Regional Difference and Prognostic Significance of Foxp3 Positive Regulatory T Cell Infiltration in Breast Cancer

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**Background:** Foxp3 is known as the most specific marker for regulatory T lymphocytes which plays an important role in immune tolerance to frustrate anti-tumor immune responses. We investigated the prognostic significance of foxp3 regulatory T lymphocyte (foxp3 Treg) infiltration in breast cancer. **Methods:** Immunohistochemical stainings for foxp3, CD4, and CD8 were performed on representative full tissue sections from 143 patients with invasive ductal carcinoma, no otherwise specified, which were separately quantified in tumor bed and tumor periphery. Foxp3 Treg infiltration, foxp3 Treg/CD4 T lymphocyte, and foxp3 Treg/CD8 T lymphocyte in tumor bed and tumor periphery were analyzed to examine the association with the clinicopathological factors and patient prognosis. **Results:** Tumor periphery was far more densely infiltrated by foxp3 Treg, CD4 and CD8 T lymphocytes. Within tumor bed and tumor periphery, high foxp3 Treg infiltration, high foxp3 Treg/CD4 and high foxp3 Treg/CD8 were associated with unfavorable prognostic factors including high Ki-67 labeling index, higher nuclear and histologic grade. High foxp3 Treg/CD4 in tumor periphery was significantly associated with estrogen receptor and progesterone receptor negativity and triple negative breast cancer. High foxp3 infiltration and high foxp3 Treg/CD8 in tumor periphery were independent predictors of tumor recurrence and shorter disease free survival. **Conclusions:** High foxp3 infiltration, high foxp3 Treg/CD4 and high Treg/CD8 were valuable indicators for breast cancer with poor pathological factors and unfavorable prognosis.

**Key Words:** Breast neoplasms; Foxp3; T-lymphocytes, regulatory

MicroRNA Expression Profile of Malignant Phyllodes Tumor

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**Background:** Phyllodes tumor of breast is a heterogeneous and complex group of tumors. Despite being evaluated into sub-classifications, the actual characteristics and prognosis of these tumors remain poorly understood because of their rarity. MicroRNAs (miRNAs) are considered as attractive candidates that may improve diagnostic, prognostic, and predictive characterization of this group of malignancies. **Methods:** A comprehensive miRNA expression analysis, in a series of 5 malignant phyllodes tumor and 4 benign (normal or fibrocystic change) breast lesions, was performed, using peptide nucleic acid-based miRNA expression profiling Kit which is consists of 135 probes for cancer- or stem cell-related miRNAs. **Results:** This analysis revealed that 48 miRNAs are detected from the malignant phyllodes tumor and benign breast lesion and among 48 miRNAs, expression of let-7c and let-7b (chromosomal region 9q22.3) miR-153 are significantly decreased in malignant phyllodes tumour than benign breast lesion, while, expression of 21 somatic region 9q22.3) miR-153 are significantly decreased in malignant phyllodes tumour and benign breast lesion. **Conclusions:** Through comprehensive miRNA profiling identified a novel set of miRNAs that might differentiate between malignant phyllodes tumor and benign breast lesion and could provide a starting point for experimental modulation of relevant targets for new diagnostic or therapeutic strategies for malignant phyllodes tumor.

**Key Words:** Phyllodes tumor; MicroRNA; Breast; Transcriptome; Malignant
Expression of Plexin-B1 in Human Invasive Breast Ductal Carcinoma, Not Other Specified

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Background: Cumulative studies have shown involvement of plexin-B1 in tumor progression. An in vitro breast carcinoma study reported that coupling with HER-2, plexin B-1 promoted migration of cancer cells. This study aims to characterize the expression of plexin-B1 in human invasive breast ductal carcinoma, and evaluate especially its relationship with HER-2 expression in regards to lymph node metastasis. Methods: Expression of plexin-B1 in 94 patients diagnosed with invasive ductal carcinoma, not other specified were explored immunohistochemically on paraffin embedded tissue sections. For each section, three best-stained hotspots and the whole-slide tumor area were evaluated using an intensity distribution score (IDS), a modified H-score system, for the expression of plexin-B1. Expression was categorized as high or low using the median score as a cutoff for statistical analysis. Results: This study demonstrated that invasive breast ductal carcinomas variably expressed plexin-B1. Eighty-two point six percent of best-stained hotspots coincided with the tumor invasive front. In addition, high average 3-hotspot IDS of plexin-B1 expression had higher numbers of lymph node metastasis ($p=0.032$). Limiting to estrogen receptor positive cases or HER-2 overexpressed cases, high plexin-B1 expression by the whole-slide assessment was paradoxically associated with absence of lymph node metastasis ($p=0.009$ and $p=0.039$, respectively). Conclusions: Heterogeneity of plexin-B1 expression in human invasive breast ductal carcinoma was demonstrated. Association between plexin-B1 expression and lymph node metastasis was complex as this association could be modulated in the context of estrogen receptor and HER-2 status. This study results contradicted the in vitro experimental results of co-expression of HER-2 and plexin-B1 in tumor progression. Key Words: Carcinoma, ductal, breast; Plexin-B1; Receptor, erbB-2

Concordance between Image Analysis to Manual HER2 Protein Scoring in Breast Cancer

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Background: HER2 gene amplification is the poor prognostic factor in breast cancer. Fluorescence in situ hybridization (FISH) is the universally gold standard method for assess HER2 status. The immunohistochemistry (IHC) study of HER2 protein overexpression was routinely performed in breast cancer targeted therapy. HER2 scoring was interpreted by American Society of Clinical Oncology (ASCO) guideline. The image analysis was also developed HER2 scoring and approved by Food and Drug Administration (FDA). This study compared HER2 scoring between Image analysis and pathologist. Methods: The HER2 IHC slides were analyzed by ScanScope, Aperio compared to routinely HER2 score in pathology report breast cancer in Srinagarind Hospital, Faculty of Medicine, Khon Kaen University, Thailand since June 2010 to December 2012. Results: The 66 slides showed concordance rate between image analyses with pathologist scoring was 56 cases (84.85%). Discordance cases found in 3 cases (4.55%) as positive HER2 by image but scoring 0/1 by pathologist. HER2 negative in 7 cases (10.61%) by image while were scored equivocally staining by pathologist. FISH were confirmed in 11 cases of concordant group, HER2 gene amplification in 6 cases of positive group and non-amplification in 5 cases of negative group. Conclusions: Image analysis is very useful for determine the HER2 status in pathology laboratory. The concordance between image analysis and pathologist interpretation is high and confirmed by FISH. Key Words: Image analysis; Genes, erbB-2; Gene amplification; Pathologist; In situ hybridization, fluorescence; Concordance

