EDITORIAL COMMENT
The management debate continues!

In order to decrease the morbidity of inguinal lymph node staging among patients with invasive penile cancer (and negative inguinal examinations) risk adapted strategies are now commonly used to select candidates who are at low risk for inguinal microscopic dissemination based upon primary tumor histology and anatomic structure invaded. There appears to be consensus that factors associated with a "high risk of metastasis" (i.e. ≥ 50% or more) include stage ≥T2, poorly differentiated tumors and those exhibiting vascular invasion. Alternatively it is also agreed that stage Tis, Ta, and T1 well differentiated tumors (aka grade 1) tumors are candidate for observation due to the low risk of metastatic disease (i.e., 0%-10%). Where the stage T1 grade 2 tumors should reside has been controversial to say the least[1] (references 2, 3, 5-6,14 in manuscript) related to the management implications of observation (i.e., no initial morbidity) versus prophylactic inguinal staging procedures (i.e., some potential morbidity) as management strategies.

The authors describe a small retrospective series of seven patients with stage T1 moderately differentiated penile cancer in who either had (n = 1) or developed (n = 3) metastatic penile cancer during follow up. Thus among the initially node negative group 3 of six (50%) developed metastatic disease within 9 months of follow up. Thus from the authors perspective these patients should be offered prophylactic inguinal staging. However to put this small series into perspective a recent study that specifically evaluated the risk of metastasis among T1 grade 2 tumors was published.[2] The value of this study is that it includes 117 tumors from two institutions that are very experienced in the evaluation and management of penile carcinoma. Overall the incidence of lymph node metastasis in this cohort was 13% and importantly among those that were lymph node negative the subsequent risk of metastasis with a median follow up of 44 months was only 9%. Thus based upon pathologists' interpretations at these institutions the biology of T1 grade 2 tumors was largely favorable and one could easily make an argument for careful observation of such patients to avoid dissection in 90% of patients that exhibited no palpable adenopathy.

The authors make the important observation that the controversy regarding the risk of metastasis in T1 grade 2 tumors could be either related to pathologic discrepancies related to grading or to molecular differences/tumor heterogeneity in what the pathologists recognize as a grade 2 tumor.

In order for us to improve the management of this specific subset of patients and all patients with invasive penile cancer and negative inguinal examinations two actions are required: 1) An expert panel of pathologists should re-examine the utility of the Broder's grading system[3] and other pathologic features to determine the optimal histological features associated with the risk of metastasis[4] and 2) Future definition of the molecular signature of metastasis at the mRNA or protein levels to further assist in stratifying tumors that appear histologically similar but that have different biologic potential. For the present however, it is incumbent for surgeons making management decisions regarding the inguinal lymph nodes to discuss the pathologic findings in the primary tumor with their pathologists to insure that adverse features that would favor an elective staging procedure are absent and importantly to offer surveillance strategies only to those compliant patients who will perform self examination and follow prescribed follow up visits. When a prophylactic staging procedure is performed it should be the one that the surgeon performs with expertise, accurately stages the patient, and minimizes morbidity. In this subset of patients we continue to balance maximizing cure with "doing no harm".

References

1. Naumann CM, Alkatout I, Al-Najar A, Beate Korda B, Hegele A, Bolenz C, Ziegler H, Klollel G, Juenemann K, vanderHorst C. Lymph node metastasis in intermediate-risk squamous cell carcinoma of the penis. *BJU Int* 2008;102(9):1102-1106.
2. Hughes BE, Leijte JAP, Kroon BK, Shabbir MA, Swallow TW, Heenan SD, Corbishley CM, vanBoven HH, Perry MJA, Watkin N, Horenblas S. Lymph node metastasis in intermediate-risk penile squamous cell cancer: a two-centre experience. *Eur Urol* 2009,doi: 10.1016/j.eururo.2009.7.004
3. Broders AC. Squamous cell epithelioma of the skin. *Ann Surg* 1921;73:141-143.
4. Cubilla AL. The role of pathologic prognostic factors in squamous cell carcinoma of the penis. *World J Urol* 2009;27(2):169-177.
5. Muneer A, Kayes O, Ahmed HU, Arya M, Minhas S. Molecular prognostic factors in penile cancer. *World J Urol* 2009;27(2): 161-167.

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