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ASSESSMENT OF THE ROLE OF ALPHALIPOIC ACID IN PREVENTION OF CHEMOTHERAPY INDUCED PERIPHERAL NEUROPATHY

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Introduction: Chemotherapy induced peripheral neuropathy (CIPN) is a common dose limiting side effect of many chemotherapeutic agents. It is considered the second most common acute side effect after hematologic toxicity .It affects ~ 30 % of patients receiving chemotherapy. Causes of CIPN in not exactly known and well understood. However treatments that are used to treat this condition have been found to be ineffective and have many undesirable side effects. Alpha Lipoic acid (ALA) is a physiological anti-oxidant that has been found effective in diabetic neuropathy, but hasn't been investigated thoroughly for the use in CIPN.

Material and Methods: This is a prospective clinical trial conducted at Clinical Oncology Department in Suez Canal University Hospital, where one hundred patients received chemotherapy causing peripheral neuropathy were included in our study; they were divided into two equal groups, study and control group. Study group received ALA 6oo mg three times daily for 12 weeks from the start of chemotherapy, control group received no treatment. Assessment was done before starting treatment and after each cycle by using FACT/GOG-Ntx score.

Results: A total of 100 patients were included in this study, 83% were females and 17% were males. 62% of patients had breast cancer and 17 % had GIT cancer.65% of patients received single neurotoxic agent causing peripheral neuropathy while 35% received combined agent causing peripheral neuropathy. 96% patients completed the study (12 weeks). There was a statistically significant difference between the ALA and the control groups for FACT/GOG-Ntx scores.

Conclusions: CIPN is one of the most severe adverse effects of chemotherapy; with a significant impact on the Quality of life .This strategy of oral ALA administration was effective at preventing neurotoxicity. LA as a neuroprotective agent has shown some promise.

Future studies to explore ALA as a neuroprotective agent should take heed of the barriers confronted in this study.

Keywords: Alpha lipoic acid, Chemotherapy-induced peripheral neuropathy, Taxol

HYPOFRACTIONATED RADIATION THERAPY IN THE MANAGEMENT OF BREAST CANCER: ANALYSIS OF 350 PATIENTS TREATED IN THE NATIONAL INSTITUTE OF ONCOLOGY OF RABAT, MOROCCO.

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Purpose: Radiation therapy constitutes an important arm in the management of breast cancer, and the hypofractionated regimen represents a good alternative, it has demonstrated its effectiveness in local control, with a tolerable toxicity.

The aim of our study is to relate our experience on hypofractionated radiotherapy in the management of breast cancer at the National Institute of Oncology (NIO).

Material and methods: This is a retrospective study including all women followed in radiotherapy department of NIO for invasive breast cancer (IBC) during 2010, and treated with hypofractionated regimen.

We have excluded from the study, patients irradiated with conventional regimen, and non-irradiated patients.

The Statistical analysis was done by SPSS 20.0.

Results: Between January and December 2010, 350 patients with IBC and treated with hypofractionated regimen were reviewed. The average age was 48.08 years ($\pm$ 10.23), 43.6% were menopausal. 51.3% of tumors were located in the right breast, 48.1% in the left breast, and 0.6% were bilateral. Ductal carcinoma was predominant (91.7%), followed by lobular carcinoma (4.8%). SBR

grade 2 was predominantly (52.6%), hormone receptor positive (70.8%), and HER-2 over expression (19%).

Regarding treatment, 67.7% received radical mastectomy, and 32.3% conservative surgery. 57.8% of patients were T2, and 65.1% had positive lymph nodes. 88.1% of patients received adjuvant chemotherapy. Adjuvant radiation therapy was performed in 15 fractions for a total dose of 42 Gy (2.8 Gy per fraction) in all patients, with a boost on the tumor bed in 31.7% of patients. The average length of treatment was 25.39 days ($\pm$ 7.02).

Regarding toxicity, lymphedema of upper limb was observed in 25.42% of patients, hyper-pigmentation in 23%, fibrosis in 15,7%, and telangiectasia in 12.3%.

With median follow-up time of 59.4 months, locoregional recurrence-free survival of 94.3% at 5years, and overall survival was 87%.

Conclusion: Our results confirm that adjuvant hypofractionated radiotherapy in breast cancer allow a local control comparable to the standard pattern, with good clinical tolerance.

RESULTS OF THE STUDY "OPPORTUNITIES FOR SURGICAL TREATMENT OF PATIENTS WITH NEWLY DIAGNOSED ADVANCED BREAST CANCER" PERFOMED BY RUSSIANASSOCIATION OF ONCOMAMMOLOGISTS (RAOM).

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Introduction: Every tenth breast cancer patient has distant metastases detected at diagnosis. To date, there is no clear understanding of the importance of cytoreductive surgery in the treatment of disseminated BC. The most debatable issue is the eligibility of patients for this treatment, since it is unclear what plays a decisive role in the selection process: localization of metastases, sensitivity to systemic treatment, tumor biological characteristics, or a combination of these factors.

Material and methods: This study covers the analysis of treatment outcomes in 608 patients with newly diagnosed advanced breast cancer (newly diagnosed ABC) between 1990 and 2015 as reported by 5 health care institutions. The mean follow-up period was 56 months. The study and control groups were recruited retrospectively. The study group comprised patients with newly diagnosed ABC who underwent primary tumor surgery were receiving systemic anticancer therapy. Patients in the control group were receiving only systemic anticancer therapy. The groups were composed by pairwise matching, i. e. each patient in the study group was matched with a control patient of similar prognostic characteristics. Study groups were well balanced by the main prognostic factors. Data were analysed using univariate and multivariate correlation techniques. The Kaplan Meier method was used to calculate the patients' survival; 3- and 5- year survival rates were assessed. Only deaths attributable to BC were considered. The log-rank test was used to compare the survival rates between the groups; relative risks of death were calculated using the Cox proportional hazards model, which allows to predict the risk of an event occurring in a certain time period in view of the contribution of each independent prognostic factor and excluding the correlation between such factors.

Results: Removal of primary tumor in newly diagnosed ABC was found to increase the average life expectancy from 23 up to 35 months (p < 0.01). The 3-year overall survival was reported to increase from 47% to 65%, with the 5-year survival increasing from 21% to 45% (p = 0.001). The most impressive effect of surgical treatment is observed in patients with bone metastases, one or two metastatic lesions in one organ, positive response to systemic treatment, high expression of estrogen/progesterone receptors, and in cases where it is possible to achieve clean resection margins.The independent prognostic factors found to significantly increase the risk of death in patients with newly diagnosed ABC are multiple lesions (> three lesions in one organ), visceral metastases (in particular liver metastases) or involvement of multiple organs and systems, absence of response to systemic therapy, absence of ER/PR expression, childbearing age, unoperated primary tumor, cancer cells in resection margins in postoperative patients.

Conclusions: Removal of primary tumor is effective treatment for selective patients with newly diagnosed ABC.

EVALUATION OF THE ROLE OF 1% METHYLENE BLUE DYE IN SENTINEL LYMPH NODE BIOPSY POST-NEOADJUVANT CHEMOTHERAPY

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Abstract

Background: Surgical management of the axilla in breast cancer has evolved greatly in the last 20 years. SLNB which was first investigated in the early 1990s, has replaced routine axillary lymph node dissection (ALND) with its associated greater morbidity in early stage node negative patients. However, the role and timing of SLNB, management of the axilla, and technical aspects of the procedure in patients treated with neo-adjuvant chemotherapy (NACT) are matters of controversy. Although data on SLNB and NACT are accumulating, the value of SLNB in relation to long-term outcomes remains to be seen.

Objectives: Evaluation of the use of 1% Methylene Blue die as a single agent tracer for the detection of sentinel lymph node (SLN) after neoadjuvant chemotherapy for locally advanced breast cancer (LABC) with the calculation of the identification rate and false negative rates (FNRs), compared to other single tracers used in SLN in LABC.

Methods: Thirty-one patients with **cT3-4(a-c) cN1-3, M0** breast cancer post NACT who have shown downstaging of their nodal status (**N0**) were injected 1% methylene blue, retroarelarly or perituromaly followed by axillary lymph node dissection and results compared to detect FNR, and identification rate.

Results: The median age of the patients was 48 with 83.8% of the patients above the age of 40. Identification rate was found to be 83%, a false negative rate of 11.5% was detected. FNRs were found to be less when more than 3 SLNs were dissected, with no statistically significant difference of FNRs related to the initial nodal state of the disease.

Conclusion: The use of 1% MB in post NACT showed a comparable identification rate and FNRs to other single tracer techniques, yet all single tracer techniques are lesser than ideal in this group of patients.

Keywords: Sentinel Lymph Node Biopsy, identification rate, False Negative Rates, Locally Advanced Breast Cancer

ASSESSMENT OF PATHOLOGICAL RESPONSE TO PREOPERATIVE THERAPY IN RELATION TO MOLECULAR SUBTYPE IN BREAST CANCER PATIENTS

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Abstract

Introduction: Preoperative therapy in breast cancer has many established short and long term advantages with pathological complete response (pCR) being the most important endpoint. Correlating response to molecular subtypes may further identify potential candidates for preoperative therapy and consequently allow for better treatment tailoring.

Materials and methods: This retrospective study reviewed electronic medical records of 110 female patients with histologically diagnosed breast cancer who received preoperative chemotherapy $\pm$ targeted therapy during the period of April 2007 to March 2014. The records of99patients were analyzed in the study with a total of 104 tumors. Seventy nine patients received chemotherapy alone and 20 patients received chemotherapy and anti HER2 targeted therapy. Patients were treated at the university hospital of Saarland in Homburg, Germany.

Results: The study included 38.8% triple negative tumors, 23.3% luminal B HER2-, 17.5% luminal A, 10.7% HER2 overexpression and 9.7% luminal B HER2+ tumors. Twenty six percent of tumors were initially T3-T4 versus 8% T3-T4 tumors postoperatively, and 68.3%were node positive versus 39.8% node positive postoperatively. Downstaging was observed in 76.5% of tumors versus 23.5% that were either stable or progressed. Pathological complete response was achieved in 29.3% of patients. Molecular subtypes were found to be of statistical significance when correlated to pCRrates(P value 0.007). Only one luminal A tumor out of 18 (i.e. 5.6%) achieved pCR whereas 6 out of 10 tumors (60%) with HER2 overexpression showed pCR.Luminal B HER2+, triple negative, and luminal B HER2- subtypes achieved pCR in 50%, 35.6%, and 16.7% respectively.

Conclusion: preoperative therapy achieved pCRin 29.3% of patients. Molecular subtypes impact the probability of achieving pCR with HER2 overexpression subtype achieving highest rates followed by Luminal B HER2+ then triple negative subtypes. Luminal A subtype was the least sensitive to preoperative chemotherapy.

Keywords: preoperative therapy- breast cancer-molecular subtype-pathological complete response

CHARACTERISATION OF GYNECOLOGICAL CANCER NEO-ANTIGENS AND THEIR RECOGNITION BY TUMOUR INFILTRATING LYMPHOCYTES

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Introduction: Gynaecological malignancies are the cause of death among 250000 women each year. Some patients have few treatment options leading to poor prognosis and due to that novel treatment strategies are needed. The presence of T cells is associated with improved progression-free

survival. This suggests that immunotherapies are likely to benefit patients. Adaptive cell transfer using TILs has shown promising results in melanoma and renal cell carcinoma. The hypothesis of this project is that tumour reactive TILs recognise neo-antigens could be exploited for immunotherapy. The main aims include isolation and expansion and characterisation of the immune phenotype of TILs in gynaecological tumours and compare them with matched peripheral blood samples. Additionally, evaluate the functional activity of TIL population using cytokine release assay byco-culturing with the autologous tumour.Finally, to identify tumour neo-antigens using whole exome sequencing and confirm the finding by synthesising and assessing the peptides.

