II-1

“A case report of breast cancer occurrence in conjunction with Turner syndrome”

Kyoto University Department of Breast Surgery

*Miru Okamura, Eiji Suzuki, Itsumi Uno, Maki Namura, Ryutaro Mori, Wakako Tsuji, Megumi Takeuchi, Takayuki Ueno, Hiroshi Ishiguro, Toshiyuki Kitai, Tomoharu Sugie, Masakazu Toi

We report a 35-year-old female who was diagnosed with breast cancer in conjunction with Turner syndrome. She has been administered hormone replacement therapy (HRT) , estrogen and progestin, for about 25 years with a diagnosis of Turner syndrome. Her chief complaint was nipple discharge and a tumor mass in her right breast. Breast ultrasound revealed a 60mm size cystic mass around E area. With mammotome biopsy, it was diagnosed as invasive ductal carcinoma. HRT was stopped and a mastectomy of the right breast and sentinel lymph node biopsy was implemented. Pathology after surgery confirmed it as invasive ductal carcinoma, pT1aN0(sn). Grade 1(3-1-1). ER:100%. PR:100%. HER2:1+. Ki-67:0.5%. E2 after surgery was not detected. Taking into consideration the hormonal environment of Turner syndrome, HRT was paused as an adjuvant hormonal therapy and conventional adjuvant therapy such as TAM was not applied. As she suffered from breast cancer in conjunction with Turner syndrome we report this case with bibliographic discussions.

II－2

“Pretracheal lymph node metastasis from occult thyroid carcinoma was difficult to distinguish of metastasis from breast cancer -the patient was treated with TC-FEC as a neo-adjuvant therapy”

Saiseikai Shigaken Hospital Department of Surgery 1) Pathology 2)

Kenichiro Fukuda 1), Yuji Fujita 1), Yosuke Ariyoshi 1), Hisataka Matsuo 1), Shin Nakajima 1), Junshin Fujiyama 1), Mamoru Masuyama 1), Masamichi Baba 2)

We report a 38-year-old female who came to see our department complaining rt. Breast tumor with pain. Invasive ductal carcinoma, ER(-), PgR(-), HER2(-) was diagnosed by needle biopsy. It was recognized that FDG accumulation were found at the primary focus, right axilla and pretracheal lymph nodes by PET and we diagnosed as T3N2aM1(pretracheal lymph nodes) StageIV. Then Chemotherapy of TC→FEC was administered. After the chemotherapy, the primary legion as well as axillary lymph node shrunk significantly. The accumulation persisted only in the pretracheal lymph node. Therefore we performed Bp and Ax and pretracheal lymph node excision. The result of pathology was pCR for the primary breast lesion and axillary lymph node and the pretracheal lymph node was diagnosed papillary thyroid cancer metastasis. Further examinations of thyroid was performed, however the apparent tumorous legion was not identified. Therefore in consultation with the patient, we decided not to performe a total thyroidectomy but planned regular examinations. Radiotherapy after surgery was given at the conserved breast, the supraclavicular fossa and para-sternum which was at the back side of the dissected pretracheal lymph node. Three years have passed since the surgery but no recurrence has been detected. It was considered that excision is preferable for all areas that it is possible to dissect in the case of isolated metastasis to diagnose pathologically.

II-3

“A case in which an additional partial excision of the breast towards the positive margin was performed after wide excision and breast reconstruction by autologous free dermal fat graft”

Kobe City Medical Center General Hospital, Department of Surgery 1), Department of Nursing 2)

Mariko Tokiwa 1), Yuichiro Kikawa 1), Hironori Kato 1), Satoshi Kaihara 1), Ryo Hosotani 1), Yumiko Fujimura 2)

