens among the Moroccan blood donors

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Background & Aim: The frequency of Human Platelet Antigens (HPA) varies among populations. And so far, typing of HPA systems has not been carried on the Moroccan population. Therefore, the frequencies of these antigens, their risk of alloimmunization and their clinical implications and complications associated with the Moroccan population are unknown. The anti-HPA alloimmunization of the platelets concentrates receivers is frequently manifested by transfusion platelets inefficiency. In addition, the anti-HPA alloimmunization can have serious consequences, such as fetal and Neonatal Alloimmune Thrombocytopenia (NAIT). The study aims in defining allele frequencies and genotypes in the Moroccan population of the five HPA1-5 systems and evaluate the potential risk of platelet alloimmunization in the Moroccan population.

Method: The gene polymorphisms of HPA-1, -2, -3, -4 and -5 were determined by the (PCR-SSP) technique on a sample of 103 Moroccan blood donors for the system HPA-1, 104 for the HPA-2 system, 99 for the HPA-3 system, 106 for the HPA-4 system and 105 blood donors for HPA-5 system.

Result: Alleles frequencies for the HPAs systems are, HPA-1a: 0.709, HPA-2a: 0.683, HPA-3a: 0.798, HPA-4a: 0.99 and HPA-5a: 0.686. The alleles HPA-1b: 0.291, HPA-2b: 0.317, HPA-3b: 0.203, HPA-4b: 0.01 and HPA-5: 0.314. Theoretical genotype frequencies in the descendants at risk of alloimmunization are 0.206 for HPA-1, 0.216 for HPA-2, 0.161 for HPA-3, 0.009 for HPA-4 and 0.215 for HPA-5.

Conclusion: The study of HPAs polymorphism helped us to infer the genetic constitution of the population and to predict the risk of anti-platelet alloimmunization. This will allow anticipating the size and causes of NAIT and the inefficiency of platelets transfusion in our community by the definition of the most possible allo-antigens involved in these phenomena.

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Curcumin sensitizes kidney cancer cells to TRAIL-mediated apoptosis via ROS-JNK- CHOP activation

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The Holy Grail in cancer therapy is to find an agent that is able to eradicate cancerous tumors without harming normal tissues. Much research has focused on fulfilling this goal. The use of TRAIL in cancer therapy has been considered an attractive option to kill different types of tumors with minimal toxicity on normal cells. However, the development of resistance against TRAIL by many tumor cells is the major obstacle that limits TRAIL's therapeutic applications in clinical settings. Curcumin induces apoptotic cell death through caspase dependent and independent mechanisms. It has been found that curcumin at low doses induces apoptosis by the down-regulation of proteasomes and increasing levels of ROS. The sensitization of the cancerous cell leads to activating many transcriptional factors and signaling pathways, resulting in activating apoptotic pathways and ultimately cell death. We investigated whether the combination of curcumin with TRAIL induced synergistic anti-tumor effects. Also, we assessed if the mechanism of cell death was via the induction of apoptosis and was caspase-dependent. Furthermore, the effect of curcumin or curcumin/TRAIL combination on general oxidative stress of cells was tested. As well as this, we examined whether oxidative stress can induce the activation of Mitogen Activated Kinases (MAPK) and Endoplasmic Reticulum (ER) stress. Curcumin was shown to cause a higher degree of sensitization of ACHN cells to TRAIL induced apoptosis than silymarin. The highest degree of synergy was observed at the combination of 25 μ M curcumin with 50 ng/ml TRAIL. Curcumin, by itself or in a combination with TRAIL, did not only cause a cellular inhibition, but they also permanently induced a caspase dependent apoptotic ACHN cell death. The apoptotic cell death process was associated with the activation of both the intrinsic and the extrinsic pathways of apoptosis. Treating ACHN cells with curcumin or curcumin/ TRAIL combination can induce ROS production, therefore, increased the general oxidative stress of the cells. Curcumin induced ROS production was associated with an increase of ER stress and the dysregulation of MAPK pathways. Curcumin, alone or in combination with TRAIL was found to induce the expression of stress associated protein kinases, JNK and P38, while suppressed the expression of the survival kinase ERK. The pretreatment of cells with the free radical scavenger, NAC, abolished the effect of curcumin or curcumin/TRAIL combination on CHOP and MAPK protein expression. The pre-treatment with the JNK inhibitor Sp600125 abolished curcumin-induced CHOP activation.