Materials and methods: Solid tumour biopsies were disaggregated into single cell suspension using GentleMACSdissociation, and cells mitogenically stimulated with CD3/anti-CD28 T cell expander beads and IL-2. TILs were expanded in for 21 days and characterised phenotypically before and after the expansion. The functional activity was determined by co-culturing expanded TILs against autologous tumour cells and measuring IFN-γ and IL-2 production.

Results: Clinical specimens were collected from 58 patients with breast cancer and 9 patients with endometrial cancer. After tumour digestions surface markers were determined using flow cytometry. TILs were successfully expanded from 40/58 (68%) of the breast and from 6/9 (66%) of the endometrial specimens. The phenotype characteristic of TILs after expansion showed a significant increase in OX40 and CD69markers and a decrease in PD-1 marker compare to day 0. Recognition of autologous tumour was observed in 43% of the expanded TILs as detected by the production of IFN-γ.

Conclusion: TILs can be expanded from gynaecological tumours and the expanded TILs maintain autologous tumour recognition *in vitro*. The future stage is to focus on testing the neoantigens identified form the sequencing with theautologous TILs for positive responses. These could then potentially be used as a therapeutic approach.

FATTY ACID SYNTHASE, HER2/NEU, AND E2F1 AS PROGNOSTIC MARKERS OF PROGRESSION IN NON-MUSCLE INVASIVE BLADDER CANCER

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Abstract

Introduction: Non-muscle-invasive bladder cancer (NMIBC) is a heterogeneous disease which has unpredictable risk of stage progression to muscle-invasive bladder cancer (MIBC) and could be managed either conservatively by trans-urethral resection of bladder tumor (TURBT) or more aggressively by radical cystectomy. The selection of patients who may benefit from early radical intervention is a challenge. Molecular tumor markers are greatly needed to improve the risk stratification and hence help to personalize treatment options. To define the useful prognostic markers for progression, we analyzed the immunohistochemical expression of Fatty Acid Synthase (FASN), Her2/neu, and E2F1 in 60 cases of NMIBC.

Patients and Methods: The immunohistochemical expression of FASN, Her2/neu, and E2F1 was assessed in 60 patients with NMIBC who underwent TURBT and adjuvant intravesical bacillus-Calmette-Guérin (BCG). Their predicting role for tumor recurrence, progression, recurrence-free survival (RFS) and progression-free survival (PFS) was analyzed.

Results: High FASN expression was observed in 56.7% (34/60) of NMIBC cases, and FASN expression was significantly associated with the tumor size, histologic grade, and tumor stage (p= 0.003, p< 0.001, p<0.0001 respectively). Positive Her2/neu was noted in 18.3% (11/60) of the cases, and its expression was significantly associated with the tumor size, histologic grade, and tumor stage (p= 0.001, p= 0.002, p=0.011 respectively). High E2F1 expression was detected in 40% (24/60) of the cases, and it was associated with tumor size, histologic grade, and tumor stage (p < 0.001 for each). Analysis of follow-up period revealed that NMIBC with high FASN, positive Her2/neu, and high E2F1 expression exhibited a potent relation with tumor progression, shorter RFS, and poor PFS.

Conclusion: High FASN, Her2/neu and E2F1 are considered as adverse prognostic factors of tumor recurrence and progression in NMIBC patients and these patients should be followed carefully. Therefore, we suggest that FASN, Her2/neu and E2F1 should be considered and evaluated during the selection of the appropriate management strategy for NMIBC patients

INTRAOPERATIVE RADIOTHERAPY PROVIDES ADVANTAGE IN SHORT-TERM OUTCOMES FOR PATIENTS WITH LOCAL BREAST CANCER.

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Introduction: the combination therapy of localized breast cancer (LBC) with external beam radiation therapy

(EBRT) is accompanied by a number of particular problems and needed more time to treat patients. Goals, to demonstrate that intraoperative radiotherapy (IORT) would be modest compared to the external beam radiation therapy (EBRT).

Methods: We performed retrospective analysis of short-term outcomes of 100 breast cancer patients, who underwent breast-conserving surgery(BS) combined with radiotherapy (RT) (2017). patients are in the under 62 ± 3, the tumor size was 2.5 cm with luminal biological subtype of tumor. The Intraoperative radiotherapy (IORT) was carried out using «INTRABEAM PRS 500», the external beam radiation therapy (EBRT) was conducted with the help of «Electra Synergy».

Results: The patients were divided into 2 groups. The first group consists of 42 breast cancer patients with stage I and 8 breast cancer patients with stage II. The BS was combined with the IORT on «INTRABEAM PRS500». A single dose in first group ranged from 12 to 20 gy. The overall time of BS + IORT was 70-120 minutes. At the first group the post radiotherapy skin is not revealed. The average time of the treatment is approximately 35 ± 4 days. The second group of patients (41 breast cancer patients with stage I, 9 patients with stage II) were followed by external beam radiotherapy on «Electra Synergy» after the BS during 3-5 weeks after the surgery. The single tumor dose was 2,5 gy., Time of EBRT ranged from 50 to 80 minutes. The post-operative drawbacks connected with radiotherapy are epidermitis- 88%, dermic ulcers – 0.1%. The average time of the treatment is approximately 35 ± 4 days.

Conclusions: The analysis of the results showed that the using of IORT slightly increases the time of the operation, completely eliminates the possibility of skin manifestations of radiation therapy. Treatment regimen using IORT has several advantages and can be considered as an alternative treatment option in a strictly selected category of patients with LBC.

BREAST CANCER DURING PREGNANCY: RETROSPECTIVE STUDY AND LITERATURE REVIEW

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Abstract

Introduction: Breast cancer is the most common type of cancer diagnosed during pregnancy, frequently it is diagnosed in advanced stage, and it needs a special treatment.

Material and Methods: We conducted a retrospective study to evaluate the efficacy and the safety of chemotherapy used during pregnancy in 19 women and to appreciate maternal and fetal prognosis.

Results: 15 women received chemotherapy during pregnancy,the prognosis was quite good for women and their child,two women died due to progression of the disease,and two newborn died, the both have been exposed to chemotherapy and were prematurely delivered.

Conclusions: Treatment of breast cancer during pregnancy is difficult for doctors, it requires a multidisciplinary approach, collaboration between the pediatrician, the gynecologist and oncologist, treatment decisions must include the wish of the patient and her family.

NEUTROPHIL-TO-LYMPHOCYTE RATIO AND PLATELET-TO-LYMPHOCYTE RATIO AS PROGNOSTIC MARKERS IN PATIENTS WITH INVASIVE DUCTAL BREAST CARCINOMA:A RETROSPECTIVE COMPARATIVE STUDY

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Abstract

Background: The pretreatment neutrophil/lymphocyte ratio (NLR) and platelet/ lymphocyte ratio (PLR), derived from differential white blood cell counts, has been previously associated with poor prognosis in breast cancer. Growing evidence nowadays suggests that oncogenesis is associated with systemic inflammation. The present study investigated white blood cell and platelet indices, whose values change during the inflammatory response, in women with invasive ductal breast carcinoma.

Aim: To compare the overall survival rates(OS) and disease free survival (DFS) of patients having invasive ductal breast carcinoma in relation neutrophil/lymphocyte ratio (NLR) and platelet/ lymphocyte ratio (PLR)at the time of diagnosis.

Subjects and Methods: A retrospective analysis of prospectively collected data conducted on 106 patients, the number of patients divided by high NLR/PLR and low NLR/PLR ratio into two groups. The median follow-up time was 34 months (range 17 –72 months).

Results: The mean lymphocyte, neutrophil and platelet counts were 1.2, 4 and 231.3, respectively. The mean PLR and NLR were 159 and 1.8, respectively. The univariate analysis revealed that elevated NLR and PLR (P-value =0.004 and P-value =0.001, respectively) were linked with poor OS and DFS. As regard multivariate analysis showed also association between Tumor size (P-value =0.002), Tumor grade (P-value =0.001) with reduced OS and DFS.

Conclusion: NLR and PLR at the time of diagnosis are useful parameters for newly diagnosed invasive ductal breast cancer patients and can affect OS and DFS. However, more studies are required to confirm the findings of the current study, which may allow making strategy of prognostic factors for patients with breast cancer to plan treatment options in the future.

Keywords: invasive ductal breast carcinoma, neutrophil/lymphocyte ratio, platelet/ lymphocyte ratio, survival.

BRCA1 AND BRCA2 GERMLINE MUTATIONS IN UNSELECTED YOUNG BREAST CANCER PATIENTS FROM MOROCCO

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Introduction:In Morocco, breast cancer is described as young women disease. The median age for breast cancer diagnosis is a decade younger and the frequency among young women is significantly higher compared to Western countries. This higher frequency suggests a strong contribution of BRCA1/2 mutations. However, no study has been designed to test this hypothesis and available data are inconsistent and non-conclusive.

Material and Methods: Germline mutations in the BRCA1 and BRCA2 genes were analyzed by nextgeneration sequencing (NGS) in a group of 33 patients diagnosed with breast cancer at the age 40 or younger, regardless of the presence of a family history of breast and/or ovarian cancer.

Results: Overall, 5 of 33 patients (15.1%) carried a deleterious BRCA mutation.Three mutations were identified in BRCA1 (9%) and two mutations in BRCA2 (6%). These are three frameshift mutations (c.798_799delTT, c.2125_2126insA, c.5116_5119delAATA), one missense (c.116G> A) and one nonsense mutation (c.289G> T). Among these mutations, c.5116_5119delAATA has been considered as the first non-Jewish founder mutation identified in North Africa and was found in a single patient. In addition to these deleterious mutations, two variants of uncertain significance were identified in BRCA2 (c.4090A> G; c.6322C> T). The great majority of mutations carriers (80%) did not have a family history and the presence of this factor influenced only slightly the mutation rate (16.7%).

Conclusion: Our results suggest that BRCA alterations alone do not explain the higher frequency of breast cancer in Moroccan young women. Besides, young age alone seems to be a sufficient criterion to indicate a systematic genetic screening and that the age limit of ≤40 years is an adequate threshold

SCLEROSING STROMAL TUMOR OF THE OVARY: CAN NOVEL MR TECHNIQUES NAMELY MR PERFUSION HELP IN ITS PREOPERATIVE DIAGNOSIS? A CASE REPORT

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Introduction: Sclerosing stromal tumors of the ovary (SST) are benign tumors which are always misdiagnosed as malignancy. This report aims atemphasizing the added role of MR perfusion weighted imaging(MR PWI) in preoperative identification of these tumors to guide the surgical decision and avoid unnecessary radical surgeries in women aiming to preserve fertility.

Materials and Methods:A 30-year-old virgin female underwent MR PWI using rapid Dynamic Contrast enhanced T1-weighted gradient-echo. Regions of interest (ROIs) were drawn in the solid part of the ovarian tumor and on the outer myometrium. PWI was analyzed using descriptive, Time Signal intensity curve and semiquantative parameters (Relative Enhancement (RELENH), Maximum Enhancement (MAXENH), Maximum Relative Enhancement (MAXRELENH), Time to Peak (TTP), and Wash in Rate (WASHIN) and Wash out Rate (WASHOUT). Time intensity curve and semiquantative parameters results were correlated to the histopathological result.