Metastasis-Associated in Colon Cancer 1 Predicts Poor Outcomes in Patients with Breast Cancer

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Background: Metastasis-associated in colon cancer 1 (MACC1) plays a role in cancer invasion and metastasis through upregulation of hepatocyte growth factor/MET-pathway, which is known as a critical regulator of the mitogen-activated protein kinase (MAPK) cascades. However, the potential involvement of MACC1 in breast cancer has not been assessed. Methods: To investigate MACC1 expression as a prognostic marker in breast cancer, we performed immunohistochemical staining for MACC1 expression in tissue microarrays consisting of 198 invasive breast carcinomas. To show the potential correlation of MACC1 and MAPK cascades, phospho-p44/42 MAPK was also analyzed. Results: Expression of MACC1 was detected in 109 of 198 (55.1%) invasive breast carcinomas. MACC1 expression was associated significantly with several clinicopathologic parameters, including estrogen receptor negativity ($p<0.01$), progesterone receptor negativity ($p<0.01$), and HER-2 positivity ($p<0.01$). The percentage of metastatic relapse was significantly higher in the MACC1-positive group (36/41, 87.8%) than the MACC1-negative group (73/157, 46.5%) ($p<0.001$). MACC1 expression significantly correlated with phospho-p44/42 MAPK expression ($p<0.05$). In a univariate survival analysis, a significant association was observed between MACC1 expression and decreases in disease-free survival ($p=0.001$) and overall survival ($p<0.001$). MACC1 expression was one of the statistically significant independent risk factors for disease-free survival ($p=0.001$). Conclusions: Our results suggest that MACC1 may serve as a new parameter for the prognostic prediction in patients with invasive breast carcinoma. MACC1 is likely to be involved in the regulation of MAPK cascades in invasive breast carcinoma. Key Words: MACC1; Breast neoplasms; Neoplasm metastasis; Mitogen-activated protein kinase 1
Low-Grade Periductal Stromal Tumor of the Breast Associated with Synchronous Bilateral Breast Carcinoma: A Case Report

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Low-grade periductal stromal tumor is an extremely rare biphasic tumor of the breast, which is characterized by a nodular and periductal stromal proliferation around open tubules and ducts devoid of a phylloides pattern. We report a case of low-grade periductal stromal tumor with synchronous bilateral breast carcinoma. A 45-year-old woman presented with bilateral palpable breast masses. Core-needle biopsy demonstrated invasive carcinoma in the left breast and ductal carcinoma in situ in the right breast. Fibroepithelial lesion with increased stromal cellularity was also observed in the right breast. Patient underwent bilateral breast-conserving surgery. The right breast showed a circumscribed nodular tumor (4.5 × 4.0 cm) and another smaller nodule with pale-yellow flecks (1.5 × 1.2 cm). Microscopically, the circumscribed tumor was composed of spindle cells that formed cuffs around multiple open tubules and ducts. The spindle cells had significant atypia with nuclear pleomorphism and moderate mitotic activity. The tumor cells were immunohistochemically positive for CD34 and vimentin, but were negative for smooth muscle actin, CD117, and estrogen and progesterone receptors. A diagnosis of low-grade periductal stromal tumor was established. The smaller nodule was an invasive carcinoma of no special type, grade II with a predominant intraductal component. In the left breast a grade II invasive carcinoma of no special type (maximum diameter, 1.5 cm) was discovered. Adjuvant chemotherapy and hormonal therapy were planned. To our knowledge this is the first case of low-grade periductal stromal tumor of the breast with synchronous bilateral breast carcinoma reported in the English-language literature.

Key Words: Breast neoplasms; Neoplasm, fibroepithelial; Synchronous; Carcinoma

Ki-67 Marker Index Indicating the Malignant Degree of Invasive Ductal Carcinoma Mammae

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Background: Breast cancer as important health problem in developed and developing countries. In Indonesia, according to the data of health department of 2008, the rank of it shift from the second to the first among 10 most frequent cancers in females, The majority of breast cancer is ductal invasive type. Uncontrolled cell proliferation represents malignant characteristic of neoplasia as breast cancer, represented by Ki-67 proliferation marker immunohistochemically. This study to analyze the index of Ki-67 according to the malignant degree of invasive ductal carcinoma mammae. Methods: The study using a cross-sectional method, utilizing twenty formalin fixed paraffin embedded specimen with histologically diagnosed as ductal invasive type of breast cancer were tested for Ki-67 immunohistochemical staining, with antigen-retrieval to block endogen peroxidase by heat procedure using microwave. The proportion of Ki-67 positive nuclei was enumerated and 20% cut off value was used to distinguish low and high proliferation index, statistically analysis was done using the chi-square test. Results: Histologically, high grade malignancy 12 cases (60%), and low grade malignancy 8 cases (40%). The half of patients showed low Ki-67 index and the rest high Ki-67 index. Seven cases (70%) with Ki-67 index <20% showed low grade while 9 cases (90%) with ≥20%, showed high grade malignancy. Statistical analysis showed positive correlation significantly (p < 0.025) between Ki-67 index with histological grading of the tumor. Conclusions: The higher the Ki-67 marker index the higher the grading.

Key Words: Breast neoplasms; Ductal invasive type; Neoplasm grading; Ki-67 antigen; Proliferative marker

Morphologic-Molecular Recurrence Predictive Model for Invasive Breast Carcinoma in a Standard Treatment Setting

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Background: Morphologic features and molecular subtypes are associated with recurrence in invasive breast carcinoma (IBC). Their independent role and correlation have not been well established. Methods: To identify independent predictors of recurrence, morphologic features, including histologic grade (HG), fibrotic focus (FF), extensive intraductal component, lymphocytic infiltrates (LI), lymphovascular invasion (LVI), necrosis, margin, and TNM stage, and molecular subtypes approximated by immunohistochemistry were analyzed in 624 patients with IBC receiving standard treatment and available follow-up data. A recurrence predictive model was constructed and validated in another independent population. Results: Ninety-eight recurrences were observed (mean follow-up period, 75 months). Morphologic features, including high HG (p = 0.003), LVI (p = 0.004), mild LI (p = 0.011), FF (p = 0.017) and high TNM stage (p < 0.001), and molecular subtypes, namely HER2OE (p = 0.010) and basal-like (p < 0.001) were independent predictors of recurrence. The correlation of morphologic features and molecular subtypes varied, with luminal A showing features correlated with better prognosis, including low HG and low level of its three contributing factors (p < 0.001), non-LVI (p = 0.009), non-necrosis (p < 0.001), low pT (p = 0.002), pN (p = 0.028), and TNM (p = 0.001) stage, but mild LI (p < 0.001). A recurrence predictive model was constructed and validated with independent cohorts. Prognostic index based on these seven predictors showed a strong significant correlation with recurrence (chi-square, 80.7; p < 0.001). Conclusions: Both morphologic features and molecular subtypes are independent recurrence predictors of IBC. A model based on these morphologic-molecular features is powerful to predict recurrence and can be validated. Morphologic features correlated with better prognosis are prone to be identified in luminal A subtype.