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Spectrum of bone marrow changes in patients of chronic kidney disease

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Statement of the Problem: Chronic Kidney Disease (CKD) is a health problem present worldwide. CKD is a collective term covering a number of primary disease processes resulting in structural or functional kidney abnormalities or both persisting for at least 3 months. It is related with premature mortality and decreased quality of life. Untreated cases can end up in End Stage Renal Disease (ESRD) finally necessitating dialysis. In Pakistan more than 21 million people are affected by this disease. Almost every patient of advanced CKD suffers from some degree of hematological abnormalities. The purpose of this study is to analyze various hematological manifestations of advanced stage CKD in peripheral blood and Bone Marrow (BM) of the patients, referred to us from the nephrology unit of our tertiary care medical set up.

Method: Patients of both genders and all age groups with CKD stage III, IV and V were included in this study. Patient's histories were recorded. Complete blood counts, bone marrow aspiration and trephine biopsies were done and evaluated microscopically. Mean blood counts of the patients in three groups of CKD were compared. Frequencies of various bone marrow findings in CKD patients were calculated.

Findings: Out of 57 patients, 41 (71.9%) were males while 16 (28%) were females. Mean age was 60 years. There was no statistically significant difference between the mean hemoglobin, mean white cell count and mean platelet count of the patients in three groups of CKD. Reactive changes due to underlying CKD and inflammation were the most frequent finding in the BM of the patients.

Conclusion: Anemia of mild to moderate severity and reactive changes in the BM are the most frequent hematological findings encountered in patients suffering from advanced stage CKD. Since CKD is predominantly a disease of the elderly so it is not rare to find the co-morbidities including plasmacytosis, malignancies and their effects on the BM in the patients of CKD.

Recommendations: We should focus our attention on primary prevention of anemia by strictly adhering to the treatment guidelines, adapting healthy life styles and dietary modifications as early recognition can slow the progression of the disease to ESRD. Public awareness is very essential to halt the advancement of disease.

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Assessment of coagulation profile, fibrinogen, protein C, protein S, antithrombin and vitamin K levels among Sudanese neonates with proven sepsis in Omdurman Maternity Hospital, Sudan

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Background & Aim: Neonatal sepsis represents one of the most common causes of neonatal morbidity and mortality worldwide, non-specific clinical remarks makes earlier diagnosis difficult. Locally in Sudan, in less than five years mortality, sepsis comes on the top of mortality leading causes (14%) in 2012. In 2013, for a less than one-year mortality, sepsis frequency was 658 deaths which is more than seven-fold mortality cases among 1-4 years for the same period. The study aimed to assess the platelet counts, Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT), Thrombin Time (TT), fibrinogen, protein C, protein S, Antithrombin (AT) and vitamin K in Sudanese neonates with sepsis and compare them with healthy neonates in order to study hemostatic alteration among septic neonates.

Method: The study was a prospective case control study conducted in Omdurman Maternity Hospital in the period from June 2013 to April 2015 to a total of 100 samples divided into case and control group (50 for each), blood culture was done routinely for all neonates with suspected sepsis, the first 50 neonates with a positive culture were taken as case group. Platelets were counted by the cell counter (hematology analyzer Sysmex KX-21). PT, APTT, TT, fibrinogen, protein C and protein S were assessed by the clotting procedure by use of semi-automated coagulometer (Stago Start four). AT was assessed spectrophotometrically by the turbidimetric method by use of semi-automated chemistry analyzer (Mindray BA-88A). Vitamin K was assessed by the HPLC (High Performance Liquid Chromatography) Shimadzu 10 ADVP. Data were tabulated and analyzed by the (SPSS 20) via one sample t test (95% confidence interval (P value)).

Result: The gender distribution was 23, 27 and 24, 26 males and females for case and control respectively, in the case group, 17 neonates with early onset sepsis (from birth-7 days) and 33 with late onset (7-28 days). 10 from test group died (20%). Platelets count was decreased, PT and APTT were prolonged, TT was shorted, fibrinogen was increased, PC, PS, AT and vitamin K were decreased (means 60,289 c/mm³, 16.6 sec, 47.8 sec, 18.6 sec, 482.2 mg/dl, 34.4%, 33.4%, 183.9 mg/ml, and 0.86 ng/ml. And 212,030 c/mm³, 13.9 sec, 37.5 sec, 20.6 sec, 393.7 mg/dl, 36.8%, 34.7%, 221.5 mg/ml and 1.23 ng/ml for case and control, respectively).