In the case where wide excision, that is no less than quadrantectomy, is necessary, judging from the preoperative imaging tests to examine the extension of breast cancer, we should assume the possibility of a positive margin and an additional re-excision because the accuracy of frozen sections is limited. We should endeavor to adopt the plastic surgery taking such possibilities into consideration. When using a procedure of the relocation of the remnant mammary gland, identification of a positive margin will be difficult. Therefore we adopt autologous free dermal fat grafting in order to obtain both good cosmetic results and easy identification of a positive margin after breast wide excision. The advantages of autologous free dermal fat grafting are reported to be that it is a simple and convenient procedure with better survival of the grafted fat. Moreover as it necessitates no mobilization of the remnant mammary gland and the graft is en bloc, the identification of a positive margin and an additional re-excision are relatively easy, which we believe are great advantages. We report a case in which we performed wide excision and autologous free dermal fat grafting after confirming negative margins by frozen sections during surgery for a breast cancer which had extensive intraductal spread in the right A-E area, and implemented an additional re-excision including the positive margins after the postoperative intensive histopathological tests.

II-4

“Study of a case of spindle cell carcinoma which we experienced at our hospital”

Saiseikai Kyoto Hospital Department of Surgery

Tatsuya Kotani, Hiroshi Nishi, Hideaki Tsurudome, Kei Naito, Shoichiro Hikami

Spindle cell carcinoma is a special form of breast cancer which is a rare histological type of around0.1 to 0.2% of whole breast cancers.

Case 1

57 years old female with no family history of breast cancer came to the hospital after self identification of tumor mass in the left nipple-areola region 3 days before the first consultation. Examination by touch radius of 1.7cm, elasticity hard, surface smooth, mobility good, no dimpling. No enlarged axillary lymph nodes, we suspected breast cancer by looking at the screening, however during cytological diagnosis there was a small amount of spindle-celled tissue only, therefore judgment was difficult. Tumor marker before surgery was within normal range. Soon after, the tumor enlarged rapidly and the axillary lymph node enlargement also became expressed, therefore we urgently implemented breast muscle conserving mastectomy. Pathologically, most was made up of spindle-cells and we identified through screening an apparent cancer focus of epithelial nature moving towards spindle-cell, therefore we have diagnosed the case as spindle cell carcinoma.

WHO histological grade 3 (tubular formation;3, nuclear atypia;3, mitosis counts;3), axillary lymph node positive for metastasis (2/15), At immunohistochemical staining, it was triple negative of ER(-), PgR(-). HER2(-). AE1/AE3(+), vimentin(+), SMA(±) and it was resistant to anti-cancer drug (Epirubicin,cyclophosphamide). Lung metastasis, cardiac metastasis were expressed and the patient died after only about 5 months (and about 4 months after surgery) from her first consultation.

Case 2

59 years old female with no family history of breast cancer. She became aware of a tumor mass in her right breast lower-inner quadrant region and came to our hospital. It was identified on

examination by touch radius 1.0cm, elasticity hard, border clear, mobility good. With ichnography it was identified as 12x10mm, internal echo homogeneous, posterior echo there was enhancement, anterior border of the mammary gland no interruption. It was suspicious for malignancy at fine needle aspiration cytology. We implemented wide excision as well as sentinel lymph node biopsy, taking her age into consideration.

The pathological diagnosis was spindle-cell cancer. Lymph nodes (0/7), margin negative. WHO histological grade2, (tubular formation;3, nuclear atypia;2, mitosis counts;1). At immunohistochemical staining, it was triple negative of ER(-), PgR(-), HER2(-).

AE1/AE3(+), desmin(-), SMA(-), CK 7 (-), CK20(-), CD10(-), E-cadherin(-). After surgery the patient is making a satisfactory recovery and radiation therapy is implemented at 50Gy. As a supplement chemotherapy the patient has taken oral tegafur-uracil (UFT) for 2 years. There has been no recurrence since and the patient is alive.

Regarding prognosis of spindle-cell cancer, the connection with nuclear grade is speculated upon however the reports are various. There are reports of extremely bad prognosis, however there is no certain observation for effective supplementary treatment.

