LETTERS TO THE EDITOR

Uncertainties in the management of pleomorphic lobular carcinoma in situ of the breast still remain

Dear Editor,

Pleomorphic lobular carcinoma in situ (PLCIS) is a rare variant of LCIS that shares radiographic, histologic, and molecular profile pattern as observed in ductal carcinoma in situ (DCIS). The absence of E-cadherin expression by immunohistochemistry is the main characteristic of PLCIS compared to DCIS. Controversy exists as to whether a diagnosis of PLCIS on core needle biopsy (CNB) warrants follow-up surgical excision (FSE) to exclude an associated invasive malignancy. Guo and colleagues investigated the clinicopathological features and correlation with subsequent excision in 37 patients with PLCIS diagnosed by breast core biopsy (BCBx) [1]. They confirmed its aggressive biology and frequent association with multifocal invasive lobular carcinoma (ILC), as well as frequent presentation in patients with a family history of breast cancer. Associated with this, Fasola et al. [2] reviewed 78 cases of PLCIS diagnosed from 1998 to 2012 and confirmed the results of Guo et al. study [1]. Among all cases, 47 (60%) were associated with invasive carcinoma and/or DCIS after final surgical excision. As in Guo et al. study [1], most of the invasive pathologies were ILC (18 cases were classical ILC, 18 cases were PILC). The authors reported two local recurrences at a median follow-up of 50 months with both relapses in patients with PLCIS present at the surgical margin. Therefore, surgical re-excision or radiation therapy should be considered in cases of close or positive PLCIS surgical margins. Taken all together, PLCIS is a rare lesion with a poorly understood natural history and limited long-term clinical data. Further studies with larger cohorts of patients and longer follow-up period are urgently warranted.

References


Kadri Altundag
MKA Breast Cancer Clinic, Tepe Prime, Ankara, Turkey

Correspondence to: Kadri Altundag, MD.
E-mail: altundag66@yahoo.com

Preserved lenalidomide efficacy in a recurrent isolated subcutaneous mantle cell lymphoma relapse

Dear Editor,

A rare hematologic malignancy, mantle-cell lymphoma (MCL) is frequently an aggressive disease whose typical evolution includes repeated relapses, with only a small subset of patients having an indolent clinical course. Cutaneous involvement is very rare, only a few cases being reported. In this report we present of a patient with recurring isolated subcutaneous relapse of MCL, successfully re-treated with the immunomodulatory drug lenalidomide. An 83-year-old woman in very good shape presenting with malaise, minor recent weight loss of 1 kg, and diarrhea was diagnosed with Ann Arbor stage IVAX MCL. Computed tomography scan examination described the presence of a large (13x8 cm) mass in the right iliac fossa, with disseminated pelvic, abdominal, and mediastinal lymph node enlargement, and right pleural effusion. A biopsy of the pelvic mass found a diffuse proliferation with a typical cyclin D1+ MCL phenotype, and t(11;14)(q13;q32) translocation was present. The patient had an absolute lymphocyte count of 1.7 G/L, but with 45% CD19+ CD5+ cells showing peripheral blood involvement. Bone marrow cytological examination described no abnormal cells. Corticospinal fluid examination was also negative. Lactate dehydrogenase levels were elevated. The patient was treated with one course of COP, followed by one course of CHOP plus rituximab, then, because of poor tolerance (gastrointestinal symptoms), switched to 6 courses of bendamustin plus rituximab, achieving complete remission. She was continued on 6 two-monthly cycles of rituximab maintenance. One and a half years later, the patient presented with an isolated right lumbar subcutaneous mass of about 4x5 cm. A punch biopsy confirmed MCL relapse. Due to the advanced age, the patient was treated for a year with 4-weekly cycles of 21 days of lenalidomide 10 mg daily associated, for the first 6 cycles, with rituximab. The tolerance of the treatment was good with only grade 1 diarrhea as adverse event. A complete clinical and metabolic remission was documented at
CA 15-3 elevation during post-metastasectomy period may occur in breast cancer patients with oligometastatic liver metastases

