

Chapter 34

Considerations: Imaging in Penis Carcinoma

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Introduction

Malignant tumors of the penis consist of 95% of the cases of squamous cell carcinoma. The other 5% comprises of other tumors originating in the skin, like melanoma and basal cell cancer, or tumors arising from elements of cavernous tissue like soft tissue tumors [1–3]. Ideally, imaging modalities should help the clinician in deciding on the appropriate therapy of the primary tumor by exactly delineating the extent of the tumor and invasion in various structures of the penis, like the cavernous tissues and the urethra. Squamous cell carcinoma shows a very strong tendency for lymphatic spread first, with hematogenic spread in very advanced cases only [4]. Timely management of lymph node metastasis is of utmost importance [5, 6]. Imaging should also inform the clinician on the absence or presence of regional metastases in the groin area. In more advanced cases knowledge of spread to second echelon lymph nodes in the pelvic region and further spread to retroperitoneal lymph nodes is essential for a rational approach.

Imaging of the Primary Tumor

The extent of the primary tumor in squamous cell carcinoma of the penis has important prognostic and therapeutic implications. The prognostic difference between deeply infiltrating tumors and superficially growing tumors has been recognized for a long time and is expressed already in the first TNM classification system for squamous cell carcinoma of the penis [7]. Size of the tumor was surpassed by depth of infiltration as a classification criterion in the most recent classification [8]. A distinction was made between tumors infiltrating into the deeper structures of the penis and tumors

Table 34.1 1987 TNM Classification [8]

T-Primary tumor
T X Primary tumor cannot be assessed
TO No evidence of primary tumor
Tis Carcinoma in situ
Ta Non-invasive verrucous carcinoma
TI Tumor invades subepithelial connective tissue
T2 Tumor invades corpus spongiosum or cavernosum
T3 Tumor invades urethra or prostate
T4 Tumor invades other adjacent structures
N-Regional lymph nodes
NX Regional lymph nodes cannot be assessed
NO No regional lymph node metastasis
NI Metastasis in a single superficial inguinal lymph node
N2 Metastasis in multiple or bilateral superficial inguinal lymph nodes
N3 Metastasis in deep inguinal or pelvic lymph node(s), unilateral or bilateral
M-Distant metastasis
MX Distant metastasis cannot be assessed
MO No distant metastasis
MI Distant metastasis
Stage grouping
Stage 0 Tis NO MO Ta NO MO
Stage I TI NO MO
Stage II TI NI MO T2 NO, NI MO
Stage III TI N2 MO T2 N2 MO T3 NO, NI, N2 MO
Stage IV T4 Any N MO Any T N3 MO Any T Any N MI

invading the superficial layers only (Table 34.1) This distinction, how important this may be, is not easily made on clinical grounds only.

The main issue in the management of the primary tumor is the decision whether to amputate or not. Standard partial penile amputation as a treatment for localized squamous cell carcinoma is increasingly being replaced by methods that conserve the penis [9, 10]. Main danger is the risk for local recurrence, which increases proportionally with size and depth of infiltration of the tumor. Therefore, the extension of the primary carcinoma must be assessed with great care. Staging on clinical grounds only is not always easy, as the often accompanying infection can give the impression of deep infiltration while microscopic invasion can easily be missed. Comparing clinical and pathological staging in a series with almost 100 patients with squamous cell cancer

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showed the following differences: in 10% of the cases the clinical stage was higher compared to the pathological stage (“overstaging”), in 16% of the tumors the pathological stage was higher than the clinical one (“understaging”). Overall a 26% difference between clinical and pathological stage was found, almost similar to a 23% difference in a study from Maiche et al. [11, 12]. Reasons for these discrepancies were clinically undetected infiltration in the subepithelial tissue or corpus spongiosum, infection, and edema masking the real size of the tumor and giving a false impression of infiltration.

Can imaging contribute to more accurate staging? Various imaging techniques have been evaluated for this purpose [13–18].

Cross-Sectional Imaging Techniques

Ultrasound

Various distinctive structures of the penis can be depicted on ultrasound investigation and used for staging penile carcinoma. The tumor itself is mostly shown as a hypoechoic lesion (Fig. 34.1). It can be distinguished from the urethra. Introducing a urethral catheter can aid in delineating the tumor. The tunica albuginea surrounding both corpora cavernosa is seen as a hyperechoic structure (Fig. 34.2). Ultrasound was shown to reliably give the extent of infiltration into the corpora cavernosa, but was not reliable enough in discerning the true extent of infiltration into the corpus spongiosum of the glans [19].