Results: The solid part of the tumor show curve type 3 enhancement pattern. It showed higher maximum enhancement (MAXENH) and maximum relative enhancement (MAXRELENH) than the external myometrium with shorter time to peak(TTP),higher wash in (WIR)but the wash out rate (WOR)of the solid part was (WOR = 4.76) which is less than the suggested cut-off value of WOR for benignity; (WOR= 6.03) suggesting the benignity of the lesion.

Conclusion:MR PWI is useful in preoperative depiction of ovarian SST.Wash out rate is postulated that it represents only the permeability characteristic of the capillary wall with no relation to the microvascular density. So we can depend upon WOR cutoff value to exclude the false positive cases with high diagnostic accuracy (up to 85%).

FREQUENCY OF GERMLINE MUTATIONS BRCA1 AND BRCA2 IN OVARIAN CANCER PATIENTS AND THEIR EFFECT ON TREATMENT OUTCOME

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Abstract

Introduction: The frequency of BRCA1 & 2 mutations in ovarian cancer patients is unclear. Aim of this work is assessment of the prevalence of BRCA1/2 in ovarian cancer patients and their effect on treatment outcome.

Materials and methods: 104 patients with epithelial ovarian cancer were recruited and analyzed for sequencing of all translated exons and immediately adjacent intronic regions of BRCA1/2 genes. Responses to multiple lines of chemotherapy and effect of BRCA gene mutation on progression free survival (PFS), and overall survival (OS) were assessed.

Results: Pathogenic BRCA1/2 mutations were found in 21.15% of patients. BRCA1 represented 68.2% of the mutations. Age at diagnosis and family history of cancer were strong predictor of the presence of a pathogenic BRCA1/2 mutation. 3/4 of patients with pathogenic BRCA mutation were diagnosed at an advanced stage. Women with high grade serous tumors had higher incidence of pathogenic mutation P= (0.07).

Response rate to neoadjuvant chemotherapy was 93.9%. All patients underwent surgery which was optimal in (73.1%). Adjuvant chemotherapy was received in 85.6% of patients.

After primary treatment 45.2% of patients relapsed, BRCA mutation carriers experienced visceral metastasis more often compared to non carriers P=0.01. BRCA mutation status didn't affect platinum sensitivity at time of relapse.

Patients carrying pathogenic BRCA1/2 mutation had a longer median PFS of 42.43 ms (95%CI 32.04-52.83) compared to 22.24 ms (95% CI 14.83-29.58) for non carriers, P=0.08. Patients carrying a mutation had a median OS of 64.32 ms (95%CI 38.09-90.06) compared to 56.63ms (95%CI 50.05-63.21) for non carriers, P=0.04.

In multivariate analysis early stage at diagnosis and optimal debulking were the only independent predictors of better PFS and OS.

Conclusion: BRCA mutation status has influence on survival in ovarian cancer patients and can be an additional stratifying factor in clinical trials. Mutation status may be able to contribute to decision making and systemic therapy selection.

PROGNOSTIC IMPACT OF EXPRESSION OF FORKHEAD BOXP3 (FOXP3) AND CYCLOOXYGENASE-2 (COX2) IN BREAST CANCER: A SINGLE-INSTITUTIONAL STUDY

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BACKGROUND: FOXP3 is a forkhead box transcription factor that plays an important role in the development and function of (Tregs).

Besides, COX-2 is widely expressed and profoundly linked to poor prognosis in a variety of malignant tumors. Therefore, COX-2 might be a potential prognostic factor to predict the survival in patients with cancers. This retrospective study was conducted on archival cases of Egyptian female patients newly diagnosed with breast cancer in Menoufia University Hospitals, Egypt during the period between January 2010 and March 2015.

METHODS: Two sections, 4 μm in thickness, from each case were stainedfor (FOXP3) and (COX2). The method used for immunostaining was streptavidin-biotinamplified system.

RESULTS: Sixty-six archival specimens.

I.   All positive cases showed cytoplasmic pattern of expression. (95.5%) showed positive expression of FOXP3, while 3 (4.5%) showed negative expression. All positive lymphocytes showed nuclear pattern of expression. Five (7.8%) were of score 0, 18 (28.1%) were of score 1+, 19 (29.7%) were of score 2+ and 22 (34.4%) were of score 3+. Six (10.3%) were of score 0, 12 (20.7%) cases were of score 1+, 16 (27.6%) cases were of score 2+ and 24 (41.4%) cases were of score 3+.

II.   A relationship was found between increasing H. scores of FOXP3 expression in peri-tumoral lymphocytes and younger age group of the cases of BC (p=0.010).Assessment of IHC expression of COX2. All positive cases showed cytoplasmic pattern of expression. Twenty-seven cases out of 66 (40.9%) showed positive expression of COX2, while 39 cases (59.1%) showed negative expression. A significant association was found between higher H. scores of COX2 expression and negative PR expression in tumor cells of BC cases (p=0.025).

Survival Analysis: Univariate analysis revealed improved OS in high infiltration by peritumoral infiltrating lymphocytes and high FOXP3 positive intratumoral lymphocytes scores (p=0.018 and 0.014 respectively).

Cox regression analysis revealed that FOXP3 positive intratumoral lymphocytes score was independent prognostic factors affecting patients' OS (p= 0.043).

Keywords: breast cancer, FOXP3. COX2

Conclusion: High FOXP3 expression in peritumoral and intratumoral infiltrating lymphocytes is considered as a good independent prognostic factor in the studied population .

ENHANCED PROPHYLACTIC AND THERAPEUTIC POTENTIAL OF CURCUMIN AND TAURINE ON HEPATOCELLULAR CARCINOMA.

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Introduction: Hepatocellular carcinoma is a cancer with high mortality. HCC treatment including surgical and loco regional treatment. Recent studies focus on the role of immune system thus immunotherapy represent novel approach to treat HCC because of it is immunological characteristic. Curcumin and taurine have been used to participate in HCC through activation of immune system.

Materials and Methods: Mononuclear leukocytes and serum were obtained from HCC patients (n= 15) baseline then treated oral with curcumin and taurine after three weeks, and six weeks and healthy control (n= 30). IL-10, IL-6, IL-8, TNF-α, IFN-γ and TGF-α by ELISA technique and CD4+%, CD8+%, CD4+CD25+%, and CD8+CD25+% by flow cytometery were determined.

Results: Results revealed that after treatment for IL-10 there was significant decrease (P< 0.001), but for IFN-γ there was significant increase (P < 0.001). On contrast, level of IL-6, IL-8, TNF-α, and TGF-α there were no significant difference (P> 0.05). For CD4+%, CD8+%, CD4+CD25+%, and CD8+CD25+% there were significant differences (P < 0.0001, P< 0.001, P< 0.01, and P< 0.00001 respectively) compared to baseline.

Conclusion: curcumin and taurine have a protective role against hepatocarcinogenesis.

Keywords: HCC, curcumin, taurine, and cytokines.

TAMOXIFEN WITH OR WITHOUT OVARIAN FUNCTION SUPPRESSION AS ADJUVANT HORMONAL TREATMENT IN PREMENOPAUSAL BREAST CANCER PATIENTS

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Introduction: Adjuvant endocrine therapy is an integral component of care for endocrine dependant breast cancer.Adjuvant endocrine therapy with tamoxifen had been recommended for premenopausal women with hormonereceptor positive breast cancer duringthepast15 years.international consensus guidelines for breast cancer management recommending that ovarian ablation or suppression not be added routinely to adjuvant therapy in premenopausal women

Materials and Methods: This is a retrospective study Included 285 patients evaluating the disease free survival, overallsurvival and toxicity profile, the patients were divided into two groups: group I included 173 patients received Tamoxifen alone and group II included 112 patients received Tamoxifen with ovarian suppression (LHRH) agonists.Data collected from files of patients that were treated from Breast cancer in Ain shams university and Nasser Institute in period from 2012 till 2015.

Results: By the end of data collection 214 patients were still alive.The median follow up period was 33.0 months. The median OS was 49.0 months and the cumulative OS at 1 year and 2 years, were 95.4% and 88.2% respectively.Overall survival at 2 years was 89.8% among those assigned to tamoxifen alone and 85.9%among patients assigned to tamoxifen plus ovarian suppression(P=0.150).Disease free survival at 30 months was 63.1% among those assigned to tamoxifen alone and 69.3%among patients assigned to tamoxifen plus ovarian suppression (P=0.838).Treatment related adverse events were mild and manageable(P value=0.002).

Conclusion: Our study results state regarding the comparison between Tamoxifen alone and Tamoxifen with ovarian suppression (LHRH) agonists: There is no significant statistical difference between the twogroups regarding disease free survival, overall survival &toxicity profile in premenopausal breast cancer patient

CLINICO-PATHOLOGICAL VARIABLES AFFECTING UTERINE CARCINOSARCOMA, EGYPTIAN EXPERIENCE

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Abstract

Introduction: Uterine carcinosarcomas or malignant mixed Müllerian tumors (MMT) are rare tumors, accounting for less than 5 % of uterine cancers. MMT comprised of carcinomatous and sarcomatous elements. Recent evidence showed that MMT are undifferentiated carcinomas rather than uterine sarcoma, so they are considered a high-risk variant of endometrial adenocarcinoma. The most important prognostic factor affecting outcome of MMT is the stage and other risk factors include age, depth of myometrial invasion, lymphovascular space invasion and the presence of gross residual disease.

Aim of the work: Retrospective study evaluating the clinicopathological variables affecting treatment outcome in uterine carcinosarcoma patients

Patient and Methods: Study included 37 patients who received their treatment in NCI – Egypt between 2013 to 2015. Clinical and pathological data were obtained from patients' files retrospectively

Results: The median age of study group was 62 (35 – 78) years. six patients presented with metastatic disease and 36 of 37 patients had undergone pan hysterectomy. Twenty-five patients received adjuvant therapy with chemotherapy alone (7 patients) or CRT (18 patients)After median follow up 3 years, median OS was 22.9 month and median DFS was 15 months. Despite age was not significant, shorter DFS and OS were observed with premenopausal patients versus postmenopausal (p =0.015 and 0.001 respectively), delay of surgery more than 1 month adversely affected DFS but not OS (p= 0.020). OS significantly affected by FIGO stage (p= 0.004). Longer survival was observed in 19 patients who had lymphadenectomy versus 17 who had not (p = 0.026). Adjuvant therapy did not influence the outcome in our study group

Conclusion: MMT is a high-risk endometrial carcinoma subtype with overall poor prognosis, the most important factor affecting its outcome is FIGO stage and timing of surgery. Lymphadenectomy may improve prognosis and survival in MMT. Further prospective trials are needed to study this disease

Keywords: MMT, OS, DFS, lymphadenectomy

CAN KI-67 PREPICT PELVIC NODE STATUSIN ENDOMETRIAL ADENOCARCINOMA?

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Introduction: The Ki-67 marker is a nuclear protein that has a direct correlation with the degree of cells proliferation that often expressed in human neoplasm. the study objective isto evaluate utilization of Ki-67 expression as predictor for pathological nodal positivity in endometrial endometrioid adenocarcinoma.