Dear Editor,

MUC-1 is found in nearly all epithelial cells including liver cells, and its overexpression is often associated with colon, breast, ovarian, lung, and pancreatic cancers. CA 15-3 serum levels detect soluble forms of MUC-1, a transmembrane oncoprotein aberrantly overexpressed in breast cancers [1]. Systemic treatment is the main treatment method for breast cancer with liver metastases. However, some cases such as isolated oligometastatic or

[Figure 1. Combined PET/CT evaluation before (left) and after (right) 3-month single agent lenalidomide treatment on second relapse, showing complete disappearance of the right lumbar subcutaneous MCL relapse (arrows).]
Letters to the Editor

Neutrophil-to-lymphocyte ratio above 2 – advocate for lymph node dissection in prostate cancer

Dear Editor,

Neutrophil-to-lymphocyte ratio (NLR) is a marker of systemic inflammation, with implications in the carcinogenesis and tumor metastasis and has shown an association with poor prognosis in a number of malignant diseases [1].

A recent systematic review by Tang et al. [2] of 18 studies that analyzed 9,418 patients concluded that also in prostate cancer (PCa) high pre-treatment NLR is positively correlated with lymph node (LN) involvement (OR 1.616, 95%CI 1.167–2.239), but not with pathological stage (OR 0.827, 95%CI 0.637–1.074) or Gleason score (OR 0.761, 95%CI 0.555–1.044). Also, high NLR associates a higher recurrence risk in localized and locally advanced PCa (HR=1.367, 95%CI 1.126–1.636) and poorer overall survival (OS) (HR=1.628, 95% CI 1.41–1.879) for patients with locally advanced PCa in comparison with patients with lower pre-treatment NLR.

Furthermore, another meta-analysis of 14 publications and 16,266 patients confirmed the prognostic role of pre-treatment NLR for poorer OS (HR=1.44, 95%CI 1.32–1.57) and recurrence-free survival (HR=1.45, 95%CI 1.19–1.77) also in patients with metastatic castration-resistant PCa [3]. Likewise, follow-up NLR after 4 and 12 weeks of treatment with enzalutamide has a predictive significance for progression-free survival (HR=1.24, 95%CI 1.07–1.42 and HR=1.09, 95%CI 1.01–1.19, respectively) [4].

We analyzed 87 patients with localized and locally advanced PCa that underwent robotic radical prostatectomy with pelvic lymph node (LN) dissection in our department between 2009-2015. In the present study we did not include patients who received hormonal therapy or presented urinary tract infection. Lymphadenectomy was performed for a risk of positive LN on Memorial Sloan Kettering Center nomograms (MSKCC) higher than 4%. For these patients we assessed the pre-treatment NLR and we observed that it was significantly correlated with the presence of LN metastasis (p=0.008), but not with the pre-operative PSA (p=0.94), number of positive biopsy cores (p=0.06), clinical or pathological stage (p=0.48 and p=0.107, respectively), histological subtype (p=0.21) or Gleason score (p=0.797). Also, a NLR value above 2 showed a sensitivity of 77.7% and a specificity of 64.1% for the prediction of positive LN, with an AUC of 0.745 (p=0.001).

The results of our study come to support the idea that inflammation might promote metastasis progression, but it is not linked to the intrinsic tumor features, like Gleason score or tumor stage [5].

In conclusion, we consider that patients with pre-treatment NLR above 2 are at higher risk of harboring LN metastasis. We believe that NLR should be implemented in the MSKCC in order to refine the risk for LN involvement. This added evaluation should help the decision-making of the surgeon to perform a super-extended LN dissection as it might improve the oncological outcome of these patients or preserve the LN and reduce the risk of perioperative complications.

Acknowledgements

This paper was realized within the Partnership Programme in priority domains - PN-II, which runs with the financial support of MEN-UEFISCD, Project no. 247/2014.