III-1

“Individualized treatment of luminal type breast cancer”

-Study of neoadjuvant endocrine therapy at our hospital -

Department of Breast Surgery, Kyoto University

Itsumi Uno, Ryutaro Mori, Shigehira Saji, Tomoharu Sugie, Miru Okamura, Maki Minamimura, Wakako Tsuji, Eiji Suzuki, Megumi Takeuchi, Takayuki Ueno, Toshiyuki Kitai, Masakazu Toi

[Purpose] We studied neoadjuvant endocrine therapy at our hospital

[Patients] Twenty two women with ER-positive, HER2-negative operable breast cancer underwent endocrine therapy before surgery between 2007 and 2010.

[Result] Fifteen cases were Luminal A and 8 cases were Luminal B. There were no differences in age among these two subtypes and clinical tumor stage were 21 of T1-2 and 1 of T4. In Luminal A, 6 cases received LET (Letrozole) and 9 cases had LET and CPA (Letrozole+Cyclophosphamide).

In Luminal B, 1 case received LET and7 cases had LET+CPA. In Luminal A, the objective response to LET and LET +CPA were: SD 4, PR 2 and SD 4, PR 5, respectively. In Luminal B, LET and LET + CPA achieved the clinical response of: SD 0, PR 1 and SD 1, PR 6, respectively. One case underwent mastectomy and the others received breast conserving surgery. 2 cases who received LET+CPA had the PEPI score 0 after surgery.

[Conclusions] Endocrine treatment before surgery contributes for a better conserving rate but the cases of unnecessary following chemotherapy were limited

III-2

“Study of safety of using Trastuzumab for elderly HER2 positive breast cancer patients”

Shiga University of Medical Science Hospital, Division of Breast and General surgery 1), Shiga University of Medical Science, Department of Surgery 2)

Yuki Kawai 1), Hajime Abe 1), Tsuyoshi Mori 1), Kaori Tomida 1), Aya Tokuda 1), Yoshinobu Nagasawa 2), Hirotomi Cho 1), Yoshihiro Kubota 1), Tomoko Umeda 1), Eiji Mekata 2), Tohru Tani 2)

With the increase of the incidence of breast cancer recently, it is expected that the number of elderly breast cancer patients indicated Trastuzumab administration will increase. In large-scale clinical trials showed the effectiveness of the administration of the Trastuzumab, the number of registered elderly cases was few and there is insufficient data on the safety of the elderly breast cancer patients.

In this report, we have studied the safety of administering Trastuzumab for elderly breast cancer patients over 70 years old at our hospital retrospectively.

[Patients] Fifteen cases (11 cases of adjuvant treatment and 4 cases of recurrent treatment) of over 70 year’s old HER2 positive breast cancer patients who were administered Trastuzumab.

[Results] Average age was 74.5 years old. Average administration period was 15.9 months. Five cases out of 15 are still being administered, and the longest administration was 57 months. All cases were in conjunction with chemotherapy and 3 cases were in conjunction with radiation therapy.

Average of left ventricular ejection fraction (EF) before administration of Trastuzumab was 67.5%. We have experienced a case where EF decreased by 10% during and after administration who is under observation for asymptomatic. As other adverse events, 4 cases were observed the infusion reaction.

[Discussion] We did not find any serious adverse events in all cases of HER2 positive breast cancer patients over 70 years old, and it was possible to administer Trastuzumab safely.

[Summary] In this study, the safety of Trastuzumab administration for elderly breast cancer patients was suggested and it is considered that this may become a highly tolerable treatment. However there is necessary to continue to observe the progression more, carefully.

III-3

“Effectiveness and safety of eribulin mesylate for advanced recurrence breast cancer patients: study of 10 cases at our hospital”

Nara City Hospital Lacteal Gland Center

Yoshimi Umeda, Totoki Tokugawa, Hiroshi Koyama

[Background] Reporting the effectiveness and safety of 10 cases where eribulin mesylate was used.