Materials and methods: Aretrospective case control study,we evaluated 12 histopathological slides for patients with endometrioid adenocarcinoma of the uterus for percentage of expression of Ki-67. We defined high expression as Ki-67 stained > 50% of tumor cells. Main outcome measures: The correlation of Ki-67 high expression rates and pelvic node positivity in endometrioid adenocarcinoma.

Results: Our sample mean age at diagnosis is (58.25 years) and median age is (57 years). The rate of high expression of Ki-67 in tumor cells among cases with positive lymph nodes vs controls were significantly higher (83%) vs (17%), with (p-value = 0.04). There were no significant differences between the mean age in cases and controls (59.8 vs 56.67) with (p = 0.67), tumor grade (p = 0.3), myometrium invasion (p = 0.1), cervical stromal invasion (p = 0.2), lymphovascular invasion (p = 0.2). On multivariate analysis a high expression of Ki-67 continued to be independent predictor for lymph node positivity (p = 0.02).

Conclusions: This finding suggests that a high expression of Ki67 plays an important role as predictor for lymph node positivity in endometrioid adenocarcinoma. The level of expression of Ki-67 can be utilized for preoperative or postoperative risk assessment to predict for lymph node metastasis for cases with borderline indications for postoperative pelvic irradiation. Further prospective larger study is needed to validate this preliminary data.

LETROZOLE AND ANASTROZOLE IN EARLY BREAST CANCER POSTMENOPAUSAL PATIENTS IN ONCOLOGY DEPARTMENT AT SUEZ CANAL UNIVERSITY HOSPITAL

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Abstract

Background: There are limited data in the literature comparing the efficacy of aromatase inhibitors in postmenopausal hormonal receptor positive early breast cancer patients. **Aim of study:** To compare the efficacy of letrozole and anastrozole in hormone-receptor positive postmenopausal breast cancer patients. **Methods:** A retrospective study with a mean follow-up period of 64 months (about 5 years) for 74 files of early invasive postmenopausal breast cancer hormonal receptor positive patients; 39 received letrozole

and 35 received anastrozole, considering TTP as primary end point, and OS as second end points.

Results: Letrozole is not superior to anastrozole during the first 55 months of treatment (80% PFS at 5th year), and 80% OS benefit at 6th year.. Overweight patients had better (90% PFS at 5th year) than obese patients (60% PFS at 5th year).

Conclusion: Letrozole is not superior to anastrozole in efficacy in early invasive hormonal receptor positive breast cancer postmenopausal patients during the first 5 years of treatment; however, Letrozole 2nd line after tamoxifen is superior to anastrozole 2nd line after tamoxifen in treating obese patients with early invasive hormone receptor positive breast cancer.

Keywords: Suvival, TTP, PFS, AI

DOSIMETRIC COMPARISON BETWEEN VMAT AND IMRT IN ADJUVANT BREAST CANCER IRRADIATION

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Objectives: To compare the dosimetric difference between the Volumetric Modulated Arc Therapy (VMAT) & Intensity Modulated Radiotherapy (IMRT) in breast cancer patients receiving adjuvant radiotherapy, regarding the dose distribution coverage of the target volume and lung doses.

Methods: Twenty patients with breast cancer (left and right sided) who received adjuvant localized radiotherapy to the breast or the chest wall, in Dar Al Fouad hospital were included. Eclipse13.7.14 (Varian, Palo Alto, USA) planning system was used to design the VMAT & IMRT planning for each patient. VMAT plans were done using 2 half arcs while IMRT plans were made using five fields technique. The prescription dose was 50Gy/25fr/5w. All plans required 95% of the target volume receiving the prescription dose. The dose distribution of the target, conformity index (**CI**), Homogeneity Index (**HI**)and lung doses were compared.

Results: Both Rapid-Arc and IMRT plans showed comparative target coverage. Themean **UI** for Rapid-Arc and IMRT was 0.136and 0.156 (P=0.609), respectively. The mean **CI** was 0.869and 0.842(P= 0.104), respectively.V95 of plan target volume was 95.58% and 97.49% (p=1.23) respectively.Compared to the IMRT, Rapid-Arc plans had higher dosimetric parameters for the ipsilateral lung: V20 (21.46% for the VMAT vs. 18.45% for the IMRT, P=0.00963) whileV5 % for the VMAT77.84%vs. 69.41%

for the IMRT, p=0.0624). Compared toRapid-Arc plan, IMRT has increased treatment time [(132.9±7.2) s vs. (140.3±11.6) s, P=0.030] respectively. Both the machine units were almost the same [(457.0±30.4) MU vs. (484.7±44.9) MU, P=0.094]respectively.

Conclusion: VMAT planning and delivery is feasible in treatment and provides highly conformal plans with less treatment delivery times compared to IMRT. It has ability to deliver a large field mono-isocentric plan with reduction of setup uncertainty and in-room shifts. However IMRT has significant reduction in lung dose better than VMAT

TRANSARTERIAL CHEMOEMBOLISATION (TACE) IN PATIENTS WITH BREAST CANCER WITH METASTASES TO LIVER: WHAT WE CAN DO?

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Introduction: Metastatic breast cancer requires systemic therapy in most of cases but the local therapy can be used as well. The aim of this study was to determine the response and OS rates in patients with liver metastases of breast cancer who undergo TACE in combination with chemotherapy.

Materials and methods: Open-label prospective non-randomized single-center study was performed. 60 patients had history of histologically confirmed breast cancer and histologically and/or radiographically confirmed liver metastases. 26 patients (group 1) received chemotherapy and 34 patients (group 2) who had 1-2 TACE procedures (doxorubicin 30 mg/m², 5-fluorouracil 600 mg/m², 10 ml of Lipiodol and 300-500 μm Microsphere HepaSphere) following chemotherapy (taxane-contained regimes) with PR/SD as a result of treatment. Exclusion criteria: 70% damage of the hepatic parenchyma, partial or complete main portal vein thrombosis, comorbidity in decompensating, contraindications for the angiography and selective visceral catheterization. The groups were comparable according the main clinical characteristics: the age, primary stage, biological subtype and previous treatment (p>0,05).

Results: Response was assessed according RECIST by MRI. PR – 7 (20,6%), SD – 23 (67,6%), PD – 4 (11,8%). Side effects of TACE: nausea/vomiting Gd1 – 8 patients (23,5%), stomach cramps Gd1– 3 patients (8,8%). Median follow-up was 17 months. The Kaplan–Meier-estimation of the 3-year OS for the 1 group – 63,2%, for the 2 group - 43,8% (p=0,039).

Conclusion: TACE can be included to the treatment protocol of the patients with liver metastases of breast cancer with partial response/stable disease following chemotherapy for further consolidation.

TUMOR INFILTRATING LYMPHOCYTES AND TERTIARY LYMPHOID STRUCTURE AS PROGNOSTIC AND PREDICTIVE FACTOR FOR NEOADJUVANT CHEMOTHERAPY IN STAGE II & III BREAST CANCER

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Abstract

Purpose: Tumor-infiltrating lymphocytes (TILs) have a strong prognostic and predictive value in triple-negative breast cancer (TNBC) and HER2 enriched subtype but no other breast subtypes but no studies have evaluated tertiary lymphoid structure (TLS).

Materials and Methods: Eighty patients with stage II and III breast cancer in Tanta oncology and pathology department with luminal A, B and her 2 enriched and TNBC diagnosed with core needle biopsy treated with neoadjuvant chemotherapy (4 AC followed by 12-week taxol + herceptin). TIL and TLS were evaluated histopathologically using hematoxylin and eosin–stained slides. The immune cell aggregates which were TLS positive showed the presence of CD20+ B lymphocytes within the follicles, with areas of CD3+, CD4+ T lymphocytes mainly in the periphery [T-cell zone] resembling the highly organized structures of secondary lymphoid organs.

Results: TLS were detected in 53.7% of the tumors in whole breast groups, 83.7% in triple negative subgroup. Increased number of tumor infiltrating lymphocytes and tertiary lymphoid structure are associated with longer OS and DFS for TNBC and HER2-positive breast cancer.

Conclusion: For predicting treatment response in patients with TNBC and HER2 enriched subtype, TILs and TLS may be prognostic and predictive marker triple-negative breast cancer (TNBC) and HER2 enriched subtype but no other breast subtypes.

Keywords: TNBC; HER2neu; TIL; TLS; Prognostic; Predictive; Molecular; DFS; OS

PROGNOSTIC AND PREDICTIVE FACTORS OF EARLY METASTASIS IN BREAST CANCER PATIENTS

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Abstract

Introduction: Distant metastases are considered the main cause of death among breast cancer patients. About 30% of women with early-stage breast cancer will ultimately develop metastatic lesions, months or even years later. We conducted this study to assess the prognostic and predictive factors of early distant metastasis in breast cancer patients.

Material and Methods: we retrospectively reviewed 975 patients with breast cancer treated with either neoadjuvant or adjuvant chemotherapy and underwent surgery at Ain-Shams University hospital, between January 2010 and December 2013. Early metastasis was defined as patients developing metastasis in the first 2 years from time of diagnosis.

Results: Out of 975 patients with breast cancer patients, 116 developed early metastasis, population age ranged from 21 to 75 years with mean age of 47 years. Stage II and stage III represented 19% and 81% respectively. Invasive ductal carcinoma represents 88.8% of cases. Those with HR positive represented 65.5% of the population, Her2 overexpression group represented 9.48%, and those with triple negative represented 21.5%.Patients received chemotherapy either as neoadjuvant (15%) or adjuvant (85%). In most of the patients, chemotherapy received was sequential anthracyclines followed by taxanes. Post-operative radiotherapy was received in 85% of cases.Most common site of metastasis was bone (61.2%), lung and liver represented 42.2% and 31% respectively, while brain metastasis represented 25%. Patients with HER2+/HR- tumors had worse outcome (median DFS: 12 months; 95% CI: 5.526-18.474, p=0.003) and worse overall survival (median OS: 15 months; 95% CI: 11.22-18.78, p= 0.000); While those with HR+ had better outcome. High tumor grade was also associated with poor outcome (median DFS: 16 months; 95% CI: 9.746-22.254, p=0.031). Histological subtype was also found to have an impact on survival where ILC had worse prognosis (median OS: 13 months; 95% CI: 10.85-15.14, P=0.001).

Conclusion: Her2+/HR- subtype, high grade and histological subtype are prognostic and predictive factors which are associated with poor DFS and OS in patients with breast cancer.

NEOADJUVANT RADIOTHERAPY/ CHEMOTHERAPY FOLLOWED BY SURGERY VERSUS SURGERY FOLLOWED BY ADJUVANT RADIOTHERAPY FOR STAGES IB2-IIA FOR CARCINOMA OF THE CERVIX AT NCI, EGYPT

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Abstract

Aim: To assess the effect of pre-operative radio-chemo-therapy followed by surgery versus surgery followed by post-operative t radiation on survival for patients with stage IB2-IIA cancer cervix.

Patients and Methods: Data from National Cancer Institute hospital based registry used to list all patients diagnosed with carcinoma of the cervix at the period from October 2014 to October 2016.

Results: The study involved 123 female patients with stages IB2-IIA cancer cervix Squamous cell carcinoma (SCC) was the predominant histopathology; 102 patients (83.3%), while adenocarcinoma represented the remaining 21 patients (16.7%). Sixty six patients received preoperative chemo-radiotherapy followed by surgery and 57 patients underwent surgery followed by post-operative radiotherapy according to Seidles criteria. The 2 years overall survival was 35.5% for the group received preoperative chemo radiotherapy versus 30.8% for the group received post-operative radiation (p=0.833). The 2 years recurrence free survival was 70.4% for the group received preoperative chemo-radiotherapy and 58.2% for the group received post-operative radiation (p=0.467). The 2 years metastasis free survival was 58.2% in the group received preoperative chemo-radiotherapy and 73.2% for the received post-operative radiation (p=0.5).