CT Scanning

Computerized tomography is limited by its ability to image in one plane only and the poor soft tissue contrast. While it has been used extensively for the detection of nodal metastases, it has been used rarely for imaging the primary tumor, as the tumor and surrounding corporal bodies are poorly differentiated [18, 20, 21]. One can conclude that CT scanning does not play a role in the imaging of the primary tumor.

Magnetic Resonance Imaging (MRI)

In contrast to CT scan, MRI imaging is not limited by imaging in one plane. Moreover, soft tissue contrast is much better than with CT scan. Lont et al. analyzed the accuracy of MRI staging of the primary tumor [17]. MR images were obtained in the axial plane using T1-weighted spin echo (T1-SE) and T2-weighted turbo-spin echo (T2-TSE) sequences. Sagittal images were acquired using a short inversion recovery

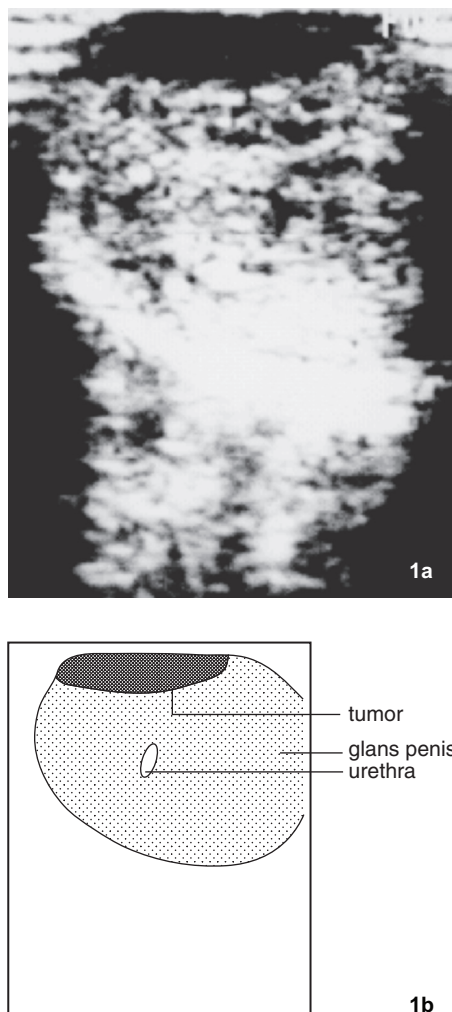


Fig. 34.1 Ultrasound examination of penile carcinoma (a) with schematic representation of distinct structures (b), showing a hypoechoic lesion

sequence and T1-SE sequences, before and after administering an intravenous contrast agent (gadolinium based). Tumor identification was mainly based on the presence of lesions with low signal intensity relative to the corporal bodies on the T1- or the T2-weighted images (Figs. 34.3 and 34.4). It was concluded that because of the possibility of imaging in various planes and because of the ability to visualize other structures of the penis, MRI can be useful in doubt of the true proximal extent of the tumor.

In order to improve imaging of the primary tumor, MRI was combined with artificial erection and compared with pathologic staging in nine cases of penile cancer. T1-weighted and T2-weighted MRI with and without contrast was obtained using a phased array coil. The MRI and pathologic staging coincided in eight of nine patients. In one patient no tumor was detected at MRI. Despite the differences between clinical staging and MRI staging, this had no therapeutical consequences [22].