References


Kadri Altundag
MKA Breast Cancer Clinic, Tepe Prime, Ankara, Turkey

Correspondence to: Kadri Altundag, MD.
E-mail: altundag66@yahoo.com
Chemotherapy dose adjustment in obese locally advanced or early breast cancer patients might affect survival outcome

Dear Editor,

The effect of obesity in breast cancer patients undergoing neoadjuvant chemotherapy (NAC) or adjuvant chemotherapy remains controversial. Liu and colleagues investigated the association between obesity and survival in breast cancer patients receiving adriamycin/taxane-based NAC [1]. They reported that obesity may negatively impact survival, with differences among tumor subtypes. However, the authors did not report about the adjustment of the chemotherapy dose to the patients’ exact body surface area (BSA) values. Karatas et al. recently reported that obesity had an adverse effect on pathological complete response (pCR) among women receiving NAC [2]. However, the authors did not uniformly adjust the dose to the patients’ exact BSA values, limiting them at a lower level of 2 m² to prevent side effects. Contrary to Karatas et al. study, Farr et al. found that obese women receiving full uncapped doses of anthracycline-taxane-based NAC had increased pCR and favorable progression-free survival and concluded that this could result from increased dose intensity with increased efficacy and toxicity [3]. Furthermore, Schwartzman and colleagues [4] tried to find out if weight gained during adjuvant chemotherapy was associated with worse survival outcomes among 1998 early-stage breast cancer patients. They reported that BMI increase of >0.5 kg/m² compared to maintaining body mass index (BMI) was marginally associated with increased locoregional recurrence risk (HR:2.53; 95% CI 1.18-5.45; p=0.017), adjusting for grade, stage, and radiation delivery on multivariate analysis. However, the authors did not give information about dose adjustment in patients gaining weight during the adjuvant chemotherapy period. Taken all together, dose adjustment in obese breast cancer patients receiving NAC or adjuvant chemotherapy might have an impact on survival and should be taken into consideration.

References

Kadri Altundag
MKA Breast Cancer Clinic, Tepe Prime, Ankara, Turkey

Correspondence to: Kadri Altundag, MD.
E-mail: altundag66@yahoo.com

Endocrine therapy in early-stage breast cancer care: defining the appropriate regimen and time frame

Dear Editor,

Endocrine therapy after breast cancer resection seems to play an important role in the management of patients with estrogen receptor (ER)-positive early-stage breast cancer. Women receiving adjuvant endocrine therapy have a reduced risk of locoregional and distant recurrence as well as death from breast cancer compared to no endocrine therapy [1]. Tamoxifen and aromatase inhibitors have been approved by the FDA as adjuvant hormone treatment regimens for both premenopausal and postmenopausal women with ER-positive early-stage breast cancer.

Several trials have assessed the efficacy of these regimens. In a trial comparing 5-year tamoxifen versus no
endocrine therapy, recurrence rate in the tamoxifen group was 50% lower during the first 5 years, while cancer-related deaths were 50% lower during 15 years compared to the no treatment group [2]. In postmenopausal women, recurrences while on aromatase inhibitors were by one-third fewer compared to tamoxifen with about 15% fewer deaths during the first decade [3]. A recent study by Pan et al. [4] found that distant recurrences in early-stage, ER-positive breast cancer women who received adjuvant endocrine therapy for 5 years only, occurred steadily within 20 years showing a strong relationship with the respective TN status of the tumor. Women in this cohort received different types of endocrine therapy (65% tamoxifen, 17% aromatase inhibitors and 20% a combination of them) [4]. However, this study did not provide a subgroup analysis of each individual treatment regimen, which would help clarify some matters.

In real life, women may switch from one regimen to another and also extend the hormone treatment period beyond the usual 5 years. For instance, women may receive additional treatment with an aromatase inhibitor after 5 years of tamoxifen or even switch to an aromatase inhibitor after 2 or 5 years of tamoxifen, for a total of 5 or more years of hormone therapy. It has been shown that extending endocrine therapy beyond 5 years may further reduce the risk of recurrence and mortality [5]. However, this is counterbalanced by some bothersome and even sometimes life-threatening side effects related to the continued hormone therapy: menopausal symptoms, osteoporosis, pulmonary embolism and endometrial cancer [5].

It is true that poor applicability of trial results to routine clinical practice is the most frequent criticism by clinicians of randomized trials. Importantly, clinical criteria for receiving adjuvant therapy do not always coincide with the breast cancer trials criteria (range, 17-56%). Community-based and trial populations sometimes differ significantly; therefore, results of trials should be more thoughtfully interpreted and wider applicability of trials is necessitated. Decisions about the type of adjuvant hormone therapy should be made on an individual basis. Finally, extending the duration of treatment beyond 5 years should balance the benefits against the additional side effects.