Conclusion: No difference in survival or local control was found between post-operative hysterectomy after chemo-radiotherapy versus hysterectomy followed by postoperative radiotherapy for stages IB2-IIA cancer cervix.

Keywords: cancer cervix, chemo-radiotherapy, Seidles, survival

ULTRASONOGRAPHIC ASSESSMENT OF EX-VIVO SENTINEL LYMPH NODE BIOPSY IN EARLY BREAST CANCER

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Abstract

Background: Breast cancer is the most common type of cancer and the second leading cause of cancer deaths among women. Early-stage diagnosis of breast cancer increases the chances of survival and, therefore, reduces mortality rates. Accurate staging and proper management of axillary lymph nodes are important for the treatment of breast cancer. Sentinel lymph node biopsy (SLNB) provides accurate assessment of nodal status. Ultrasound staging of the axilla is increasingly used to identify suspicious axillary nodes.

Objective: Evaluation of the accuracy of Ultrasonographic ex-vivo assessment of SLNB in patients with early breast cancer patients (T1-2 N0) in comparison to intraoperative frozen section examination and final paraffin histopathological examination.

Methods: Thirty female patients with early breast cancer (T1-2 N0) were subjected to ultrasonographic ex-vivo assessment of SLNB before sending it to frozen section examination then managed according to ACOSOG Z0011 criteria with follow-up of average 6 months.

Results: The mean age of the study population was 49.97 ± 11.3 years. SLNB was done using 1% MB with identification rate 100% in all surgical specimens. The overall ultrasonographic assessment of ex-vivo lymph nodes revealed 17 cases of the studied group (56.7%) with positive ultrasonographic signs suggestive for malignancy. Frozen section examination of the lymph nodes revealed 12 cases of the studied group (40%) with positive histological signs suggestive for malignancy and the number of positive cases (by frozen section examination) who required axillary lymph node dissection (ALND) was 2 cases out of 12 (16.7%). Paraffin section examination revealed 10 cases of the studied group (33.3%) with histological signs for malignancy, these 2 false positive cases in frozen section examination did not need ALND, so the discordance between frozen section examination and paraffin section examination did not affect management of the cases. The retrieved lymph nodes' length was significantly related to paraffin section examination (p value =0.045) with cut off value of 13.6 mm. The retrieved lymph nodes' cortical thickening was significantly related to paraffin section examination (p value =0.008) with cut off value 2.65 mm. Known complications from MB injection as allerigic reaction, superficial sloughing of the skin permenant pigmentation of the skin did not appear in any patient of the studied group. Follow up of the patients for an average of 6 months showed no locoregional recurrence in any patient.

Conclusion: One % MB dye is very effective as a single agent in SLNB in early stage breast cancer with very high identification rate compared to patent blue and radiocolloids. Ultrasonographic assessment of ex-vivo SLNB is a good negative test but not good positive test and is inferior to frozen section examination in detecting positive cases of SLNB. Applying ACOSOG Z0011 criteria to the patients shows no locoregional recurrence after 6 months follow up.

Keywords: Ultrasonographic assessment; Ex-vivo sentinel lymph node; early breast cancer.

THERAPY FOR DISABLING PARESTESIA INDUCED BY CHEMOTERAPY FOR BREAST CANCER: CLINICAL EXPERIENCE

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Introduction: Chemotherapy-induced polyneuropathy (CIP) is common in cancer patients receiving chemotherapy. Thenumbnessandpain in the extremities are sometimes disruptive. In previous studies, duloxetine has been reported as them osteffective treatment option in patients with neuropathic pain. There is no consensus on treatment in patients with symptoms of paresthesia. We aimed to discuss the efficacy of antiepileptic treatment in breast cancer patients who had paresthesia after chemotherapy.

MaterialandMethods: The data of 17 female patients refer red to theneurology out patient clinic after chemotherapy were analyzed retrospectively. Complaints of the patients were severe in the hand sand/or feet and had started with in 6 month safter chemotherapy. Three months follow-up results were evaluated. Gabapent in was administered at doses of 300-1800 mg/day and pregabalin 75-600 mg/day. Patients were asked how much they got benefit from the treatment.

Results: Themeanage was 55.8 (34-78) years. Eleven patients received paclitaxel, one patient docetaxel, 2 patients cisplatin, 3 patients 5-fluorouracil + epirubicin + cyclophosphamide. Gabapentin 300-1200 mg/day and pregabalin 75-600 mg/day were more than 50% beneficial in 7 patients. Four patients were followed up without any drug and one patient could not tolerate gabapent in due to side effects.

Conclusions: Taxanesandplatinums can causes ensory CIP. The symptom type and severity are variable and them echanism is not fully understood. In our observations,it was observed that both gabapent in and pregabaline were effective for parestesia on variable doses at 3-month follow-up. Reducing the dose of chemotherapy, vitamins, antioxidants, antide pressants and antiepileptics can be applied according to clinician preference. However, there is a need for extensive studies which are performed considering drug to lerability, side effects and drug interactions.

PHASE III TRIAL OF WEEKLY LOW DOSE PACLITAXEL VERSUS OBSERVATION AS MAINTENANCE TREATMENT IN PATIENTS WITH ADVANCED OVARIAN CANCER IN COMPLETE RESPONSE AFTER PACLITAXEL/PLATINUM-BASED CHEMOTHERAPY

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Abstract

Objective: to assess whether weekly intravenous 60mg/m2 paclitaxel for 21 weeks is effective and feasible as maintenance treatment in patients with advanced ovarian cancer who achieved complete response after paclitaxel/platinum based chemotherapy versus observation alone.

Patients and methods: Prospective study included one hundred patients with stage III/IV epithelial ovarian, fallopian tube and primary peritoneal cancer who are in complete response after paclitaxel/ platinum based chemotherapy were randomly allocated from September 2015 till September 2018 to either observation alone (50 patients i.e control arm) or to receive 21 doses of weekly paclitaxel 60mg/m2 (50 patients i.e maintenance arm).

Results: All 50 patients in maintenance arm completed the planned cycles of weekly paclitaxel. The worst toxicities were grade 2 neutropenia in 30.6 %, grade 2 sensory neurotoxicity in 26.5%, grade 2 motor neurotoxicity in 14.3% in the paclitaxel arm patients, The median survival time was 28 months (95% confidence interval [CI] 23.8 to 32.2) and 30 months (95% CI, 23.9 to 36.1) for the control and maintenance arm respectively, which was not statistically significant(P value = 0.472), The median progression free survival was 9 months (95% CI, 7.5 to 10.5) and 10 months (95% CI, 8.3 to 11.7) for the control and maintenance arm respectively, which was statistically significant (P value= 0.002) in favor of the maintenance arm.

Conclusion Weekly low dose paclitaxel is an effective, well tolerated maintenance treatment in patients in complete response after paclitaxel/platinum based regimens.

CIRCULATING MICRORNA-34A AND MICRORNA-125B AS PROMISING NON INVASIVE BIOMARKERS IN EGYPTIAN LOCALLY ADVANCED BREAST CANCER PATIENTS

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Abstract

Introduction: Breast cancer (BC) is the second most common cancer worldwide. MicroRNAs are a group of noncoding, single stranded RNAs of ~ 22 nucleotides, which regulate gene expression at the post-transcriptional level. Circulating miRNAs have been found as potential blood based predictive biomarkers. Material and methods We aim to evaluate 2 potential biomarkers: miR-34a & miR-125b in diagnosis and to predict outcome from neoadjuvant chemotherapy in Egyptian BC patients. Quantitative assessment of circulating plasma miR-34a & miR-125b expression was performed by quantitative real-time PCR. Thirty nine newly diagnosed locally advanced BC female

patients and 10 age and sex matched healthy volunteers were included in the study as control group.

Results: miR-34a & miR-125b expression were significantly higher in BC patients compared to controls with p value <0.001 & 0.004, respectively. We performed ROC curve analysis to evaluate the diagnostic value for the miR-34a with AUC = 0.997 and a cutoff point < 0.0001 with sensitivity 100%, specificity 90.0%, and accuracy 98.0%. miR-125b had AUC = 0.790 and a cutoff point < 0.001 with sensitivity 74.4%, specificity 70.0% and accuracy 73.5%. miR-34a & miR-125b expression levels in non-responsive BC patients were higher than the levels in responsive cases, however, it didn't reach statistically significant difference with P value = 0.150 & 0.9, respectively. Finally, we noticed direct highly significant statistical correlation between miR-34a and miR-125b expression levels with r = 0.77 & P value <0.001.

Conclusions: miRNAs became a rising issue in cancer genetics. miRNAs are crucial candidates for novel molecular targeted therapies due to their capability to regulate numerous genes in molecular pathways. Our data suggest that circulating miR-34a and miR-125b expression levels are promising non-invasive biomarkers in diagnosing BCs and predicting chemotherapeutic resistance associated with higher expression levels in non-responsive patients.

Keywords: Breast cancer, Circulating microRNA, Biomarker, Neoadjuvant Chemotherapy

MANAGEMENT OF ABEMACICLIB-ASSOCIATED ADVERSE EVENTS IN PATIENTS WITH HORMONE RECEPTOR POSITIVE (HR+), HER2- ADVANCED BREAST CANCER: ANALYSIS OF THE MONARCH TRIALS

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Introduction: Abemaciclib is a CDK4&6 inhibitor dosed continuously with demonstrated efficacy and acceptable safety profile in HR+, HER2- advanced breast cancer patients as monotherapy (MONARCH-1) and in combination with endocrine therapy; with fulvestrant (MONARCH-2) or non-steroidal aromatase inhibitors (MONARCH-3). We describe management of common adverse events (AEs) in MONARCH trials.

Material and Methods: Study designs and key eligibility criteria of MONARCH 1,2,3 have been reported. Patients were advised to initiate antidiarrheal therapy at first sign of diarrhea and notify the investigator. Treatment was suspended until diarrhea resolved. Dose reductions required for grade≥3 or persistent grade2 diarrhea. For grade3 neutropenia, abemaciclib was held until ≤grade2. Dose was reduced for recurrent grade3 or grade4 neutropenia.

Results: Totally 132 patients in MONARCH-1, 441 in MONARCH-2, and 327 in MONARCH-3 were included. Across MONARCH, median time to onset of diarrhea was between day 6&8. First dose reductions for diarrhea occurred at a median of 28-41 days. Dose holds for diarrhea were brief, constituting 1.7-3.8% of total treatment time. Median time to onset of grade3/4 neutropenia was 29-36.5 days, and resolved at a median of 11-15 days. AEs were managed by dose adjustments and/or supportive medication. Diarrhea (any grade) was reported in 119 (90.2%), 381 (86.4%), and 269 (82.3%) patients in MONARCH-1/2/3, respectively. In MONARCH-1/2/3, grade1, 2, and ≥3 diarrhea was experienced by 50.4%/48.6%/46.1%, 24.4%/23.6%/19.3%, and 25.2%/27.8%/34.6% of patients, respectively. Antidiarrheal treatment was given to 60.6%/75.5%/69.1%of patients in MONARCH-1/2/3. Neutropenia (any grade) was reported in 49 (37.1), 203 (46.0), and 143 (43.7) patients in MONARCH-1/2/3, respectively. Respectively, study treatment was discontinued by 0/1.6%/2.8% of patients in MONARCH-1/2/3.