Key Words: Breast; Carcinoma; Recurrence
Clinical Significance of EZH2 Expression in Invasive Lobular Carcinoma of the Breast
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Background: Invasive lobular carcinoma (ILC) is the second most common histologic type of breast cancer, but the prognosis of ILC is still controversial. Enhancer of zeste homolog 2 (EZH2), the catalytic subunit of the polycomb repressive complex 2, is frequently overexpressed in various cancers. This study evaluated the relationship between clinicopathologic characteristics and prognostic factors of ILC and EZH2 expression. Methods: We retrospectively reviewed the medical records of 54 patients with ILC and selected 48 cases. Immunohistochemistry for EZH2 was undertaken. Results: We defined ILCs as dis cohesive cells with a linear or nonlinear growth pattern. No statistically significant difference was found for most variables, including multifocality, tumor stage (pT), lymph node stage (pN), estrogen receptor and progesterone receptor. In contrast, nuclear grade was statistically significant and EZH2 expression was associated with high nuclear grade. In total, 80% of nuclear grade 3 had an EZH2 score of 4 and 86% of nuclear grade 1 had EZH2 scores of 1 and 2. Our cases had a score of 3 for tubule formation and a score of 1 for mitoses and so the histologic grade consisted of grades 1 (7 cases) and 2 (42 cases) depending on the nuclear grade. Conclusions: EZH2 expression was associated with high nuclear grade and most ILCs have histologic grade 2 with nuclear grade 2 or 3. Therefore, our opinion is that if ILC is diagnosed by separating the classic type and variants and considering both EZH2 expression and nuclear grade, the Nottingham grading system would be a more accurate prognostic factor.

Key Words: Breast; Carcinoma, lobular; EZH2

Co-existent Lesions in the Mucocele-like Lesions of the Breast
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Background: Mucocele-like lesions (MCL) are commonly observed in the needle biopsy section obtained from "microcalcification." The aim of this study is to evaluate the prevalence of coexistent lesions with MCL in the ipsilateral and contralateral breasts. Methods: The materials were 105 MCL cases during recent 5 years. Based on pathological findings, bilaterality, presence of atypia of MCL, and coexistent lesions in the both breasts were evaluated. Results: Bilateral MCLs were noted in 8 cases (7.6%), and malignant MCL was only one case (1.0%). MCL was the most commonly occurred in fourth decade (44.8%), third decade (25.7%), second decades (14.3%), fifth decades (12.4%) and over 50 (2.9%), respectively. In the ipsilateral breast, columnar cell lesions (CCL) were coexistent in 59 cases (56.2%), and atypical CCL or atypical ductal hyperplasia, ductal carcinoma in situ, and invasive carcinoma were noted in 11 (10.5%), 5 (4.8%), and 6 cases (5.7%). In the contralateral breast, CCL was found in 18 cases (17.1%), atypical CCL/typical ductal hyperplasia in 4 cases (3.8%) and invasive carcinoma in 5 cases (4.8%). Conclusions: MCL might be closely related with CCL, and more worrisome lesions in the ipsilateral or contralateral breast in 21.0% and 8.9%. Careful follow-up is needed if MCL was identified in the needle biopsies.

Key Words: Mucocele-like lesion; Columnar cell lesion; Breast

Re-appraisal of p53, Ki-67, and COX-2 Expressions According to the Immunophenotypes of Breast Cancers
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Background: The prognostic and predictive roles of Ki-67, p53, and cyclooxygenase 2 (COX-2) expression in the invasive ductal carcinoma (IDC) were well known, however, the cutoff values for these markers were not standardized yet. In this study, re-interpretation of these markers using new cutoff values was done. Methods: Immunophenotypes of 290 IDC cases were re-evaluated based on Ki-67 labeling index (<10%, 10-20%, >20%). p53 expression was interpreted as negative, low (<2/3) and high (>2/3), which was regarded as "positive," and COX-2 expression was categorized into negative, weak/focal (<50%) and diffuse (>50%), which was regarded as "positive." The significances of p53 and COX-2 expression based on new cutoff values were analyzed. Results: The proportions of luminal type A and luminal type B were 54.1% and 9.8%, but those were changed into 27.0% and 36.8%, respectively, after application of Ki-67 labeling index (>20%). Positive rate for p53 expression was decreased from 31.0% to 24.8% after applying new cutoff value. It was higher in basal-like and HER-2 types, and correlated with histological grade, but not with T and N stage. Positive rate for COX-2 expression was decreased from 87.9% to 65.5% based on new cutoff value, and was higher in luminal type A and B, HER-2, triple negative and basal-like type in decreasing order, and negatively correlated with histological grade, but not with T and N stage. Conclusions: For the determination of immunophenotypes, application of new Ki-67 cutoff criteria will be needed. New cutoff value for p53 would not be so significant, but that of COX-2 might be informative in some extent.

Key Words: Breast neoplasms; Tumor suppressor protein p53; Ki-67 antigen; Cyclooxygenase 2

Characteristic Histopathologic Features after Chemotherapy Mimicking High Grade Carcinoma of the Breast Cancer
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Background: The characteristic and diverse histopathologic features after neoadjuvant chemotherapy in advanced breast cancer are well-known. However, in some circumstances these pleomorphic features mimicking the high grade carcinoma or apocrine carcinoma. This study aims to describe the morphological features found in breast cancer after chemotherapy because these have not been detailed previously. Methods: Histological sections were examined from 21 cases of advanced breast carcinoma that had been treated by preoperative chemotherapy. The morphology was compared with any pretreatment biopsy specimens or cytology that had been performed. Results: We observed a characteristic pattern of cellular fibrous tissue with peribulbar lymphocytic infiltrate and pronounced stromal changes, macrophages, coagulative necrosis of range from 5% to 60%, and characteristic bizarre nuclear and cytoplasmic features. The nuclear features include giant bizarre nuclei, bi- or multinucleation with prominent nucleoli, chromatim clumping, and karyorrhexis. The cytoplasm reveals large clear, vacuolar changes, abundant eosinophilic and dense condensed cytoplasm. In 2 patients, only microscopic, scattered or no tumor cells were left after chemo-therapy, but the tumor cells were present all the axillary nodes. Conclusions: Because preoperative chemotherapy is being increasingly in the management of advanced breast cancer, pathologist should be aware of the resultant morphological features and to differentiate from high grade carcinomas or apocrine-type carcinomas. In those cases accurate tumor typing and grading is impossible. The number of cases in this study is small, and more large numbers of cases of prospective studies with follow up will be necessary to determine a good morpho-logical response to chemotherapy.