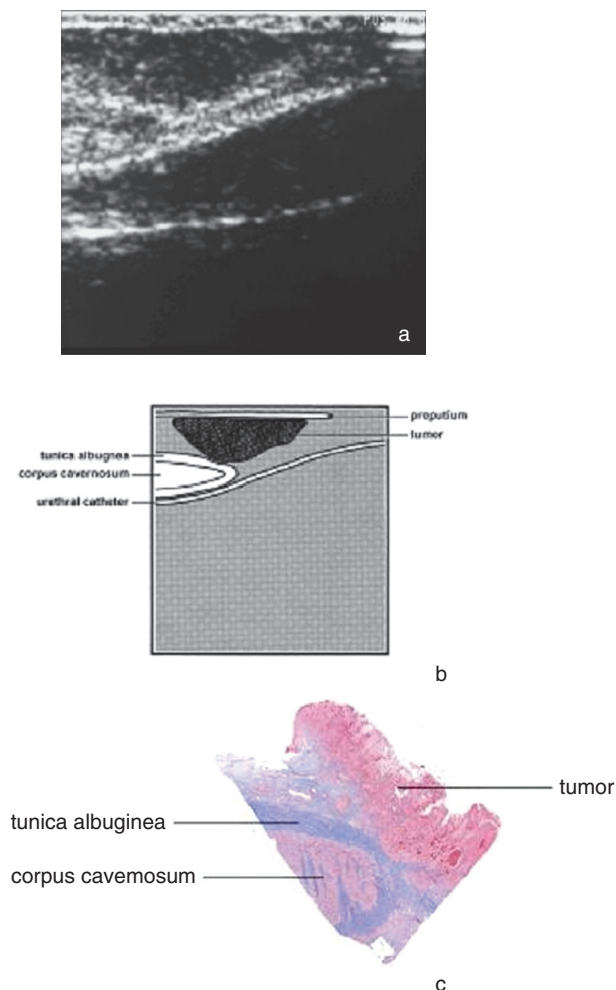


Fig. 34.2 Ultrasound examination of penile carcinoma (a) with schematic representation of distinct structures (b), showing the tumor abutting the tunica albuginea, without invading it. Histology (c) confirms the ultrasound observation (tumor not invading the tunica albuginea)



Fig. 34.3 MRI (T1 SPIR) with contrast in the transversal plane at a distal level of the penis in a patient with a T2 tumor. The tumor is seen as a low signal mass, clearly distinguished from the glans penis (T = tumor, G = glans penis, arrow indicates urethra)

Accuracy of Physical Examination, Ultrasound, and MRI

The accuracy of physical examination, ultrasound investigation, and magnetic resonance imaging (MRI) was compared in 33 patients [17]. All patients underwent a radiological evaluation with ultrasonography and MRI, the former using an SDD 280 LS scanner (Aloka Corp., Tokyo, Japan) with a 7.5 MHz linear-array small-parts transducer, and the latter using a 1.5 T Magnetom scanner (Siemens GmbH, Germany) with a small surface coil. An ultrasonography gel pad was used to avoid artifacts, and a urethral catheter was introduced for identification. The tumor was identified by the presence of hypoechoic lesions on the ultrasonograms that were not consistent with normal penile anatomy. Tumor size was determined in two directions using standard calipers on the ultrasonogram and in three planes on MRI. Invasion by tumor of the subepithelial stroma, corpus spongiosum, corpora cavernosa, and urethra was assessed. Infiltration depth was measured. After comparing the findings of the various investigations with histopathology, physical examination was more reliable for assessing tumor size than were ultrasonography and MRI. Furthermore physical examination predicted corpus cavernosum infiltration with the highest positive predictive value and was accurate for determining the presence of deep infiltration, missing substantial infiltration in only 2 of 33 patients (Table 34.2). For infiltration into the corpus spongiosum of the glans, the following values for positive predictive value and sensitivity were found: 94, 92, and 91% and 68, 92, and 80%, respectively, for physical examination, ultrasonography, and MRI. There were no false-positive findings of infiltration. MRI was the most sensitive method for determining cavernosal infiltration but at the cost of some false-positive results.

Imaging of Lymph Nodes

Squamous cell carcinoma of the penis metastasizes first to the inguinal lymph nodes and from there to the pelvic nodes. Metastases to the pelvic nodes without inguinal involvement (skip metastases) have hardly been observed, except an occasional case. By definition clinically occult metastasis are not detected by physical examination. These clinically node-negative patients present a challenge for additional imaging as approximately 20% will harbor clinically undetectable metastases. Non-invasive methods to detect these metastases are unreliable, but there is a clinical need to find occult metastases at the earliest possible stage, because survival is related to presence and extent of nodal involvement [5, 6, 23]. The optimum management of patients with clinically node-negative groins is controversial. A surveillance