[Subject matter] 10 cases where eribulin mesylate was used for either surgery impossible cases or recurrence breast cancer cases between August and December 2011. Average age was 54.8 years old (44 to 66 years of age), average regimen number before chemotherapy was 5.1 regimens (2 to 7 regimens). All cases were administered at the outpatient department.

[Result] Administration cycle number average was 2.8 cycles (1 to 5 cycles). Of 6 cases, effect is to be assessed in the future and 3 cases where we have judged effectiveness were all PD. Of 1 case, the patient died after first administration by primary disease. The outset of side effects on the patients with expression of more than Grade3 was 1 case and we identified neutropenia and poor appetite. We acknowledged a total of 4 cases (40%) of neutropenia but we didn’t identify febrile neutropenia.

[Observation] In 90% of cases, eribulin mesylate was safely administered as outpatients. During the current study, we didn’t reach success. However, we consider by using it at an earlier stage of recurrence treatment in the future, we can expect a life extending effectiveness while maintaining QOL.

IV-1

“A novel method to set area of resection for breast conserving surgery at 10 MicroMark II® indwelling cases”

Kyoto Prefectural University of Medicine, Department of endocrine and breast surgery

Midori Morita, Koichi Sakaguchi, Mari Soushi, Aya Imai, Katsuhiko Nakatsukasa, Naruhiko Mizuta and Tetsuya Taguchi

As breast cancer screening using mammogram (MMG) has become more popular, many women can be screened and diagnosed in the early stages. Under such circumstances, DCIS with micro calcification without tumor formation is increasing.

There is no question that biopsy using stereo-guided Mammotome® (MMT) is the most effective way to diagnose calcifying lesion without tumor. At the same time, MicroMark II® is usually placed at the site of stereo-guided biopsy. However, it is difficult to confirm the exact location of MicroMark II® and all surgeons face with a great difficulty to set area of resection for breast conserving surgery. In many situations, relying on hematoma or scar of the biopsy, using the hook wire method, using radioscopy method, or differential THI method etc were applied to set area of resection. However, each method requires a special instrument and expert technique, moreover requires modality which is invasive to the patients.

Now, we will make suggestions on how to locate Micro Mark II® in non-invasive technique. By targeting MMG in the direction towards ML/CC with placing a metal chip on the skin which identifies the exact location of MicroMark II®, we are able to perform partial excision centering around it. With this method, no special instruments other than MMG are required and it is possible to set area of resection easily and precisely.

IV-2

“Study of optimum excision area by sequential MRI after drug therapy before surgery”

Japan Red Cross Wakayama Medical Center

Lacteal Gland Surgery Department 1), Radiology Department 2), Pathological Diagnosis Department 3)

Harumi Yamada 1), Hiroshi Yoshibayashi 1), Kanako Yamada 1), Mako Yamoto 1), Tomomi Nishimura 1), Kyohei Nakamura 2)

Kotaro Shimada 2), Kazuo Ono 3), Hiroaki Kato 1)

[Background] Drug therapy before surgery for primary carcinoma is being implemented in order to achieve the better breast conservation rate or to see the effect of drugs. However, the optimum excision area after drug therapy before surgery varies according to each institution’s policy.

[Purpose/ Method] We have studied retrospectively 53 cases of primary infiltrating carcinoma where we have implemented surgery after administrating drug therapy and before surgery at our hospital and we studied the optimum excision area by sequential MRI.

[Result] An accidental error of within 1 cm of which we made assumption from sequential MRI and pathological remaining tumor radius were 90.9% (30/33) in the chemotherapy group before surgery and 70.0% (14/20) in the endocrine therapy group before surgery. Also within the endocrine therapy group, there were 85.7% (12/14) post-menopause in the group and 33.3% (2/6) in the group pre-menopause.