Key Words: Postchemotherapy; Histopathology; Breast neoplasms

Clinicopathologic Analysis of Breast Cancer According to Subtypes Determined by Immunohistochemistry
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Background: Treatment and prognosis of the breast cancer can be affected by molecular subtype determined by gene expression profiling as well as stage. Classification according to immunohistochemistry (IHC) results is consistent with the molecular subtype. The purpose of this study is to classify subtypes according to IHC and to analyze the differences in clinicopathologic features among the subtypes. Methods: Subtypes were determined by IHC expression of estrogen receptor, progesterone receptor, human epithelial growth factor receptor 2 (HER2) and ki-67 index in 299 cases of invasive ductal carcinoma: luminal A (LA), luminal B (LB), HER2-enriched (HE), and triple negative (TN). We analyzed the association with the subtypes and clinicopathologic characteristics. Results: Nuclear and histologic grades and p53 overexpression were the highest in HE and TN, followed by LB and LA. Breast cancer with no ductal carcinoma in situ component was more frequently observed in TN than the other subtypes. Pathologic T stage of TN was higher than those of LA and LB. Ki-67 proliferation indices of HE and TN were higher than those of LB and LA. Pathologic N stage and patients' age were not significantly different among subtypes. Conclusions: This study showed each subtype had its specific clinicopathologic features. It will help to select the most effective way to predict the prognosis and determine the treatment plans for a patient with breast cancer.

Key Words: Breast neoplasms; Immunohistochemistry; Molecular subtype; Pathology

Molecular Classification of Metaplastic Carcinoma of Breast Using Surrogate Immunohistochemical Staining
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Background: The purpose of this study is to investigate molecular subtyping and implications on metaplastic carcinoma according to surrogate immunohistochemical staining. Methods: Following tissue micro-array on 34 cases of metaplastic carcinoma, immunohistochemical staining for cytokeratin 5/6 (CK5/6), epidermal growth factor receptor (EGFR), claudin-3, claudin-4, claudin-7, E-cadherin, signal transducer and activator of transcription 1 (STAT-1), androgen receptor (AR), and glutamyltransferase (GGT) were performed and classified as the following: basal-like type (CK5/6 positive and/or EGFR positive), molecular apocrine type (AR positive and/or GGT-1 positive), claudin low type (claudin-3, claudin-4, or claudin-7 negative, and/or E-cadherin negative), immune-related type (stromal STAT positive), mixed type (more than 2 types mixed), and null type (not belonging to any other subtype). Association with triple negative breast cancer subtype and clinicopathologic parameters was investigated. Results: Among the 34 cases of metaplastic carcinoma, 13 were basal-like type (35.2%), 9 were mixed type (26.5%), 8 were null type (23.5%), 3 were claudin-low type (8.8%), and 1 was molecular apocrine type (2.9%). Depending on cell type, there were differences between molecular subtypes with the matrix-producing type occupying the largest proportion in the basal-like, null, and mixed types. The spindle cell type represented the largest proportion in claudin-low type and molecular apocrine type and the squamous cell type served as the largest proportion in basal-like type. Conclusions: After molecular subtype classification of metaplastic carcinoma using surrogate immunohistochemical markers, the largest number of cases was classified as basal-like type, followed by mixed type, null type, claudin-low type, and molecular apocrine type. There were differences between molecular subtypes according to cell types.

Key Words: Breast; Metaplastic carcinoma; Molecular subtype; Immunohistochemistry

Expression of Nerve Growth Factor and Heme Oxygenase-1 Predict Poor Survival of Breast Carcinoma Patients
Sang Jae Noh • Jun Sang Bae • Urangoo Jamiyandorj • Ho Sung Park

Background: The characteristic and diverse histopathologic features after neoadjuvant chemotherapy in advanced breast cancer are well-known. However, in some circumstances these pleomorphic features mimicking the high grade carcinoma or apocrine carcinoma. This study aims to describe the morphological features found in breast cancer after chemotherapy because these have not been detailed previously. Methods: Histological sections were examined from 21 cases of advanced breast carcinoma that had been treated by preoperative chemotherapy. The morphology was compared with any pretreatment biopsy specimens or cytology that had been performed. Results: We observed a characteristic pattern of cellular fibrous tissue with peribulbar lymphocytic infiltrate and pronounced stromal changes, macrophages, coagulative necrosis of range from 5% to 60%, and characteristic bizarre nuclear and cytoplasmic features. The nuclear features include giant bizarre nuclei, bi- or multinucleation with prominent nucleoli, chromatim clumping, and karyorrhexis. The cytoplasm reveals large clear, vacuolar changes, abundant eosinophilic and dense condensed cytoplasm. In 2 patients, only microscopic, scattered or no tumor cells were left after chemo-therapy, but the tumor cells were present all the axillary nodes. Conclusions: Because preoperative chemotherapy is being increasingly in the management of advanced breast cancer, pathologist should be aware of the resultant morphological features and to differentiate from high grade carcinomas or apocrine-type carcinomas. In those cases accurate tumor typing and grading is impossible. The number of cases in this study is small, and more large numbers of cases of prospective studies with follow up will be necessary to determine a good morpho-logical response to chemotherapy.

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Key Words: Breast; Metaplastic carcinoma; Molecular subtype; Immunohistochemistry

Expression of Nerve Growth Factor and Heme Oxygenase-1 Predict Poor Survival of Breast Carcinoma Patients
Sang Jae Noh • Jun Sang Bae • Urangoo Jamiyandorj • Ho Sung Park
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Background: Nerve growth factor (NGF) is a member of neurotrophins and has been suggested to induce heme oxygenase-1 (HO1) expression. Although the role of HO1 in tumorigenesis still remains controversial, recent evidence suggested NGF and HO1 as a tumor-progressing factor. However, the correlative role of NGF and HO1 and their prognostic impact in breast carcinoma (BRCA) is unknown. Methods: We investigate the expression and prognostic significance of the expression of NGF and HO1 in 145 cases of BRCA. Results: Immunohistochemical expression of NGF and HO1 was seen in 43% and 57% of BRCA, respectively. The expression of NGF and HO1 was significantly associated with each other, and both have a significant association with HER2 expression and latent distant metastasis. The expression of NGF and HO1 predicted shorter overall survival (OS) and relapse-free survival (RFS) of BRCA by univariate analysis. Multivariate analysis revealed NGF expression as an independent prognostic indicator of OS and RFS. Combined expression pattern of NGF and HO1 was an also significant prognostic indicator of OS and RFS by univariate and multivariate analysis. Interestingly, the patients have a tumor co-expressing NGF and HO1 showed the shortest OS and RFS. Conclusions: This study has shown that the expression of NGF and HO1 could be prognostic indicators of BRCA and suggest that NGF-HO1 pathway could be a therapeutic target of BRCA patients.