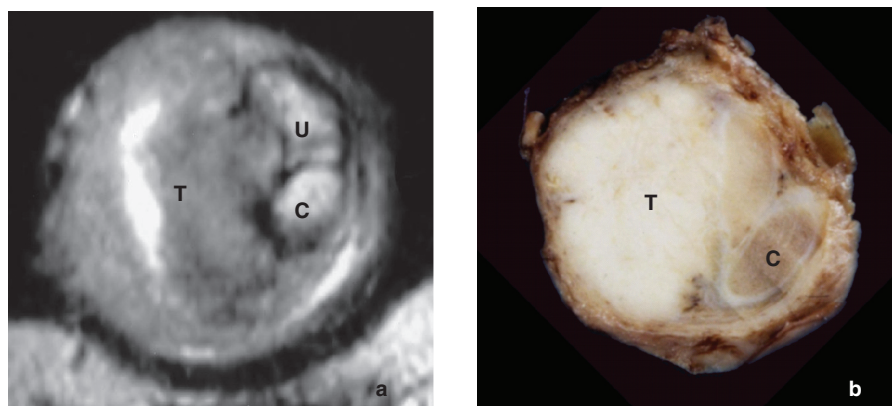


Fig. 34.4 (a) MRI (T1 TSE) without contrast in the transversal plane at a more proximal level of the penis in another patient with a T2 tumor. The tumor is seen as a mass with increased signal involving the corpus cavernosum. Some fluid collection between the preputium and the tumor is visible (T = tumor, C = corpus cavernosum, U = urethra). (b) Cross-section of the corresponding macroscopic specimen illustrates the findings on MRI, with macroscopic involvement of the corpus cavernosum (T = tumor, C = corpus cavernosum). The urethra was dissected during surgery

Table 34.2 The positive predictive value, sensitivity, and specificity of infiltration of the corpus cavernosum, as determined by physical examination, ultrasound, and MRI

Cavernosum infiltration	Positive predictive value	Sensitivity	Specificity
Physical examination	100%	71%	100%
Ultrasound	67%	57%	97%
MRI	75%	100%	91%

policy risks the patients presenting with metastasis at a stage where cure is no longer possible. On the other hand, early inguinal lymphadenectomy in all clinically node-negative patients is unnecessary in up to 80% and associated with substantial morbidity [24]. Thus better staging procedures are mandatory to improve the detection of occult metastasis and to decrease the number of unnecessary lymph node dissections. Detection of lymph node metastases in the groin and pelvis on CT scan or MRI is detected mainly by change of size. Lymph nodes smaller than 1 cm are usually considered normal. A distortion of the internal architecture by a small metastatic deposit without change of size was only visible by lymphangiography until recently [11]. Promising techniques, like modern ultrasound and MRI, using ultrasmall particles of iron oxide (USPIO), are underway to detect these occult metastases more reliably.

Patients presenting with inguinal lymph node enlargement are easily detected by physical examination. However, on average only half of them harbor lymph node metastasis, the other half is due to benign enlargement because of the often concomitant inflammation [25]. A distinction between absence and presence of lymph node metastases can be made on the basis of fine-needle aspiration biopsy guided by ultrasound or CT scanning. Understandably only a tumor-positive outcome is reliable. In patients with proven inguinal lymph

node metastasis, imaging with CT scan or MRI is useful for the determination of the extent of metastatic spread.

Cross-Sectional Imaging Techniques

Ultrasound

Thanks to the high-resolution probes, ultrasound scanning is increasingly reliable in detecting occult metastases. Modern ultrasound not only visualizes alteration in size, shape, and contour of lymph nodes but also depicts changes in the cortical and hilar morphology and texture that can reflect the presence of underlying metastasis [26]. Changes in the architecture of the node occur before the node enlarges and these are identified by the radiologist. Currently the spatial resolution limit is around 2 mm. Due to overlap of sonographic features of benign and suspicious lymph nodes, fine-needle aspiration cytology (FNAC) of sonographically suspicious nodes provides a more definitive diagnosis than ultrasound alone. Potential applications have been demonstrated in a number of malignancies [27–30]. In 2001, ultrasound-guided FNAC was introduced as standard staging procedure at the Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital to improve staging of clinically node-negative penile SCC patients (Figs. 34.5 and 34.6).

The sensitivity of ultrasound-guided FNAC to reveal clinically occult lymph node metastases was 39%, with a 100% specificity. In contrast to penile cancer, ultrasound-guided FNAC has been used extensively in assessing lymph nodes in other malignancies such as breast cancer and melanoma. Sensitivity and specificity rates are about the same as reported for these tumors. With a sensitivity of 39% there is a false-negative rate of 61%, necessitating other means to

