Ultrasound Examination and Fine Needle Aspiration Cytology—Useful for Followup of the Regional Nodes in Penile Cancer?

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Abbreviations and Acronyms

DSNB = dynamic sentinel node biopsy

FNAC = fine needle aspiration cytology

US = ultrasound

Accepted for publication August 20, 2013.

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Purpose: Routine followup of the groins of patients with penile squamous cell carcinoma after primary treatment consists of physical examination together with ultrasound of the groins, followed by fine needle aspiration cytology if suspicious. We assessed the value of this routine followup.

Materials and Methods: Using ultrasound and fine needle aspiration cytology we assessed 247 patients during followup who were treated from 2004 to 2010 and underwent dynamic sentinel node biopsy only or observation of the inguinal regions. A negative result was defined as no evidence of metastatic disease after at least 2 years of followup. We calculated the sensitivity, specificity, and positive and negative predictive values of ultrasound and ultrasound guided fine needle aspiration cytology using standard statistical methods.

Results: Recurrence was diagnosed in 47 of 247 patients (55 groins). In 40 of 55 groins (73%) recurrence was detectable by physical examination. In 12 of 15 cases of nonpalpable recurrence (80%) ultrasound guided fine needle aspiration cytology revealed the recurrence. We considered 217 groins to be suspicious on ultrasound followed by fine needle aspiration cytology. Fine needle aspiration cytology revealed tumor in 49 groins and showed false-positive findings in 1 patient after negative completion lymphadenectomy. Sensitivity and specificity were 87.3% (48 of 55 cases) and 99.9% (1,304 of 1,305), respectively.

Conclusions: Although inguinal recurrence manifests clinically in most patients, ultrasound guided fine needle aspiration cytology detected 80% of metastatic disease in patients with nonpalpable disease. Therefore, it has great value for detecting lymph node metastases during followup.

Key Words: penis; lymph nodes; carcinoma, squamous cell; biopsy, fine-needle; ultrasonography

Ultrasound together with FNAC is widely used to clinically stage the groin in patients with penile squamous cell carcinoma. High resolution probes visualize alterations in the size, shape and contour of lymph nodes and also show changes in cortical and hilar morphology, and texture that can reflect the presence of metastasis.[1] Vassallo et al described characteristics suggestive of metastases.[2] The lymph node shape (length-to-width ratio), cortex (peripheral hypoechoic) and hilus (central echogenic) are reviewed by US. Features suspicious for nodal involvement are a length-to-width ratio of less than 2, a concentrically or eccentrically wide cortex and a narrow to absent hilus.

0022-5347/14/1913-0652/0
THE JOURNAL OF UROLOGY®

http://dx.doi.org/10.1016/j.juro.2013.08.046
Vol. 191, 652-655, March 2014
Printed in U.S.A.

Changes in node architecture occur before the node enlarges and becomes clinically detectable. FNAC of nodes suspicious on US provides a more definitive diagnosis than US alone due to overlap of the US features of benign and suspicious lymph nodes.[3,4] This was also noted when staging the groin in women with vulvar cancer.[5–8]

In patients with clinically node negative penile cancer US is routinely done at our institution before DSNB. US detects occult metastases and decreases the rate of false-negative DSNBs.[4,9,10] US is also routinely performed to follow groins after DSNB, followed by US guided FNAC if suspicious nodes are seen, according to European Association of Urology (EAU) guidelines.[11,12] In the United States the National Comprehensive Cancer Network® guidelines are applied, which do not currently include the same recommendations.[13,14]

We assessed the role of US guided FNAC for detecting lymph node metastases of the groin during followup.

PATIENTS AND METHODS

Followup

Penile cancer followup has been standardized since 1988. After analyzing recurrence patterns the followup scheme was adjusted in 2001, adding routine US of the groin at each followup visit according to current EAU guidelines.[12,15] In nodes suspicious on US immediate FNAC is performed. Since 2004, all ultrasound images have been available digitally.

Patients

This study was performed in accordance with institutional ethical guidelines based on good clinical practice. A total of 247 patients after DSNB or patients in whom the inguinal regions were observed were under followup with US from 2004 to 2010. Median age was 64.9 years (range 33 to 97) and median followup was 38 months (IQR 27–54). Data on physical examination of the groins (eg palpable nodes), US and FNAC are prospectively maintained in our database of patients with penile cancer. Patients who underwent therapeutic inguinal lymph node dissection were excluded from analysis. The 2009 TNM classification for penile squamous cell carcinoma was used for staging.[12]

US Guided FNAC

Seven radiologists were involved in US guided FNAC of the inguinal regions of patients with penile cancer. Lymph nodes were classified according to the criteria of Vassallo et al.[2] FNAC was performed with a 23 gauge (0.6 mm) needle in suspicious nodes only and in an outpatient setting. If more than 1 node was detected, the radiologist aspirated the most suspicious node. Aspirated, smeared material was air dried and stained with May-Grunwald Giemsa. Patients underwent complete inguinal lymph node dissection on the ipsilateral side when FNAC was tumor positive. A negative result was considered truly negative if there was no evidence of metastatic disease after at least 2 years of followup.[15]

Statistical Analysis

Sensitivity, specificity, and positive and negative predictive values were calculated using standard statistical methods. To account for possible correlations between observations in patients we used the ratio estimator of the SE to calculate the CI.[16] All statistical analysis was done with IBM® SPSS®, version 20 and R, version 2.15.2 (R Project for Statistical Computing, Vienna, Austria).

RESULTS

In 247 patients a total of 1,360 groins were examined by US. A total of 55 groins were positive for tumor in 47 patients with a median age of 69 years (range 37 to 91) and a mean followup since diagnosis of 45 months (IQR 24–74) (see figure). The table lists tumor characteristics in these patients.

On US 217 of 1,360 groins (16%) were considered suspicious and were aspirated, of which 49 contained tumor cells. In the other 165 groins FNAC showed normal lymphoid cells or no cells.

Two patients with 3 tumor positive groins received palliative chemotherapy only and 5 with 5 tumor positive groins underwent radiotherapy only. In the other 41 patients with 48 groins completion inguinal lymph node dissection was performed. In 1 patient results in a single groin were false positive after lymphadenectomy. Thus, US guided FNAC detected 48 of 55 tumor positive groins, resulting in 87.3% sensitivity (95% CI 78.9–95.6), 99.9% specificity (95 CI% 99.8–100), 98.0% positive predictive value (95% CI 93.9–100) and 99.5% negative predictive value (95% CI 99.1–99.9).

Of the 55 groins positive for tumor 40 (73%) were already suspicious on physical examination. However, 15 groins had no palpable lymph nodes. Lymph node involvement was revealed by US guided FNAC in 12 of these groins. In the other 3 groins metastatic disease was missed by US guided FNAC but repeat DSNB together with treatment of the local recurrent tumor revealed metastatic disease. Consequently, in patients with regional recurrence but negative physical examination US guided FNAC detected 80% of metastases (12 of 15).

DISCUSSION

This study shows that 73% of inguinal recurrences were detectable by physical examination. In patients with normal groins on physical examination 80% of inguinal recurrences were discovered by US guided FNAC. This result demonstrates the value of US guided FNAC in the followup of inguinal nodes in penile cancer cases, underscoring the EAU guidelines recommendation.[12]