Conclusions: The dose adjustment strategy used in the MONARCH studies was effective at managing AEs by dose adjustment and/or supportive medication. Understanding the safety profile of abemaciclib can inform AE management and can extend time on treatment.

Disclosure: Previously presented at ESMO 2018, FPN 339P, Rugo HS et al. Reused with permission.

SECRETORY BREAST CARCINOMA:A CASE REPORT

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Abstract

Introduction Secretory breast carcinoma is a very rare and distinct subtype of invasive breast cancer, characterized by the presence of intracellular and extracellular secretory material

Secretory breast carcinoma (SBC) is also known as juvenile carcinoma, Although secretory carcinoma may occur in adults, the median and mean age are 33 and 40 years, respectively.

Secretory breast carcinoma has a good clinical outcome and systemic involvement is rare. The literature mentions nodal involvement in 15% of the patients at presentation.it is useful to report every such case, in order to make as much information as possible available in the medical literature.

We present a case of 33-year-old female diagnosed as secretory breast cancer appropriate surgical management offered to the patient according to a multidisciplinary approach.

Material and methods: Data registry were revised to demonstrate the burden of secretory breast carcinoma in the literature, prognosis and various management options.

Results: Secretory breast carcinoma is a rare, invasive type of breast cancer which represents<0.1% of all cases of invasive breast cancer.Secretory breast carcinoma (SBC) was known as juvenile carcinoma,Subsequent studies have reported secretory carcinoma in adults, then the disease is termed as secretory breast carcinoma by Tavassoliand Norris,based on the histopathological characteristics of the tumor, with cells containing a vacuolated cytoplasm and the presence of intracellular and extracellular secretory material.

Conclusion: secretory breast carcinoma is a rare oncological entity requiring multidisciplinary approach for each case, onco-plastic breast surgery widens the range of breast conservation with no compromisation of oncological safety, More studies are required to define the role of targeted therapy in secretory breast carcinoma being expressing basal cytokeratines.

TRENDS IN DEMOGRAPHICS AND REPRODUCTIVE FACTORS IN BREAST CANCER IN EGYPT: A STORY OF 25 YEARS

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Background: Several factors have been associated with the international variation in breast cancer incidence rates; these include epidemiologic, reproductive, hormonal and lifestyle factors. Trends in these risk factors are important to demonstrate changes over time.

Patients and methods: Cross-sectional study including 200 breast cancer patients diagnosed during the year 2015 (group III) for the aim to compare their epidemiologic, reproductive and hormonal characteristics with two previous studies conducted in 1990(group I) and 2005 (group II)

Results: Over the past 25 years, the mean age of the patients at diagnosis became significantly older, p=0.009; (45.7, 46.1 and 49.1 years for group I, II and III respectively). The mean age at menarche became significantly younger over time (13.5, 12. 5and 12.6 years for group I,IIand III respectively; p=0.003) and the percentage of patients had their menarche under the age of 12 years was significantly higher in groups II and III compared to group I (P= 0.001) while the age at menopause became significantly older (45.7, 48.5 and 48.2 years for group I, II and III respectively, p=0.006). The percentage of patients got married after the age of 25 years old showed significant increase; it was 8.2%, 18.9% and 19.8% for group I, IIandIII respectively, p=0.005. Consequently, age at first full term pregnancy was significantly increased also while breast feeding tends to increase significantly over time. The percentage of oral contraceptive pills intake significantly increased; it was 46.5%, 51.6 and 61% in group I, IIandIII respectively, p=0.013, while the percentage of working women significantly increased over time.

Conclusion: There are significant changes in reproductive and hormonal pattern in Egyptian females diagnosed with breast cancer over the past 25 years. These trends should be taken into account when planning for any future national breast cancer screening or prevention plans.

EFFICACY AND OUTCOMES OF DEFINITIVE TREATMENT IN EGYPTIAN PATIENTS WITH CERVICAL CANCER: A RETROSPECTIVE STUDY IN AIN SHAMS UNIVERSITY HOSPITALS

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Abstract

Background: cancer cervix is the fourth most common malignancy in females worldwide, there were 527,600 new cases worldwide, it remains a leading reason of cancer-related death for females in developing countries. Cancer cervix remains a significant cause of morbidity and mortality in females. The highest incidence rates were in Central and South America and sub-Saharan Africa. The lowest rates were in the Middle East, Northern America, Australia and New Zealand, China, and Western Europe.

Aim of the work: this study aimed to analyze retrospectively the efficacy of concurrent chemo- radiotherapy with or without brachytherapy in the cervical cancer patients and outcomes in terms of: overall survival (OS) and progression-free survival (PFS) of patients at Department of

Clinical Oncology and Nuclear Medicine at Ain Shams University Hospitals

Results: the files of 69 patients with cervical cancer were reviewed. 11 patients were excluded from the analysis (10 patients had adeno-carcinoma and 1 patient died before treatment planning). Among the remaining 58 patients, 20 patients did not receive treatment and lost follow up after treatment planning, 2 did not complete treatment (1 died and 1 lost follow up) and 36 completed the planned treatment.

Conclusion: cancer cervix is usually diagnosed at an advanced stage and outcomes are still poor. The use of concurrent chemo-radiotherapy followed by brachy-therapy and the treatment duration were the most important prognostic factors identified in our study.

Recommendations: to reduce the incidence and mortality of cancer cervix in Egypt, we should educate and inform females about risk factors and prevention. Also, it is recommended to educate patients and their families about the nature of the disease, the importance of follow up and its impact on their outcomes.

VITAMIN D AND PARATHYROID HORMONE AND THEIR ASSOCIATION WITH SYMPTOMS OF FATIGUE AND QUALITY OF LIFE IN ADVANCED CANCER EGYPTIAN PATIENTS

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Adequate Vitamin D is crucial in sustaining human health; prevent multiple chronic illnesses and several physiological processes. Vitamin D deficiency has been mainly known for its association with fractures and bone diseases; however, its newly recognized association with risk of several types of cancer is receiving considerable attention. New data suggests that the high prevalence of vitamin D deficiency may account for several thousand premature deaths from various types of cancer annually. Vitamin D deficiency has been associated with symptoms of fatigue, muscle weakness, depression, increase in falls and secondary hyperparathyroidism (HPT), which leads to cortical bone loss in both cancer and non-cancer patients. In our study, we assessed the relationship between Vitamin D deficiency and parathyroid hormone (PTH) with health-related quality-of-life issues, fatigue, and physical functioning in advanced Egyptian cancer patients. Among 58 Egyptian patients with advanced cancer, patients were predominantly female (31%), with a median age of 50 years (range, 25-75 years). Colorectal (17%), Anal (12%) and Endometrial (10%) cancers were prevalent. All patients were vitamin D deficient with serum levels ranging from 4 to 18 ng/ml, whereas PTH was higher in cancer patients compared to controls with serum intact levels ranging from 70 to 120 pg/ml. This demonstrates the negative correlation between vitamin D and PTH. There was an evident direct association between health-related quality of life, fatigue, performance and vitamin D serum level and PTH levels. Low vitamin D levels were highly prevalent among advanced cancer Egyptian patients, which correlated with high symptoms of fatigue, low-performance status and poor quality of life.

ASSESSMENT OF THE EFFICACY OF TRASTUZUMAB AS ADJUVANT CHEMOTHERAPY IN CORRELATION WITH CLINICOPATHOLOGICAL FEATURES IN PATIENTS WITH HER/2NEU POSITIVE BREAST CANCER ATTENDING SUEZ CANAL UNIVERSITY HOSPITAL

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Abstract: The aim of this study was to evaluate clinicopathological features of early stage breast cancer patients who are epidermal growth factor receptor 2 (HER2) overexpressed/ amplified (HER2+), the efficacy of trastuzumab treatment and survival results.

Materials and Methods: Patients with HER2- positive early stage breast cancer receiving adjuvant trastuzumab were investigated retrospectively. Clinicopathological features of 88 patients and treatment outcome were analyzed. To evaluate survival rates, the Kaplan-Meier method was used. Univariate and multivariate analyses were conducted with the Cox regression model.

Results: In trastuzumab group: 61 patients received trastuzumab, 60.7% of them were less than 50 years, 60.7% were premenopausal, 93.4% of patients had invasive ductal carcinoma and 52.5% of the patients had T2 carcinomas. 77% of patients were nodal positive, 86.9% of patients had grade 2 carcinomas, stage IIIA and stage IIIC were the most common among the study group represent about 26.2% and 27.9% respectively, 55.7% of patients were ER negative and 65.6% were also PR negative. Most of the patients underwent modified radical mastectomy but only 16.4% of the patients did conservative breast surgery. Of overall 61 patients who received trastuzumab, 83.6% of them completed one-year trastuzumab treatment. In the non-trastuzumab group: 27 patients didn't receive trastuzumab, 51.9% of them were 50 years or more and 51.9% of them were premenopausal. 92.6% of the patients had

invasive ductal carcinoma. most of the patients (55.6%) presented with T2 carcinomas and 51.9% of them presented with N3 tumors. 81.5% of the patients had grade 2 carcinomas and 51.9% of them had stage IIIC tumors. 59.3% of the patients were ER positive while 51.9% of them were PR positive. 81.5% of the patients underwent modified radical mastectomy while conservative breast surgery was done in the rest of the patients. In patients who received trastuzumab (trastuzumab group), the median follow-up was 24 months (8.0-40.0 months). Relapse-free survival (RFS) was 31.2 months (95% CI: 28.0-34.4) and overall survival (OS) was found to be 34.9 months (95% CI: 32.3-37.5). The 3-year OS for all patients was 76.9% and RFS was 62.3%. In non-trastuzumab group: the median follow-up was 26 months (8.0-40.0 months). They were followed up during the course of treatment and it was found that relapse-free survival (RFS) was 30.18 months (95% CI: 25.2-35.1) and overall survival (OS) was found to be 32.0 months (95% CI: 27.3-36.6). So, the 3-year OS for all patients was 59.8% and RFS was 48.3%. Univariate analyses indicated larger tumor size, positive nodal involvement, and positive estrogen receptor status were significantly associated ($p < 0.05$) with RFS. Multivariate analyses of covariates displaying $p < 0.05$ identified positive lymph node involvement (HR=1.8, 95%CI 1.1 - 3, p=0.01) as an independent prognostic factor.

Conclusion: it was established that trastuzumab had a satisfactory safety profile and treatment efficacy as in other clinical studies and that among clinicopathological factors evaluated, only positive lymph node involvement had a significant effect on RFS. The occurrence of relapse with adjuvant trastuzumab makes it necessary to identify molecular predictors, which will define this group better and help explain resistance to anti HER2 based therapies

PERSISTANT MULLARIAN DUCT SYNDROME (PMDS)

A case report with review of literature.

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Introduction: Persistent mullerian duct syndrome (PMDS) is a form of male intersex caused by a defect in the mullerian inhibiting substance (MIS) system. Patients are phenotypically male and usually present when young with unilateral or bilateral cryptorchid testes and an inguinal hernia into which prolapses an infantile uterus and fallopian tubes. Familial cases have been reported with a probability of sex-limited autosomal recessive or X-linked recessive inheritance.