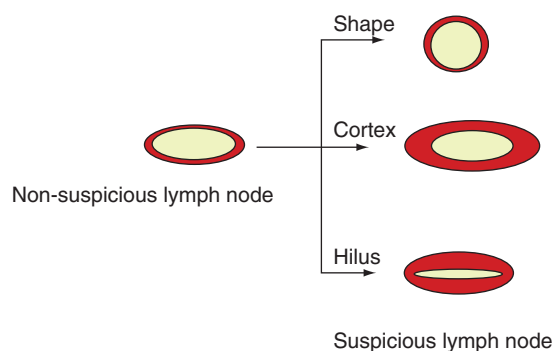


Fig. 34.5 Sonomorphologic lymph node features according to Vassallo et al. lymph node shape, cortex (normal or wide), and hilus (normal, narrow, or absent). Suspicious features for nodal involvement are a round shape, a wide cortex, and a narrow to absent hilus

assess the regional lymph nodes. At our institute we favor a so-called dynamic sentinel node biopsy (DSNB). So far ultrasound-guided FNAC cannot replace DSNB. However, it is a useful tool for preoperative screening of the clinically node-negative groins in patients with penile cancer scheduled to undergo DSNB. The commonest cause of a false-negative DSNB procedure is gross involvement of the sentinel node by tumor cells which prohibits tracer uptake with a false-negative procedure as a result [31]. These nodes in particular might be detected by ultrasound-guided FNAC. Moreover, nodal recurrences, which can occur after a false-negative DSNB procedure, might be detected earlier when compared to physical examination.

What are the causes of false-negative ultrasound results? First, the lymph node may appear abnormal and indeed contain metastatic disease, but the aspirate may fail to extract abnormal cells. This relates to erroneous sampling and can be difficult to overcome in a node with a small metastasis where placement of the needle is crucial. Second, microscopic small foci of metastases might be beyond the resolution of the transducer and therefore not show up on the images [28]. In order to improve the efficiency of ultrasound

scanning, the future effort should focus on the reduction of false-negative results. To this end, at least two strategies might be useful. First, the introduction of echogenic contrast has been advocated to increase ultrasound diagnostic power by allowing the identification of indirect features of lymph node metastases. Second, increasing the ultrasound probe ultrafrequency might ameliorate the resolution power, thus allowing the detection of lesions smaller than 2 mm [30]. In addition, a learning phase of the radiologist performing ultrasound-guided FNAC cannot be denied.

CT Scanning

Only one study exists in which the value of CT scanning in detecting regional lymph node metastases is assessed. Regional lymph node invasion that escaped clinical examination was not detected by CT [11]. Positive findings were found only in patients with clinically suspected nodes. Clinical decisions with respect to the management of regional lymph nodes should therefore not be based on negative CT findings. In patients with proved metastasis additional imaging may be of some help in the detection of pelvic node invasion and the determination of the extent of involvement (Fig. 34.7).

MR Imaging

Like in CT scanning, clinically occult metastases will not be detected by conventional MR imaging. MR imaging may be of some help in the detection of pelvic node invasion and the determination of the extent of involvement in patients with proved metastasis.

Recently, however, a promising technique has emerged with the potential to identify occult lymph node metastasis: MRI and ultrasmall particles of iron oxide (USPIO). This novel technique makes use of a lymph node-specific contrast

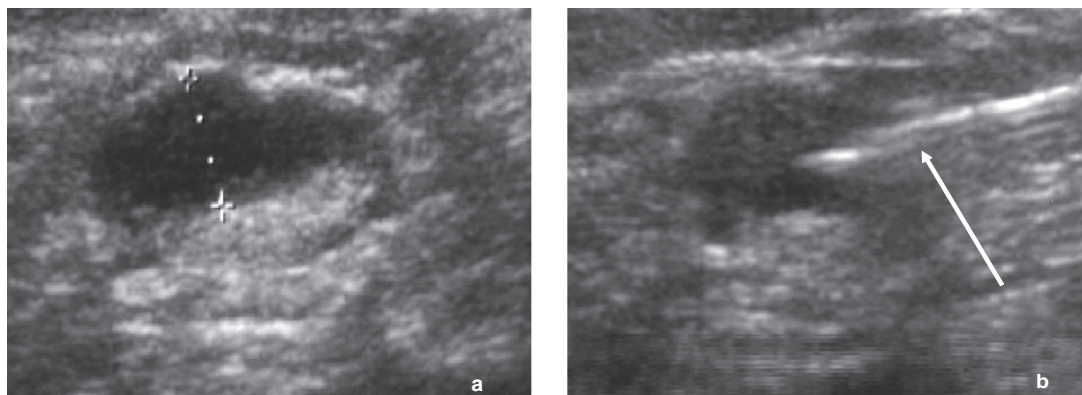


Fig. 34.6 (a) Ultrasound image of suspicious node with a wide cortex. (b) Ultrasound image of FNAC of the same node (arrow indicates needle)