Key Words: Breast; Carcinoma; Prognosis; Nerve growth factor; Heme oxygenase-1

Clinicopathologic Correlation of the Initial Surgical Margins of Breast Conserving Surgery in Association with Preoperative Biopsy Methods
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Background: We studied to evaluate the clinicopathologic variables and the impact of preoperative biopsy types with the positive initial surgical margins in the breast conserving surgery. Methods: Intraoperative frozen section analyses of 306 patients who underwent breast conserving surgeries were carried out and re-excisions were done when surgical margins were positive. Clinicopathologic variables including age (<45 years or ≥45 years), tumor size (≤2 cm or >2 cm), histologic grade (G1/G2/G3), histologic morphology (carcinoma in situ/invasive ductal/invasive lobular), presence of lymphovascular invasion, extensive intraductal component (present/absent), axillary nodal status (present/absent), estrogen receptor, progesterone receptor, HER-2 status (negative/positive), and pre-operative biopsy types were evaluated for correlation with the positive surgical margin. Results: In the 35 out of the 306 patients (11.4%) who had positive initial surgical margins, each of the preoperative core needle biopsy, VABB, and excision, showed positive initial surgical margins in 10%, 25%, and 16%, respectively (p = 0.35), and the re-excision rates for each were 8.2%, 20%, and 8.7%, respectively (p = 0.39). The independent predictors of positive initial surgical margins were presence of extensive intraductal component (EIC; p = 0.004), invasive lobular carcinoma (p = 0.003), and histologic grade (p = 0.004) and the remaining variables did not show significant correlation. Conclusions: Patients with invasive lobular carcinoma, EIC and high histologic grade require thorough preoperative and intraoperative assessments when deciding on the extent of the surgical margins in breast conserving surgery. Even though preoperative biopsy method was not an independent predictor, preoperative VABB had higher rates of positive surgical margin and re-excisions compared to core needle biopsy.

Key Words: Mastectomy, segmental; Vacuum assisted breast biopsy; Initial surgical margin

Prognostic Significance of Tumor Associated Macrophages in Invasive Breast Carcinoma, No Special Type
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Background: Macrophage is one of the major cellular components of tumor microenvironmnet, are polarized into M1 type, and M2 type. M1 has been known as antitumoral, whereas M2 as protumoral. Tumor associated macrophages (TAM) is a subpopulation of M2 macrophages, which enhance tumor growth, suppress immune response, and facilitate invasion and metastasis. Purpose of this study is to evaluate the M2 TAM, and M1, to clarify the prognostic significance of TAM in breast cancer, including the impact of TAM in tumor angiogenesis. Methods: A total of 194 cases of breast cancer were used for immunohistochemical expression of NGF and HO1 to clarify the prognosis of TAM in breast cancer. Microvessel density and overall survival (p = 0.004), invasive lobular carcinoma (p = 0.003), and histologic grade (p = 0.004) and the remaining variables did not show significant correlation. Conclusions: Patients with invasive lobular carcinoma, EIC and high histologic grade require thorough preoperative and intraoperative assessments when deciding on the extent of the surgical margins in breast conserving surgery. Even though preoperative biopsy method was not an independent predictor, preoperative VABB had higher rates of positive surgical margin and re-excisions compared to core needle biopsy.

Key Words: Breast neoplasms; Tumor associated macrophage; CD163 antigen
**AP03-PP-0022**

**Tumor-Associated Macrophages as Predictive Marker in Breast Cancer with Neoadjuvant Chemotherapy**

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**Background:** Tumor-associated macrophages (TAM) are well known having anti-tumorigenic and pro-tumorigenic roles in various organs. However, it is still unclear how those function in the field of neoadjuvant chemotherapy. The purpose of the present study was to investigate whether TAM count from diagnostic biopsies could predict the outcome of 157 breast cancer patients who had received neoadjuvant chemotherapy. **Methods:** All tumors were subclassified into luminal A, luminal B, HER-2 positive, and triple negative group. Average numbers of TAM were numerically counted in high-power fields of immunohistochemical stained slides for HLA-DR (M1) and CD163 (M2) on core needle biopsy and divided into low and high groups each. Each group was statistically analyzed to correlate with pathologic complete response. **Results:** Pathologic complete response was achieved in 1.49% (1/67) in luminal A, 5.88% (1/17) in luminal B, 29.03% (9/31) in HER-2 positive, and 19.05% (8/42) in triple negative. Odds ratio was significantly higher in HER2 positive breast cancer as much as 4.745 (95% confidence interval, 1.730 to 13.020; p=0.001). **Conclusions:** TAM of each group was not statistically correlated with pathologic complete response. In this study, HER-2 positive group demonstrated better chemosensitivity than the others and TAM may not be a predictive marker of neoadjuvant chemotherapy. **Key Words:** Tumor-associated macrophage; Neoadjuvant chemotherapy; Breast neoplasms; Pathologic complete response

**AP03-PP-0023**

**p40 (ΔNp63) Expression in Breast Disease and Its Correlation with p63 Immunohistochemistry**

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**Background:** p63 protein is widely used to identify myoepithelial cells in breast disease. There have been no comparative studies of the p63 expression profiles of p63 protein in benign proliferative diseases and malignant tumors of the breast, and analyze their diagnostic utility and clinical implications. **Methods:** We selected 32 adenoses, 34 intra ductal papillomas, 31 ductal carcinoma in situ (DCIS), 257 invasive ductal carcinomas (IDCs), and 36 metaplastic carcinomas, which were excised and diagnosed at Severance Hospital, and created tissue microarray blocks from them. We investigated the expression patterns of the pan-p63 and p40 antibodies in various forms of breast disease using immunohistochemical assay. **Results:** We determined that p63 and p40 (Diagnostic BioSystems, DB) expression in myoepithelial cells was broadly similar and showed cognate clinicopathologic features, unlike p40 (CalBiochem, CB1). p40 (CB) was more sensitive (99.0%) but less specific (85.8%), and p63 was less sensitive (93.8%) in adenosis, intraductal papilloma, and DCIS. In IDCs, p63 and p40 (DB) had similar expression in cancer cells; p40 (CB) expression, however, was statistically different. In metaplastic carcinomas, both p63 and p40 (DB) had distinct expression profiles, according to their histologic subtypes. **Conclusions:** Finally, we conclude that p40 antibodies as well as pan-p63 antibody are specific and sensitive myoepithelial cell markers. Interpretation of p40 (CB) positivity in cancer cells, however, should be considered carefully, due to its relatively lower specificity. **Key Words:** p63; p40; Breast diseases