Methods: A normal looking adult male aged 41years presented with abdominal irregular mass and hematuria. The preoperative investigations include radiological examination, hormonal assay and tissue biopsy revealed spindle cell neoplasm, however not reach the definite diagnosis. The case is very rare and has to need multidisciplinary group managements. A case of Persistent Mullerian Duct Syndrome was not diagnosed early because no patient complain and the patient is clinically free long time. Excision biopsy of the mass was performed. Gross dissection and microscopic examination was performed.

Results: Gross findings revealed The received sample was consists of uterus with upper part of vagina, bilateral fallopian tubes, two vas deferens and two ovoid gonadal organs with smooth surfaces appear like testis. On microscopy, gonads showed testicular tissue. The uterus comprising normal-looking endometrium and myometrium .Both tubal structures showed both epidydimal tissue and fallopian tubal tissue.

Conclusion PMDS is an autosomal recessive inheritance disease. It is a rare condition that reported few in literatures. Awareness amongst the surgeons about this rare conditions, its presentation and its alliance helps in appropriate management. Serum AMH measurement should be done and it can be helpful in assessing the gonadal function and screening of close relatives is important for detection of familial cases.

Keywords: PMDS., hematuria., undescended testis. Pseudohermaphroditism

INCIDENCE OF CANCER RELATED FATIGUE (CRF) ININIDANWOMEN WITH BREAST CANCER; ANOVERVIEW OF PSYCHOLOGICAL ISSUES IN BREAST CANCER PATIENTS RECEIVING CHEMOTHERAPY.

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Introduction: Fatigue is one of the most disabling and distressing symptoms affecting physical and emotional wellbeing of patients diagnosed with cancer or receiving treatment for it thereby, posing detrimental impact on their Quality of Life (QOL). Although its assessment and identification has been enormously acknowledged in oncology care, however it's being seldom addressed, reported and treated in majority of Indian patients.

Material and Methods An exploratory design was adopted for the study. Using purposive sampling method, patients (N=88) undergoing chemotherapy at RGCI, Delhi, India; aged 30-77 years were included. The level of fatigue was assessed using 16-item Multidimensional assessment

of Fatigue (MAF) scale and asemi structured in-depth interview schedule. These interviews were recorded, transcribed and analyzed.

Results: Irrespective of age, and education, 88% patients experience clinically significant fatigue, of which extreme level of fatigue was reported by 47% patients requiring immediate clinical intervention and 41% patients reported moderate level of fatigue, which is also clinically significant. Top three psycho social issues reported were apprehension of chemotherapy side effects (20%), anxiety during CT (19%) and combination of multiple psycho social issues (14%), followed by loss of appetite (13%), financial issues (12%) and fear of pain during CT (10%). Among all the patients, (66%) were aware of their diagnosis, of which 11% were either fully aware or partially aware about the prognosis (20%).

Conclusion: Fatigue remains one of the most important clinical parameters among majority of the patients receiving chemotherapy, with females reporting it more as compared to their male counterparts.Indianpatients should be evaluated for treatable conditions that might contribute to this symptom. Exercise, educational material and psychotherapeutic interventions should also be developed to prepare and support them during their treatment phase, which will ultimately lead to reduced symptoms and better quality of life

PATHOLOGIC COMPLETE RESPONSE BY BREAST CANCER MOLECULAR SUBTYPE AND LONG TERM OUTCOMES FOLLOWING NEOADJUVANT CHEMOTHERAPY ±TRASTUZUMAB IN LOCALLY ADVANCED BREAST CANCER: DOES MOLECULAR SUBTYPE MATTER?

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Background: Locally advanced breast cancer (LABC) is the most common breast cancer presentation in developing countries with incidence of 33-70%. It has a substantial risk of recurrence, metastasis and death, with a 5-year overall survival rate of approximately 57%.

Methods: Patients with LABC (T2-T4, N0-N2, M0), received neoadjuvant chemotherapy plus trastuzumab if HER2 positive, followed by definitive surgery and locoregional radiotherapy ± hormonal therapy if indicated. The primary end point was pathologic complete response (pCR) in breast and axilla in separate HER2 negative and HER2 positive cohorts with final analysis on long term outcomes.

Results: Six hundred eighty-one patients were eligible. Median age 44 years, premenopausal 73%, median tumor size 7.0 cm (4–16cm), Stage IIB 27% and IIIA / IIIB 73%, ER+/ HER2 – 41%, ER–/ HER2– 23%, ER+/ HER2+ 18 %, ER– /HER2+ 19%.20% had conservative surgery and 80% had MRM.

Overall the pathological complete response (pCR) in both cohorts was 32% in breast, 44% in axilla and 23% in both breast and axilla. Analysis of (pCR) in breast and axilla, as a function of the hormonal receptor and HER2 were: ER+/ HER2-9%; ER+ /HER2+ 29%; ER- /HER2-31%; ER- / HER2+ 37%. At median follow up of 61 months (range 37-96);10-year overall survival (OS) was highest in ER+/ HER2+(pCR 91%; no pCR 80%), and ER+/ HER2- (pCR 96%; no pCR 78%) subtypes. The worst OS was in ER-/ HER2+ (pCR 93%; no pCR 56%), and ER-/HER2- (pCR 91%; no pCR 64%).pCR in breast and axilla decreased risk of relapse and death (P value =0.001).

Conclusion: Women with ER+/HER2- subtype are the least likely to have pCR, but those with HER2+and triple negative (TN) subtypes had the highest rates. Degree of response is associated with OS survival, despite the comparatively higher likelihood of achieving pCR in ER-/ HER2+ and TN subtypes, thesesubtypes experienced a survival detriment, we are the first to report that ER+/ HER2+ subtypes has the best outcomes comparing with others.

Keywords: Locally advanced breast cancer, Neoadjuvant chemotherapy, Anthracycline, Cisplatin / Docetaxel, Trastuzumab, Pathologic complete response and molecular subtypes

EVALUATION OF FNAC VS SNB OF INDETERMINATE AXILLARY NODES IN EARLY-STAGE BREAST CANCER

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Abstract

Background: Breast cancer is the most common female cancer with the incidence increasing in the past two decades.

Axillary lymph node status is an important prognostic factor and determinant of treatment for patients with breast carcinoma.Ultrasonographic (US) evaluation of the breast and axilla is increasingly being used in the pre-operative evaluation of breast cancer patients and it can classify axillary lymph nodes into pathological, indeterminate and benign.

Aim of work: The aim of our study is to evaluate the *indeterminate axillary lymph nodes* in early stage breast cancer prior to surgery and intraoperative. This is to give the patient the maximum benefit of the available tools of diagnosis, ultrasound-guided fine needle aspiration cytology (FNAC) and sentinel lymph node biopsy technique (SLNB), and consequently avoiding unnecessary axillary lymph node dissection (ALND) with its all morbidities. There will be recommendations regarding how to deal with indeterminate axillary lymph nodes in a step-wise pattern.

Methodology: This is a prospective, randomized, controlled study. Sixty Female patients diagnosed with early-stage breast cancer with indeterminate axillary nodes were admitted to the breast surgery unit in kasr Alainy university hospital, Faculty of Medicine, Cairo University,during the period from October 2017 till October 2018. We assessed and compared*sensitivity, specificity, positive and negative predictive value* of pre-operative ultrasound-guided FNAC vs upfront intraoperative SLNB and frozen section of indeterminate axillarylymph nodes then correlation of both results to final histopathological paraffin section result.

Results: Sensitivity ofSLNB was found to be 83.33% while sensitivity of the FNAC was found to be 75% with the NPV = 83.33%, and the specificity was 83.3% while PPV= 75%. space after 75%.

Conclusion: FNAC is only moderately sensitive (75%),inadequate (insufficient) sampling is another potential limit of FNAC and it is an operator-dependent technique. In addition,positive FNAC may cost the patient unnecessary ALND with its all morbidities if the patient is candidate for Z0011 ($\leq$ 2/3 or more, not matted and with no extracapsularextension) and might benefit from SNB technique avoiding ALND, thus, enabling the surgeon to give the patient the ultimate tailored management of the axilla.

Keywords: earlybreast cancer - Indeterminate lymph nodes-fine needle aspiration cytology (FNAC) - sentinel node biopsy (SNB).

CISPLATIN PLUS GEMCITABINE VERSUS PACLITAXEL PLUS GEMCITABINE AS FIRST-LINE THERAPY FOR METASTATIC TRIPLE NEGATIVE BREAST CANCER

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Abstract

Background: Despite general improvements in the management of breast cancer, triple negative breast cancer represents a continuing challenge because, when compared with other subtypes, it is associated with a higher frequency of recurrence, shorter disease-free survival, and poorer overall survival, despite similar therapeuticapproaches to other breast cancers. The median distant disease-free interval forrelapsed triple-negative breast cancer is about 1–2 years, and the median survival formetastatic triple-negative breast cancer is about 1 year.

Aim of Work: To compare the overall Response Rate of using gemcitabine/Cisplatin regimen versus paclitaxel/Gemcitabine regimen as a tool of treatment in metastatic triple negative breast cancer

Patients & Methods: The study is a randomized clinical trial study conducted on metastatic triple negative breast cancer patients at Department of Oncology and Nuclear medicine, Suez Canal University during 2016 and 2017 at Ismailia.

Eligible patients randomly assigned (1:1) to receive either:

Group (A): Cisplatin plus gemcitabine (Cisplatin 75 mg/m² on day 1; gemcitabine 1000 mg/m² on days 1 and 8)or **Group (B):** paclitaxel plus gemcitabine (paclitaxel 175 mg/m² on day1; gemcitabine 1000 mg/m² on days 1 and8) intravenously every 3 weeks for a maximum of eight cycles, or until disease progression or intolerable toxic effect develops.

Results: Triple negative breast cancer cases were **147 case (40.9%),** while metastatic triple negative breast cancer cases were **110 (30.6%)** presented to Clinical Oncology & Nuclear medicine department Suez Canal University.

During 12 months of follow up, the **Overall response rate** for Group (A) receiving Gemcitabine / Cisplatin arm were significantly higher than Group (B) receiving Paclitaxel / Gemcitabine arm (**69.1% versus 47.3% respectively**), also **Median progression free Survival** (DFS) for the Gemcitabine, Cisplatin arm was significantly higher than Median progression free Survival (DFS) for the Paclitaxel / Gemcitabine (**Mean 7.18 versus 5.49 respectively**).

Conclusion: Cisplatin plus gemcitabine could be an alternative or even the preferred first-line chemotherapy strategy for patients with metastatic triple-negative breast cancer.

Keywords: Overall response rate, Median progression free survival, Toxicity & adverse events.

OPTIMIZATION OF OPERATION TIME IN DIEP FLAP (DEEP INFERIOR EPIGASTRIC ARTERY PERFORATOR FLAP) SURGERY WITH THE HELP OF CT(A) AND 3D MAPPING

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Introduction: Autologous breast reconstruction with deep inferior epigastric artery perforator flap considered as a platinum standard of final esthetic result. More and more centers are trying to perform DIEP flap reconstruction. Without CT(a) 3d mapping average operation time of DIEP flap surgery about 10 hours in our department.