Conclusion: It has been concluded that platelets count significantly decreased both PT and APTT significantly prolonged, TT significantly shorted, fibrinogen was significantly increased and AT significantly decreased in neonatal sepsis. APTT and protein C showed significant correlation with the outcome, so both can predict early mortality, PT and TT showed significant correlation with early sepsis. Demographic data (gender, gestational age, mode of delivery and Gram stain typing) had no effect on hemostatic parameters.

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Congenital FXIII deficiency in Pakistan

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Introduction & Aim: Factor XIII (FXIII) deficiency is a Rare Bleeding Disorder (RBD) with an incidence of about one in 1-2.5 million and its incidence is higher in populations with consanguineous marriages. The aim of this study was to characterize patients and relatives from sixteen families with suspected FXIII deficiency from Pakistan and to identify the clinical characteristics and underlying mutations.

Method: FXIII deficient patients, enrolled at National Institute of Blood diseases and Bone Marrow Transplantation were included in the study. The patients' medical histories were recorded in a questionnaire. As a first indicator of FXIII deficiency, a 5M urea clot solubility test was used. Plasma FXIII A- and B-subunit antigen levels were determined by ELISA. FXIII activity was measured with an incorporation assay. Sequencing of all exons and intron/exon boundaries of F13A was performed.

Result: We analyzed 16 families in which 32 (females 18 and 14 males) were severe FXIII deficient with FXIII level <1%. 19 first-degree relatives with mean FXIII level 71.19 ± 21.1 are asymptomatic. Each family had a history of consanguineous marriages except one. 50% had significant family history of bleeding. Age at first presentation ranged from birth to 18 years. In these patients we identified 23 mutations which include 19 missense mutations, 2 splicing mutations and 2-nonsense mutations with 7 novel mutations. Bleeding after injury (78%), umbilical cord bleeding (57%), intracranial bleed (43%), hematoma, bruises (39%), abortions and menorrhagia (38%), circumcision (35%) were the main clinical manifestations. Fresh frozen plasma/cryoprecipitate were used in the management of most patients and for prophylaxis in 8 patients with grade III bleeding.

Conclusion: We have analyzed a cohort of 51 individuals from 16 families in which 32 were severe FXIII deficient (homozygous or compound heterozygous) and remaining were FXIII deficient carriers (heterozygous). We identified 23 mutations in these families leading to congenital FXIII deficiency. Diagnosis of FXIII deficiency should be made on time so that prophylaxis can be initiated immediately to prevent fatal bleeding and for genetic counseling.

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Screening for 3.7 and 4.2 deletion mutations in Sudanese patients suspected with alpha thalassemia

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Background & Aim: Alpha-thalassemia is the genetic disorders that have high prevalence in human population around all over the world, characterized by microcytic and hypochromic anemia. The carriers for the disease present with a mild anemia and like these patients in the rural medical centres especially in Sudan can be miss diagnosed as iron deficiency anemia, because of low facilities to do further investigations for differentiation, so those patients could take iron therapy without response which exposes them to the risk of hemochromatosis. The disease was not known in Sudanese and there were no published data. The 3.7 and 4.2 alpha gene deletion mutations are the most common types of the alpha thalassemia mutations in West Africa. This study aimed to screen the participant samples for the 3.7 and 4.2 deletion mutations at the molecular level and to correlate the findings with the CBC parameters in order to find out indicative criteria in routine hematological parameters that can help in diagnosis of alpha thalassemia in Sudanese patients which should be confirmed later by genetic investigations.

Method: This is a cross sectional study targeted 98 patients of highly suspected to have alpha thalassemia based on the microcytosis and hypochromasia of their RBCs, no past history of malaria (*Plasmodium falciparum* infection), normal serum ferritin level and free of any chronic diseases were selected to be screen for the 3.7 and 4.2 alpha gene deletion mutations by single tube multiplex GAP-PCR.