**AP03-PP-0024**

**Clinicopathologic Analysis of 35 Invasive Lobular Carcinomas of the Breast According to the Histologic Subtypes**

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**Background:** Invasive lobular carcinoma (ILC) of the breast is the second most common type of breast cancer. Several distinct variants of ILC have been described, however, their prognostic implications remain controversial. **Methods:** Thirty-five invasive breast cancers, which were surgically removed and diagnosed as ILC by morphologic features and no expression of E-cadherin were selected for study. The tumors were histologically divided into variants according to the criteria, and evaluated the expression of estrogen receptor (ER), progesterone receptor (PR), c-erbB2, p53, Ki-67, and gross cystic disease fluid protein 15 (GCDFP-15). **Results:** The tumors were classified as 18 classic (51.4%), 4 pleomorphic (11.4%), 4 solid (11.4%), 4 trabecular (11.4%), 3 tubulolobular (8.6%), and 2 alveolar (5.7%) variant. Tubulolobular carcinomas were included in classic type (60%), and the remaining 14 cases were categorized as non-classic type (40%) for analysis. The tumors of classic type showed lower tumor grade (p=0.053), Ki-67 labeling (p=0.053), p53 (p=0.007), and PR expression (p=0.007), compared to the non-classic type. Signet ring cell was seen in 7 cases, and histiocytoid and apocrine features were found in 6 and 2 cases, respectively. Three cases with ER negativity belonged to the classic type and had histiocytoid feature. One solid variant with signet ring cell was ER- and PR-positive and overexpressed c-erbB2, and one pleomorphic variant with apocrine feature was positive for GCDFP-15. **Conclusions:** Because classic ILCs including tubulolobular variant were associated with known favorable prognostic parameters compared to the non-classic type, subclassification of ILC is recommended in routine diagnostic practice to help in predicting the prognosis and deciding the treatment modality. **Key Words:** Invasive lobular carcinoma; Classic type; Non-classic type; Breast

**AP03-PP-0025**

**Plasma Cell Infiltration, IgG, and IgG4 in Invasive Breast Carcinoma with Medullary Feature**
**Background:** Invasive breast carcinoma with medullary feature (BCMF) is characterized by abundant inflammatory reaction. Some of BCMF show predominant plasma cell infiltration as inflammatory component. However, the nature and significance of plasma cell have been largely unknown. Significance of IgG4 deposition in some malignant tumor was reported recently. **Methods:** We selected 73 cases of BCMF, and classified as typical and atypical type. On the basis of percentage of plasma cells, we scored as 0, <10%; 1, 11-20%; 2, 21-30%; and 3, >31% in hot spot area. Immunohistochemical staining of IgG, and IgG4 was performed. Percentage of IgG, and number of IgG4 were calculated. Plasma cell score 3 were defined as plasma cell rich type. The results were compared with clinicopathological parameters. **Results:** Plasma cell scores were 0 in 17 cases (23%), 1 in 23 (31.5%), 2 in 18 (24.7%), and 3 in 15 (20.5%). The plasma cell rich group was higher in typical type (p=0.005). On immunohistochemistry, most plasma cells show IgG positivity. However, IgG4 was very rare, and was counted less than 3/HPF in 68 cases. There was no significant correlation of IgG or IgG4 score with clinicopathological parameters. Plasma cell rich group (score 3, n=15) was correlated with estrogen receptor positivity (p=0.023). **Conclusions:** Plasma cell is major component of BCMF, especially in typical type. The role of plasma cell affecting tumor microenvironment should be investigated. Most plasma cells express non-IgG4 class of IgG which suggests that BCMF is not related with IgG4.

**Key Words:** Invasive carcinoma medullary; Breast; Plasma cells; Immunoglobin G; IgG4

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**Expression of Autophagy-Related Proteins in Phyllodes Tumor of Breast**

**AP03-PP-0028**

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**Background:** Phyllodes tumors (PTs) are classified as fibroepithelial tumors and their histologic grade is determined primarily by the features of the stromal component. In this study, we examined the expression profiles of autophagy-related proteins in the epithelial/stromal component of PTs and analyzed their clinical implications. **Methods:** We selected 204 human PT samples and created tissue microarray blocks. Immunohistochemical assays for autophagy-related proteins (beclin-1, LC3A, LC3B, and p62) were then performed on these samples. **Results:** Higher grade PTs more frequently displayed cytoplasmic expression of beclin-1, LC3A, LC3B, and p62 in the stromal component (p<0.001). In univariate analysis, the following profiles were associated with shorter disease-free survival and overall survival: nuclear beclin-1 positivity in the stromal component (p=0.013 and p=0.044, respectively), LC3A positivity in the stromal component (p<0.001 and p<0.001, respectively), and p62 positivity in the stromal component (p=0.012 and p=0.004, respectively). **Conclusions:** We determined that increased activity of autophagy-related proteins correlated with a higher histologic grade and poorer prognosis in human PTs. These results lead us to conclude that the autophagy activity of the stromal cells plays a key role in the progression of human PTs.

**Key Words:** Autophagy; Breast; Grade; Metabolism; Phyllodes tumor

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**Expression of Metabolism Related Proteins in Triple Negative Breast Cancer**

**AP03-PP-0029**

**Eun Ji Oh** ∙ **Ja Seung Koo** ∙ **Min Ju Kim** ∙ **Woo-Hee Jung**

**Background:** The aim of this study is to investigate the glycolysis, glutaminolysis, mitochondrial oxidative phosphorylation related protein in triple negative breast cancer (TNBC) and to access the dominant metabolic type and its implication. **Methods:** We generated tissue microarray...
(TMA) using the formalin fixed paraffin embedded tissue from 129 patients who were diagnosed with TNBC. Immunohistochemical stainings of glycolysis related protein (Glut-1, CAIX, MCT4), glutaminolysis related protein (GLS1, GDH, ASCT2), mitochondrial enzyme (ATP synthase, SDHA, SDHB) were performed in the TMA. According to the immunohistochemical staining results, metabolic phenotypes were defined as follow; glycolysis type is positive in more than two markers out of Glut-1, CAIX, and MCT-4; glutaminolysis type is positive in more than two markers out of GLS1, GDH, ASCT2; mitochondrial type is positive in more than two markers out of ATP synthase, SDHA, SDHB. **Results:** Tumoral metabolic phenotype in TNBC is mitochondrial type (85.3%), glutaminolysis type (67.4%), glycolysis type (63.0%) in order of frequency. Stromal metabolic phenotype in TNBC is glutaminolysis type (37.2%), glycolysis type (16.3%), and mitochondrial type (14.0%) in order of frequency. Glycosis type in tumor was observed more frequently in basal like type than in nonbasal-like type (p=0.047). In both tumor and stroma, there was statistically significant correlation between glutaminolysis type and mitochondrial type (p<0.001). **Conclusions:** In TNBC, tumor cells showed the expression of glycolysis and mitochondrial metabolism related protein. Glycosis type in tumor was observed more frequently in basal like type than in nonbasal-like type.