References


Diamantis I. Tsilimigras1, Ioannis Ntanasis-Stathopoulos1, Eleftherios Spartalis1, Michael Kontos1, Demetrios Moris1 1School of Medicine, National and Kapodistrian University of Athens, Athens, Greece; 2Department of Surgery, Duke University, Durham, NC, USA

Correspondence to: Demetrios Moris, MD, MSc, PhD, FACS. E-mail: dimmoris@yahoo.com

Should androgen suppression be used in salvage radiotherapy of biochemical recurrence after prostatectomy?

Dear Editor,

Although radical prostatectomy is most effective treatment modality in clinically localized prostate cancer, biochemical recurrence (persistence PSA elevation or elevation of PSA) is observed in 17-60% of patients during follow-up and metastasis occurs in 30% of these patients. Salvage radiotherapy (SRT) is an effective therapeutic modality that can be used in biochemical recurrence. In general, 5- or 5-year biochemical control rates are 30-70% in SRT [1,2].

The role of androgen deprivation therapy (ADT) used in combination with SRT is still under investigation. Currently, ADT isn’t preferred in SRT. However, there is an ongoing debate when ADT should be used. The results of ongoing trials on this topic are awaited. The preliminary results of 2 studies (GETUG-AFU 16 and RTOG 9601) suggesting better biochemical control with adjuvant ADT used in combination with SRT were released in 2016 [2,3]. Both studies reported that additional ADT increased biochemical relapse-free survival by about 20%. In GETUG-AFU 16 trial, 754 patients with pT2-4A pN0/cN0 prostate cancer and life expectancy over 10 years were randomized to SRT alone and SRT plus short-term ADT arms. SRT was delivered with 3D conformal technique using 66.6 Gy with normofraction involving the prostatic fossa and 46 Gy were delivered to pelvic lymph nodes in 16.6% of the patients. Five-year biochemical progression-free survival increased from 62 to 80% in the SRT plus ADT arm (p<0.0001). Overall survival increased from 95 to 96%, while prostate cancer specific death decreased from 2 to 1%; however, the differences between groups didn’t reach statistical significance [2].

In the RTOG 9601 trial, unlike GETUG-AFU 16 trial, patients with persistently elevated postoperative PSA and those with rising PSA levels between 0.2-4.0 ng/mL were randomized to receive bicalutamide (150 mg/dx) or placebo for 2 years after SRT using 64.8 Gy to the prostatic fossa. After a mean 7-year follow-up, overall survival was 91% in
the ADT arm and 86% in the placebo arm. Clinically, the detection rate of metastasis decreased from 12.6 to 7.4%. It was reported that addition of ADT to SRT didn’t increase toxicity. In both studies, it is apparent that there is a need for long-term follow up although there was no benefit in overall survival; however, biochemical control was improved by 20% [5]. Both the above-mentioned studies and ongoing 4 large, prospective studies (RTOG 534, SPPORT, EORTC 2043-30041 and RADICALS) will elucidate the role of ADT in SRT.

In conclusion, the role of additional ADT in SRT is still controversial. Based on available scientific evidence, ADT therapy is essential in SRT, at least in high-risk patients. The patient subgroup which will benefit from ADT hasn’t been identified yet. There is an ongoing debate about timing and dose of SRT, extent of therapeutic regions (prostatic bed or whole pelvis) and which patients require addition of ADT.

References


3. Shipley WU, Pugh SL, Lukka HR et al. RTOG 9601, a phase III trial in prostate cancer patients: Anti-androgen therapy (AAT) with bicalutamide during and after salvage radiation therapy (RT) following radical prostatectomy (RP) and an elevated PSA. J Clin Oncol 2016;34 (Suppl 2), abstr. 3.

Yasemin Benderli Cihan
Kayseri Education and Research Hospital, Department of Radiation Oncology, 3801 Kayseri, Turkey

Correspondence to: Yasemin Benderli Cihan, MD.
E-mail: cihany@erciyes.edu.tr