Result: The revealed of these 98 patients 7 were carriers for the 3.7 deletion mutation in the alpha globin genes and only one patient was 3.7 homozygous deletion mutation and all samples were negative for the 4.2 deletion mutation. The study revealed the 3.7 deletion mutation was found in Sudanese tribes originated from West Africa which are Four, Hawsa and Rezagat Tribes. The results showed the carrier patients of the 3.7 deletion mutation RBCs and HCT were significantly increased P-value <0.05, the RBCs were $7.23 \pm 0.78 \times 10^{12}/L$ in the adult male and $7.21 \pm 0.67 \times 10^{12}/L$ in adult female while in the children were $5.07 \pm 0.87 \times 10^{12}/L$. The MCV and MCH were clearly decreased, but the MCHC slightly decreased. The Hb level revealed mild decrease without statistical significance P-value >0.05 in the adult males were 11.7 ± 0.57 g/dl and 11.25 ± 0.64 g/dl while in the children were 11.6 ± 2.95 g/dl. The ferritin level was normal and the RDW CV clearly increased. The quantitative Hb electrophoresis was normal in addition to the presence of many target cells in peripheral picture and no one of these carriers presence with clinical manifestations indicating for anemia, but the homozygous 3.7 deletion mutation patient was anemic and his basic hematological parameters were as follows RBCs $1.38 \times 10^{12}/L$, Hb 4.99 g/dl, HCT 11%, MCV 79.7 fl, MCH 35.5 pg, MCHC 44.5 g/dl, RDW CV 17.7% and the ferritin level were 1,807 mg/dl and this elevation due to the blood transfusion.

Conclusion: The study confirmed the presence of the alpha thalassemia in Sudanese population for the type 3.7 deletion mutation in the tribes that belong to the western reside of the Sudan and which is basically originated from the West Africa where the disease was already known and this transmission due to the migration.

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MiRNAs as potential biomarkers for human cancers

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Cancer is a fatal human disease capable of spreading throughout the body extremely fast. As of now, early diagnosis of cancer is the most effective method to prevent cancer development and devise the most efficient and effective treatments. Therefore, early diagnosis is critical to achieving higher survival rates for patients. Many traditional diagnostic methods for cancer are still inadequate for early, convenient, accurate and non-invasive diagnosis. Specifically, Glioblastoma Multiform (GBM) is the most common primary malignant brain tumor, which the five-year survival rate is only 0.05% to 4.7%. Thus, the need to find more effective biomarkers is paramount in insuring early discovery and effective treatments for patients. Recently, there have been reports that indicate the possibility of microRNAs (miRNAs) as potential biomarkers for cancers. In this study, we attempt to answer two questions, could the exosomal miR-21 be used as a universal biomarker for cancer? We used the meta-analysis method to evaluate ten studies involving 318 patients and 215 healthy controls. In all, the analysis covered 10 types of cancers. In addition, we also examined and evaluated many other common issues with biomarkers, including cutoff points, internal controls and detection methods. This initial meta-analysis indicates that the exosomal miR-21 from body fluids has a strong potential to be used as a universal biomarker to identify cancers. As a continuation from the first question, we also consider, could we find any miRNA biomarkers specifically for the diagnosis of GBM? In order to predict GBM related miRNAs and their targets, we used a bioinformatics algorithm-the Relative R-Squared Method (RRSM)-to analyze the miRNA and mRNA expression profiles and motif complementary sequences. Then, real-time PCR was used to confirm the predicted miRNA candidates in human GBM tissues and cancer cell lines. Furthermore, we used bioinformatics methods and molecular techniques to analyze the related gene expression and regulatory pathways. The results of these studies indicate that variations in miRNA expression have been observed in cancer tissues and biological fluids. The fact that some highly stable miRNAs circulate in the blood and Cerebrospinal Fluid (CSF) of both healthy individuals and diagnosed patients has raised the possibility that miRNAs may serve as novel diagnostic markers. Also, increased understanding of the interaction between miRNAs and mRNAs involved in GBM progression may lead to the discovery of predictive biomarkers, some of which are clinically relevant for targeted therapy and predicting prognosis. However, as this field is in the beginning, some different studies have conflicting results. In order to make more progress in the field, there is still a need to combine different advanced techniques, such as bioinformatics methods and other molecular and cellular techniques.

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