**Key Words:** Breast; Glycolysis; Glutaminolysis; Mitochondria; Triple negative

**Clinicopathologic Significance of Ezrin Expression in Breast Cancer**

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**Background:** Ezrin is a number of ezrin-radixin-moesin protein families and is involved in interactions with cytoskeleton. Ezrin was also associated with tumor progression, metastatic dissemination, and poor survival in various cancers. The aim of this study is deducing a possible relationship between ezrin expression and clinicopathological factors including clinical outcome in breast cancer. **Methods:** Immunohistochemical analysis of tissue microarray with 202 surgically resected breast cancer specimens was performed to examine ezrin expression level and location. We also correlated ezrin expression with other clinicopathological features and prognosis. **Results:** The ezrin expression was associated with larger tumor size (≥2.5 cm, p=0.012), higher histologic grade (p=0.015), high pT (p=0.032), lymph node metastasis (p=0.076), and late stage (p=0.008). The ezrin expression trended to correlate with presence of ductal carcinoma in situ (p=0.080) and extensive intraductal component (p=0.070). The ezrin expression was not associated with cancer-specific survival. **Conclusions:** Ezrin is correlated with tumor progression and lymph node metastasis in breast cancer.

**Key Words:** Ezrin; Breast neoplasms; Tissue microarrays

**Clinicopathologic Analysis of Loss of ARID1A in Breast Cancer**

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**Background:** ARID1A is a tumor suppressor gene in several tumors. The aim of this study is to explore loss of ARID1A in breast cancer and to investigate its prognostic significance. **Methods:** Immunohistochemistry was performed on tissue microarrays in 226 cases of breast cancer. We retrospectively analyzed the clinicopathologic characteristics and prognosis. Overall survival time was assessed by the Kaplan-Meier method and Cox regression model. **Results:** Loss of ARID1A was demonstrated in 97 of 226 (43%) and was associated with high histologic grade (p=0.035) and high Ki-67 proliferating index (p=0.029). The loss of ARID1A group had a significantly shortened progression-free survival (p=0.012). However, there was no statistically significant difference between loss of ARID1A and cancer-specific survival (p=0.317). Multivariate analysis also revealed that loss of ARID1A was an independent covariate for poor progression-free survival (p=0.024). **Conclusions:** Loss of ARID1A is correlated with high histologic grade, high Ki-67 proliferating index, and shortened progression-free survival in breast cancers, indicative of aggressive tumor behavior. Although the biologic function of ARID1A in breast cancers remains unknown, the loss of ARID1A can provide new prognostic information about disease progression.

**Key Words:** ARID1A; Breast; Carcinoma; Immunohistochemistry; Prognosis

**Correlation between c-Myc Expression and Histopathological Differentiation on Invasive Ductal Carcinoma of the Breast**

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**Background:** Molecular pathologic is an important role in pathogenesis of breast cancer. The aim of this study was to investigate relationship between c-Myc and various histopathological differentiation on invasive ductal carcinoma (IDC) of the breast. **Methods:** Histopathological archives of IDC between January 2009 and December 2009 at Pathology Department, Dr. Soetomo Hospital was retrieved. One hundred and seventy six cases of IDC collected. This study was performed using cross sectional observational analytic design. We used immunohistochemical methods of c-Myc to examine 30 samples of IDC. **Results:** Statistical analysis show there is a significant difference of c-Myc in various histopathological differentiation of IDC. The difference is not significant in various differentiation of IDC. **Conclusions:** It was concluded that c-Myc expression not correlated with histopathological differentiation in IDC.
Key Words: Proto-oncogene proteins c-myc; Histopathological differentiation; Carcinoma, ductal, breast

Benefit of Intraoperative Examination of Breast Specimens
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Background: Nowadays on site examination of sentinel lymph nodes in breast carcinoma is standard method. In our laboratory beside this examination we use intraoperative assessment of the resection margins.

Methods: Since 2008 till 2013 we examined in our laboratory 750 segmentectomies of breast proper carcinoma. In all cases we assess intraoperatively the resection margins. We use macroscopic assessment and touch imprint cytology. Results: From the set of 750 examinations in 25% (188) on site pathologist recommended reresection of suspicious margins in one surgical procedure. In reresected specimens, we proved malignant structures in 62 cases (32%). Conclusions: On site examination of resected breast specimens significantly decreases number of the reoperations, especially after neoadjuvant therapy of breast cancer.

Key Words: Intraoperative; Resection margins; Breast

Loss of MicroRNA-200a Expression Correlates with Tumor Progression in Breast Cancer
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Background: miRNAs are 20-22 nucleotide-long, noncoding, small RNAs, involved in post-transcriptional regulation of many target genes. miRNA-200 family has been shown to play a crucial role in epithelial to mesenchymal transition in human cancers. Methods: To investigate the expression level of miRNA-200a in breast cancer, in situ hybridization (ISH) method was used. Formalin-fixed, paraffin embedded (FFPE) tissue of normal breast, ductal carcinoma in situ (DCIS), primary cancer, and metastatic lymph node were achieved and constructed to tissue microarrays. Results: MiRNA-200a expression was demonstrated in 95.2% of normal breast tissue and 80.4% of DCIS, whereas 178 (58.0%) out of 307 breast cancer and 83.3% of metastatic lymph node sample revealed loss of miRNA-200a expression (chi-square test, p<0.001). Moreover, loss of its expression correlated with high histologic grade (chi-square test, p=0.017) and perinodal tumor extension (chi-square test, p=0.026). However, miRNA-200a expression did not predict tumor recurrence or patient’s survival. Conclusions: In conclusion, loss of miRNA-200a is frequently observed in breast cancers, especially tumors with high grade histology. The findings suggest that miRNA-200a could play an important role in breast cancer initiation and progression.

Key Words: MIRN200 microRNA, human; Breast neoplasms; In situ hybridization; Lymphatic metastasis

Expression of Basal Phenotype Marker in Triple Negative Breast Cancer in N/E Thai Patient
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Background: Triple-negative breast (TNB) cancer is a high risk breast cancer that lacks the benefit of specific therapy. The triple-negative tumors were more likely to be advanced, poorly differentiated, and larger.