[Observation] The tumor shrank centripetally in both the chemotherapy before surgery group as well as in the endocrine therapy post-menopause before surgery group. Also the accidental error which was assumed as tumor radius at sequential MRI and pathological remaining tumor radius were small. Therefore, there is a possibility of deciding an optimum excision area from sequential MRI.

IV-3

Study of breast reconstruction cases at our hospital

Matsushita Memorial Hospital Department of Surgery 1), Osaka University Graduate School of Medicine Department of Plastic Surgery 2), Takeda Clinic 3)

Ai Hironaka 1), Masahide Yamaguchi 1), Kazuhito Yamada 1), Takahito Nakano 1), Hiroaki Taiyo 1), Takeshi Shimizu 1), Hiroyuki Izumi 1), Tadao Ito 1), Naoki Tani 1), Shinji Okano 1), Akinori Noguchi 1), Tetsuro Yamane 1), Kenji Yano 2), Yasushi Takeda 3)

[Prologue] There is an increasing emphasis on the cosmetic results following curative surgical treatment for breast cancer. Reconstructive surgery is considered not only in mastectomy, but also in partial excision cases where a large margin is required and also in cases where there is cosmetic damage. Since December 2009, we have vigorously implemented breast reconstruction surgery at our hospital for patients who wish to have this procedure. Here we report our recent experiences with breast reconstruction surgery after curative breast cancer surgery at our hospital.

[Subjects] The subjects were 15 patients who underwent breast reconstruction out of 179 patients who underwent curative surgical treatment for breast cancer in our hospital between January 2010 and December 2011.

[Result] The average patient age was 48.1 years old. Four patients (one with bilateral breast cancer) were classified as Tis N0M0, 4 were T1N0M0, 2 were T2N0M0, and 5 were T2N1M0 for diagnosis before surgery. The surgical reconstruction methods were: insertion of a tissue expander for subcutaneous mastectomy in 6 patients, insertion of a tissue expander after mastectomy in 2, latissimus dorsi flap reconstruction for subcutaneous mastectomy in 2, and latissimus dorsi flap reconstruction for subcutaneous partial excision in 5.

[Summary] Out of 179 surgical patients, 15 (8.3%) wished to have breast reconstruction. The rate was highest among patients aged 40-50 at 26%. During breast partial excision with a large excision area, we achieved favorable cosmetic results with immediate latissimus dorsi muscular flap reconstruction. After curative surgery for breast cancer, it is important to consult with patients individually to select the appropriate reconstruction procudure for those who desire it.

IV-4

"Study of risk factors and prognosis of recurrence within breast after breast conserving surgery"

University Hospital, Kyoto Prefectural University of Medicine Department of endocrine and breast surgery

Katsuhiko Nakatsukasa, Mari Shoji, Hisui Morita, Aya Imai, Koichi Sakaguchi, Shigehiko Mizuta, Tetsuya Taguchi

Breast conserving surgery is recognized as a standard treatment in our country and the implementation rate has reached over 60% today.

However what is most disturbing as the implementation rate increases is the increase of recurrence within the breast. We have handled 1082 cases (RT non implemented 556 cases and RT implemented 526 cases) of breast conserving surgery, which were implemented between June 2000 and December 2008 as the subject matter, and we studied the risk factors and prognosis of beast recurrence. We report the result hereby.

We studied the margins in detail and as a result there is significantly more recurrence within the breast for a skin side positive margin cases for the non exposure of radiation group but we couldn’t see any significant difference for the group of patients who were exposed to radiation.

However for the group exposed to radiation, there was a tendency that there was more sporadic recurrence in case when the tumor is on the skin side and within 1mm and when they were positive at infiltrating focus. Also we reported in conjunction with cases when the margin was exposed. For the prognosis after recurrence within the breast, we divided them into new primary (NP) cases and true recurrence (TR) cases. We divided them again and studied them for re-conserving cases and for mastectomy cases.