ORIGINAL ARTICLE

The positive impact of radiologic imaging on high-stage cutaneous squamous cell carcinoma management

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Background: There is limited evidence on the utility of radiologic imaging for prognostic staging of cutaneous squamous cell carcinoma (CSCC).

Objective: Review utilization of radiologic imaging of high-stage CSCCs to evaluate whether imaging impacted management and outcomes.

Methods: Tumors classified as Brigham and Women's Hospital (BWH) tumor (T) stage T2B or T3 over a 13-year period were reviewed to identify whether imaging was performed and whether results affected treatment. Disease-related outcomes (DRO: local recurrence, nodal metastasis, death from disease) were compared between patients by type of imaging used.

Results: 108 high-stage CSCCs in 98 patients were included. Imaging (mostly computed tomography, 79%) was utilized in 45 (46%) patients and management was altered in 16 (33%) patients who underwent imaging. Patients that received no imaging were at higher risk of developing nodal metastases (nonimaging, 30%; imaging, 13%; P = .041) and any DRO (nonimaging, 42%; imaging, 20%; P = .028) compared to the imaging group. Imaging was associated with a lower risk for DRO (subhazard ratio, 0.5; 95% CI 0.2-0.9; P = .046) adjusted for BWH T stage, sex, and location.

Limitations: Single institution retrospective design and changes in technology overtime.

Conclusions: Radiologic imaging of high-stage CSCC may influence management and appears to positively impact outcomes. Further prospective studies are needed to establish which patients benefit from imaging. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2016.08.051.)

Key words: cutaneous squamous cell carcinoma; staging; prognosis; radiologic imaging; disease-related outcomes; nodal metastasis; squamous cell carcinoma imaging.

With an estimated annual incidence of 700,000 cases, cutaneous squamous cell carcinoma (CSCC) is rivaled only by basal cell carcinoma for commonness in the United States.[1] Most patients with dermally-invasive (non−in situ) CSCC have an excellent prognosis and can be cured by surgical excision.[2] Poor CSCC outcomes, such as local recurrence (LR), nodal metastasis (NM), or death from CSCC, are estimated to occur in 3%, 4%, and 1.5% of dermally-invasive cases, respectively.[3,4] Although the risk of developing a poor outcome is quite low, there is a subset of CSCC cases that results in less favorable prognoses due to the presence of multiple risk factors.[3] These high-stage tumors highlight the importance of early diagnosis and accurate staging to guide treatment.

While the diagnosis of CSCC is confirmed through histological examination, there are no definitive recommendations for which CSCC tumors should be subject to further work-up. Based on the National

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Comprehensive Cancer Network (NCCN) guidelines for CSCC, imaging studies are indicated for tumors presenting with a suspicion of extensive disease,[5] defined as deep structural involvement (i.e., bone), perineural disease, or deep soft tissue involvement. However, despite these recommendations, the lack of consensus regarding high-stage CSCC staging prevents uniform imaging protocols among physicians.[6] Additionally, except for the usage of magnetic resonance imaging (MRI) for perineural disease, the guidelines fail to specify which type of imaging modality to use for different staging scenarios.

CAPSULE SUMMARY

- The utility of radiologic imaging for staging high-stage CSCCs is uncertain.
- Less than half of high-stage CSCCs received imaging. Patients that did not receive imaging were at a higher risk for developing poor outcomes.
- Imaging may be beneficial in the management of high-stage CSCC.

To the best of our knowledge, there are no prior studies that evaluate the impact of radiologic imaging on treatment and outcomes of high-stage CSCC. There is some evidence regarding the use of computed tomography (CT) and MRI for perineural spread of larger caliber nerves, but these studies do not address outcomes based on the receipt or absence of radiologic imaging.[7-9] In addition, a small retrospective case series using (18) F-fluorodeoxyglucose positron emission tomography/CT (PET/CT) in 12 cases of CSCCs found lymph node involvement in 25% and distant organ metastasis in 8%; however, this study included all cases of CSCC regardless of risk factors and did not evaluate the impact of the imaging results on management.[10] The objective of this study was to review a single center's utilization of radiologic imaging of high-stage CSCC tumors to evaluate whether the imaging changed management and correlated with disease-related outcomes (DRO).

METHODS

The Department of Pathology electronic database and the Research Patient Data Registry at Brigham and Women's Hospital (BWH) were searched to locate all patients with a diagnosis of cutaneous squamous cell carcinoma from January 1, 2000, through May 30, 2013. Cases were staged based on the BWH CSCC tumor staging system.[11] Because low-stage (BWH T1 and T2a) CSCC tumors have a low risk for recurrence, only high-stage tumors (BWH T2b and T3) were included in this study.[11-13]

The electronic medical records were reviewed to determine whether radiologic imaging was performed in association with the primary treatment. Medical records were reviewed for any type of imaging modality including CT, PET, MRI, ultrasound, and x-ray; however, no tumors in this cohort underwent imaging via ultrasound or x-ray. Cases were stratified into two groups: those that received imaging and those that received no imaging. Cases in the imaging group underwent additional chart review to obtain the following information: the date, type, and results of the imaging modality; the reason why imaging was performed; and the effect of imaging on patient management. The latter was determined by chart review of clinical notes and included an alteration in surgical approach or inclusion of radiation or chemotherapy. Additionally, for all included cases, the electronic medical records were reviewed for demographic information, follow-up time, tumor characteristics, and DROs. DROs of interest included, local recurrence (LR), nodal metastasis (NM), distant metastasis (DM), and disease specific death (DSD).

Statistical analysis and model building were performed analyzing each case individually. Patient and tumor characteristics were analyzed using descriptive statistics and frequency tabulation.

Chi-square and Fisher's exact tests were used to determine whether the use of imaging significantly differed with regard to LR, NM, DM, DSD, overall death, and any DRO. The Cox proportional hazards model was used to determine univariate and multivariate associations of risk factors with the development of any DRO. Fine and Gray competing risk analysis was used and death from non-CSCC causes was treated as a competing risk.[14,15]

Multivariate models were built through forward stepwise variable addition followed by backward elimination. In this form of model building, modeling begins with the variable with the largest effect estimate on univariate modeling. Other variables added are based on the variable with the next largest effect estimate and are retained in the model if the Wald test comparing the smaller model with the larger model is significant at $P \leq .05$, or if the P value of the χ^2 test comparing the 2 models is borderline ($>.05$ to .10) and addition of the variable changes the hazard ratios by at least 10%. Models were corrected for intra-patient correlation using the robust variance estimate because the analysis was case-based, rather than patient-based. Kaplan-Meier curves were generated to illustrate event-free survival for any DRO. All statistical tests were performed using a 2-