Key Words: HRNR protein, human; S100 proteins; Breast; Neoplasms; Disease progression
Moreover, it present in women of younger age and of lower socioeconomic status. But, these subtypes are association with the basal phenotype and show varying degrees of basal cytokeratin and myoepithelial marker expression. Therefore the aim of this study was to investigate the expression of basal-like marker in N/E Thai patient. Methods: The authors examined the TNB of N/E Thai women by using immunohistochemistry staining. The subjects were stained with epidermal growth factor receptor (EGFR), E-cadherin, p53, c-kit, and cytokeratin 5/6 (CK5/6), to characterize this specific subgroup of breast cancer and to identify prognostic markers that can identify tumors with more aggressive behavior. Results: We found that CK5/6 was expressed only in triple negative breast cancer whereas non-triple negative breast were not found (p<0.05). Significant differences between triple negative and non-triple negative for EGFR, E-cadherin, p53, and c-kit were not observed. However, expression of c-kit was tending to higher in triple negative than non-triple negative breast cancer (33.3% vs 20.59%). In addition, associations of non-negative were found with loss of expression of E-cadherin (67.74% vs 48.65%) although it was no significant. Conclusions: A panel of four antibodies (estrogen receptor–, progesterone receptor–, HER2–, and CK5/6+) may be accurately identify basal-like tumors in N/E Thai patient. However, these studies show that many basal-like tumors express c-kit, which suggests candidate drugs for evaluation in these patients.

Key Words: Triple negative breast cancer; Basal phenotype marker; Receptor, Epidermal growth factor; Cadherins; Cytokeratin 5/6

Clinicopathologic Analysis of Cystic Hypersecretory Lesion of Breast

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Background: Cystic hypersecretory lesion (CHL) of the breast is rare, and characterized by dilated ducts and cysts filled with thyroid colloid-like eosinophilic secretion. In this study, a clinicopathological and immunophenotypic analysis of CHL from 22 Korean patients was conducted. Methods: In the database of pathology of Samsung Medical Center from 1994 to 2012, archival tissue was retrieved from 22 women who had undergone surgical resection for CHL of the breast. Immunohistochemical staining was performed on the paraffin sections using monoclonal antibodies, including estrogen receptor (ER), progesterone receptor (PR), HER2, p53, Ki-67, and gross cystic disease fluid protein-15. Results: Three cases were cystic hypersecretory hyperplasia (CHH), 9 cystic hypersecretory intraductal carcinomas, and 10 invasive cystic hypersecretory carcinomas. All but one carcinoma had CHH portion. Eight CHL patients had accompanying intraductal papilloma (IDP). Whereas CHL with IDP group tended to have high ER/PR expression rate (7/8, 87.5%) and negative HER2 status (8/8, 100%), CHL without IDP group yielded relatively low positivity for ER (6/14, 42.9%, p = 0.07), PR (4/14, 28.6%, p = 0.02), and HER2 (1/8, 7.7%). CHL without IDP group was more frequently associated with invasive CHL (6/14 [42.9%] vs 2/8 [25%]) and less frequently columnar cell lesion (7/14, 50% vs 6/8, 75%). One patient of CHL without IDP group developed recurrence and died 60 months later. In other patients, there was no evidence of disease after an average follow-up of 60.5 months. Conclusions: CHL without IDP group tended to behave more aggressively than CHL with IDP group. Presence of IDP can be helpful for the prognosis prediction in CHL.

Key Words: Cystic hypersecretory hyperplasia; Cystic hypersecretory carcinoma; Invasive cystic hypersecretory carcinoma; Papilloma, intraductal; Breast

A Case of Fibromatosis-like Spindle Cell Carcinoma of Breast

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Fibromatosis-like spindle cell carcinoma is a rare subtype of metaplastic carcinoma of the breast and it is difficult to make diagnosis by not only fine needle aspiration cytology but also excisional biopsy. Herein we report a case of fibromatosis-like spindle cell carcinoma of the breast. A 48-year-old woman noticed her left breast mass and visited hospital. The tumor was lobulated and 2.5×2.7×1.9 cm in size. Fine needle aspiration cytology was performed and it showed that many spindle atypical cell with mucinous material on the background. Although there was no benign ductal cell clusters, we diagnosed it as phylloides tumor with borderline malignancy. The tumor was removed and showed white, solid and hard mass. Histologically, spindle and long oval shaped cells proliferated with abundant collagen fibers. Spindle cells showed positive for vimentin, smooth muscle actin, CD10 and negative for AE1/AE3, CAM5.2, cytokeratin 7, S-100 and CD34, and diagnosed it as fibromatosis at first. And then, additional immunohistochemical analyses were performed and spindle cells showed weak positive for cytokeratin 5/6, 34BE12 and positive for p63, and finally diagnosed as fibromatosis-like spindle cell carcinoma. She had a recurrence of neoplasm a year and 9 months after the excision and resected again. The tumor showed more aggressive histological pattern, higher cell density, more mitosis and invasion to surrounding adipose tissue. When we observe spindle cell neoplasm on the breast, we should consider in the differential diagnosis of not only mesenchymal neoplasms but also spindle cell carcinoma, and should perform immunohistochemical staining of several epithelial markers.

Key Words: Fibromatosis-like carcinoma; Carcinoma; Breast

Concordance between dc-SISH to FISH for Detected HER2/Neu Oncogene in Positive HER2 Protein Breast Patient at Northeastern Thai Region

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Key Words: HER2/Neu; Breast neoplasms; FISH; dc-SISH
Background: The ability of clinical assays to correctly assign HER2 amplification status is important in breast cancer management. Even fluorescence in situ hybridization (FISH) is the universally gold standard method for assess HER2 status. However, the longer time for staining and scoring slides, requirements for specialized training and fluorescence microscopy, and loss of the signal are the disadvantages of this method. Double-colour silver-enhanced in situ hybridization (dc-SISH) can correct the deficiencies in FISH because it is a rapid, fully automated assay providing permanently stained slides and are interpreted by conventional bright field microscopy which enables pathologists to evaluate slides within the context of tissue morphology.

Methods: The current study were evaluated the concordance between dc-SISH and FISH assays in determining the status of HER2 gene in a fifty-one positive HER2 protein breast cancers (+2 and +3 by immuno-histochemistry) at Northeastern Thai region. Overall concordance between dc-SISH and FISH was identified. Results: In this study, we found the concordance rate between IHC with dc-SISH is higher than with FISH (82.35% and 74.50%, respectively). The most important that, it has some cases are positive for IHC and dc-SISH but negative for FISH. Thus, this case would be missing to Herceptin therapy and survival would be adversely affected. Conclusions: Concluded that SISH display a novel approach for determine the HER-2 status in breast cancer. The overall concordance between SISH and FISH is excellent, and the interpretation of SISH results by pathologists is most reproducible using the HER-2/CHR17 ratio.

Key Words: In situ hybridization, fluorescence; Double-colour silver-enhanced in situ hybridization; Genes, erbB-2; Breast neoplasms