Material and methods: With the help of radiology department of our institute we`ve started a new protocol of planning DIEP flap operations. We carry out CT(a) with extended fields (capturing the pelvic area). With that trick, we can track down where and how epigastric arteries move away from iliac artery. Also we can answer very important questions,The first one: What variant of DIEA according to Moon and Taylor? The second one; Caliber of perforants? With the extended fields we can also make sure that IMA/V (intramammary artery and vein) are suitable for that kind of operation. Radiologist are tracing all the perforants and choose 2 or 3 of them on the assumption of caliber, Moon and Taylor theory, length in rectus abdominis, and Hartrampf zones of perfusion. After that we do our second trick, CT(A) with narrowing of the scan field. Its some kind of target CT(A) on the area where previously radiologist chose perforants. With the we can understand motion of perforants, their twist, and give a 3D coordinates of entry into the subcutaneous adipose tissue. With that,operation time could be decreased, because surgeons team already know the navigation and how the vessel go, their twist and what perforants can be crossed during the dissection.

Results: We perform *double CT(a)* on the group of 15 patients. With the help of that tricks we have reduced operating time by more than 4 hours. We also have decreased the length of the window in the aponeurosis which led to decrease in painful sensations of the patients and in hospital stay days.

Conclusion: CT(A) with 3d mapping must be done every time before DIEP flap surgery.

ADDED VALUE OF SPECT/CT IN BREAST CANCER PATIENTS WITH EQUIVOCAL BONY LESION DETECTED ON CONVENTIONAL PLANAR BONE SCAN

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Introduction: Planar bone scan (PBS) is a standard modality for detecting skeletal metastasis. Although PBS is very sensitive, but it lacks specificity, especially when a solitary or few atypical osseous lesions depicted .The addition of SPECT/CT can greatly enhance diagnostic accuracy and help reclassify non-conclusive findings on PBS. In this work, we evaluated the added value of SPECT/CT in characterization of equivocal osseous lesions depicted from conventional PBS in breast cancer patients.

Materials and Methods: This prospective study recruited patients known to have breast cancer referred for PBS. Immediately after the conventional scan was acquired, planar images were reviewed for the presence of solitary (or few) inconclusive osseous lesion(s). If two nuclear medicine physicians agreed on these findings; SPECT/CT was acquired in the same day, to cover the suspected area.

The final status of these lesions was decided based on subsequent clinical/imaging follow-up for at least 6-12 months. Diagnostic performance indices from both (PBS&SPECT/CT) were compared against the reference standard.

Results: A total of 83 breast cancer patients were included in this study (80 females, 3 males) with median age 52 years (range: 32-84). The sensitivity, specificity and accuracy for PBS versus SPECT/CT were 89% vs. 100%, 30% vs. 87% & 57% vs. 93%; respectively; with statistically significant difference ($P = 0.013$, <0.0001); respectively. SPECT/CT changed management in 36% of breast cancer patients by downstaging and upstaging their skeletal disease status.

Conclusion: Skeletal SPECT/CT offers an important diagnostic advantage over planar bone scan for characterization of inconclusive osseous lesions in patients with breast cancer and could significantly impact patient management.

INFLUENCE OF TIME TO ADJUVANT CHEMOTHERAPY ON SURVIVAL IN BREAST CANCER PATIENTS

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Introduction: Adjuvant chemotherapy is proven to have survival benefit for breast cancer patients. Determine optimal start timing is important. A hospital-based study was performed to analyze this time factor.

Method: 456 breast cancer patients received adjuvant chemotherapy from 01/2011 to 12/2015 in Menoufia university hospitals, were included. And divided into three groups according to time to start adjuvant chemotherapy (TTC), A (started ≤30 days), B (from 30-60 days) and C (≥60 days). Patients followed till 01/2018. Main objectives were to assess influence of time on disease-free and overall survival.

Results: Median follow up duration was 3.47years. 195(42.76%), 183(40.13%) and 78(17.11%) were group A, B and C respectively.

A includes 104(53.33%) premenopausal, 91(46.67%) postmenopausal. 182(93.3%) were IDC and 13(6.7%) were lobular and others. 3(1.5%), 168(86.1%) and 24(12.4%) had grade 1, 2 and 3 respectively. 3(1.5%), 79(40.5%) and 113(57.9%) were stage 1,2 and 3 respectively. 132(67.7%), 20(10.3%) and 43(22%) were hormone-positive, triple negative and her2-positive disease.

B includes 89(48.1%) premenopausal, 94(51.9%) postmenopausal. 173(94.6%) were IDC and 10(5.4%) were lobular and others. 4(2.2), 154(84.1%) and 25(13.7%) had grade 1, 2 and 3 respectively. 9(4.9%), 73(39.9%) and 101(55.2%) were stage 1,2 and 3 respectively. 103(56.3%), 29(15.8%) and 51(27.9%) were hormone-positive, triple negative and her2-positive disease.

C includes 40(51.3%) premenopausal, 38(48.7%) postmenopausal. 69(88.5%) were IDC and 9(11.5%) were lobular and others. 0, 69(88.5%) and 9(11.5%) had grade 1, 2 and 3 respectively. 3(3.8%), 37(47.4%) and 38(48.7%) were stage 1, 2 and 3 respectively. 50(64.1%), 13(16.7%) and 15(19.2%) were hormone-positive, triple negative and her2-positive disease.

In cox model analysis, TTC was independent prognostic factor in group C versus A by HR 1.959, 95%CI (1.259-3.047) and 2.305, 95%CI (1.409-3.772) for DFS and OS respectively.

Conclusion: Delayed initiation of adjuvant chemotherapy over 60 days carry risk on patient survival.

STEM CELLS: A NOVEL TARGET FOR OVARIAN CANCER THERAPY

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Abstract: Ovarian cancer is one of the most common gynaecologic malignancies with high rate of morbidity and mortality.

The current therapy for cancer ovary include surgery and chemotherapy. Yet the results are still unsatisfactory.

Natural killer (NK) cells are immunity cells which can be used in potential trials for ovarian cancer therapy, with favorable outcomes in decreasing the tumor burden.

Thus, stem cell therapy could provide a new hope for ovarian cancer patient through NK stimulation.

Introduction: Ovarian cancer is the fifth leading cause of cancer- related death in women world wide. In Egypt; ovarian cancer ranks as the forth most frequent cancer, according to the national population- based registry programme in Egypt 2008-2011 with a number of deaths 7.4 per 100,000 women per year. It's a highly lethal disease among all gynaecologic malignancies with overall five-year survival rate was 43% from 2002 to 2008.

Ovarian cancer arises from one of three cell types: epithelial cells, stromal cells and germ cells. More than 90% of malignant ovarian tumours are epithelial in origin, 5-6% of tumours constitute sex cord-stromal tumours and 2-3% are germ cell tumours.

Actually the reason for 90% of tumours arising from the ovary surface epithelium is that stem cells reside in this area. In early stage of ovarian cancer the number of EOC stem cells can be used to predict progression of the disease.

Stem cell therapy is a novel promising therapeutic modality in different types of malignant tumours with distinguished results in breast and ovarian cancers.

The Current management of ovarian cancer: Treatment of ovarian cancer usually include combination of surgery and chemotherapy. Despite the variability of available treatment regimens, yet, the overall prognosis in most reviews don't exceed "92% stage I *v* 5% stage IV "Even in the most favorable group treated for advanced disease, about 70% will relapse within 18 months

Stem cell therapy hypothesis in cancer ovary: Stem cells (SC) are cells with the potential develop into many different types of cells in the body.

Stem cells are divided into three types:

Induced pluripotent SC (IPSC) is one of the hottest topics in SC research, IPSC "adult cells that are reprogrammed to become "pluripotent" behave like an Embryonic one including the ability to give raise to all types of cell in the body.

Natural killer (NK) cells are immunity cells which can be extracted from the peripheral blood (PB) and isolated by the depletion of peripheral blood B and T cells to estimate its ability in mediating the killing of ovarian cancer cells mousexenograft model.

In addition, NK cells are derived from induced pluripotent stem cells (IPSC) and activated in a long-term culture, to produce IPSC-NK.

The initial studies confirm that a single dose from PB NK cells or from IPSCs-NK cells reduce tumor burden by a diverse methods of actions including: detecting the cancer cells by activating of NK receptors and co-stimulatory molecules, These are modulated by inhibitory receptors that sense the levels of MHC class I on prospective target cells to prevent unwanted destruction of healthy tissues.

Also Nk cells release cytokines and chemokines that set up inflammatory responses by modulating monocyte, dendritic cells, and granulocyte growth and differentiation; and pursue subsequent adaptive immune responses.

According to this results, stem cells are considered a valuable resources for immunotherapy of ovarian cancer having the ability to differentiate widely to NK cells. And thus, they can be banked to treat ovarian cancer patients giving a new promising hope for a better survival rate and overall prognostic results.

Conclusion:

Surprisingly, stem cell based therapy knocked out traditional way by their predominating ability in reaching distant tumors or penetrating it.

Therefore, we dig into that new fangled way of therapy to take over control in late stage ovarian cancer cases.

COMBINATION OF CISPLATIN AND METFORMIN IN CUBOSOMES ENHANCES APOPTOSIS OF COLORECTAL CANCER CELL LINES

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Introduction: Colorectal cancer (CRC) remains a leading cause of death worldwide. Utilizing cisplatin in CRC is correlated with severe adverse effects and drug-resistance. Combined anticancer drug-treatment, along with, their enhanced delivery, can effectively kill cancer through multiple pathways. Nano-cubosomes are emerging as nanocarriers for anticancer therapies, hence, we constructed nano-cubosomes bearing cisplatin and cisplatin-metformin combination for investigation on HCT-116 cells.

Aim: The aim of the present study was to construct nano-cubosomes bearing cisplatin, metformin and cisplatin-metformin combination and investigate their effect on proliferation in Caco-2 and HCT-116 cell lines, as well as, tumorigenesis-associated metabolic markers in HCT-116 colorectal cancer cell lines.

Materials and methods: Nano-cubosomes bearing either cisplatin alone or cisplatin-metformin combination were formulated using emulsification technique. The loaded nano-cubosomes were characterized in-vitro and the optimized formulations were selected. Their cytotoxic effects were investigated by Sulphorhodamine-B (SRB) assayin Caco-2 and HCT-116 cells. In HCT-116 cellsthe AMPK/mTOR metabolic pathwaywas analyzed using ELISA technique.Protein levels of AKT were determined using western blotting. Glucose, ATP, NADPH oxidase, LDH, glutathione (GSH) and caspase-3 activity were measured spectrophotometrically.

Results: Nano-cubosomal formulations exhibited superior cytotoxic effect compared to unformulated drugs. This cytotoxic effect was profound upon incorporation of metformin, an indirect mTOR inhibitor, in cisplatin nano-cubosomes. The induced CRC cell apoptosis was through inhibition of several metabolic pathways, namely, AMPK/mTOR and AKT/mTOR. Drug-loaded nano-cubosomes ensued glucose and energy depletion that led to AMPK activation and thus mTOR inhibition. mTOR was additionally inhibited via p-AKT (Ser473) level suppression after nano-cubosomal treatment. Moreover, drug-loaded nano-cubosomes produced a notable escalation in ROS levels, evident as an increase in NADPH oxidase, decrease in intracellular GSH, LDH inhibition and a consequential upsurge in caspase-3 activity.

Conclusion: These results showed the influence exerted by low concentrations of cisplatin-loaded and metformin-loadednano-cubosomes on CRC cell survival. Metformin incorporation improves the anti-proliferative effect of cisplatin nano-cubosomes on CRC cells by inhibiting metabolic-mediated tumor progression suggesting their potential use as an adjuvant treatment in CRC. Further studies are needed to confirm their beneficial effect before their use in clinical settings.

Keywords: Cisplatin, Metformin,CRC, AMPK, AKT, nano-cubosomes