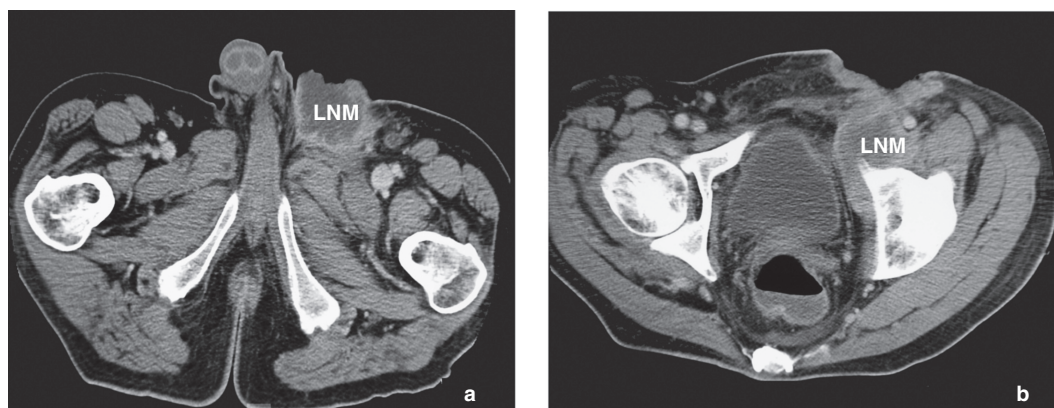


Fig. 34.7 (a) CT image in the transversal plane in a patient with a massive lymph node metastases in the left groin (LNM = lymph node metastasis). (b) Same patient at a more caudal level (LNM = lymph node metastasis)

agent that allows the identification of clinically occult metastasis. This contrast agent, known as ultrasmall particles of iron oxide (USPIO), is injected intravenously and is taken up primarily by macrophages in the lymph nodes. Presence of USPIO in the node results in signal intensity loss (darkening) on T2-weighted sequences. Metastatic growth will displace the macrophages filled with USPIO, and the metastatic part of the node therefore is high in signal intensity (whitening). Thus, metastasis within the lymph node will show as white filling defect. Metastases as small as 1 mm have been detected by using this technique [32]. In a mouse model even as few as 1,000 tumor cells could be depicted [33]. A pilot study in penile carcinoma showed a 100% sensitivity, 97% specificity, and 100% negative predictive value. Improvement of this technique could possibly replace dynamic sentinel node biopsy in the future [34].

Considerations

Primary Tumor

Small superficial tumors can be accurately staged by physical examination only. Imaging can be of help in patients in whom the extent of infiltration into the corpora cannot be determined properly by a physical examination, usually only in patients with locally extensive disease. Because of the high sensitivity for cavernosal infiltration and its precision in determining infiltration depth, MRI is the imaging method of choice. Images in the sagittal plane are particularly useful for detecting the proximal extent of the tumor. In conclusion no imaging modality is more reliable than physical examination for the assessment of the true extent of the tumor. Imaging has no important role in routine clinical management, except

where doubt exists about the proximal extent of the primary tumor.

Lymph Node Metastases

Penile carcinoma primarily metastasizes to the inguinal lymph nodes. Even in case of lymphatic metastasis many patients can still be cured. Patients presenting with inguinal lymph node enlargement are easily detected by physical examination. The diagnosis can be proven by fine-needle aspiration cytology, if possible under ultrasonographic guidance. In these patients additional CT or MRI imaging may be of some help in the detection of pelvic node invasion and the determination of the extent of involvement.

Most penile carcinoma patients, however, have no suspicious lymph nodes in their groins. This observation does not exclude the presence of disease. Approximately 25% of the patients harbor occult metastases in these lymph nodes. An important issue in the management of penile carcinoma patients is how to identify these metastases. Elective lymph node dissection is an option but will lead to overtreatment in about 75% of the patients. Moreover, inguinal lymphadenectomy is associated with major morbidity. On the other hand, a wait-and-see policy may have a negative impact on survival. Dynamic sentinel node biopsy is a minimally invasive procedure that enables detection of occult metastasis in clinically node-negative groins. To localize the sentinel node preoperatively, lymphoscintigraphy is performed after peritumoral injections of ^{99m}Tc -labeled nanocolloid tracers. Intraoperatively, the sentinel node can be identified with the aid of a blue dye and a hand-held gamma-ray detection probe. The sensitivity of dynamic sentinel node biopsy in our hands is 84%. Although minimally invasive dynamic sentinel node biopsy is burdened by an 8% complication rate. Moreover,

it requires a patient to be hospitalized. Obviously, the implementation of non-invasive staging methods, i.e., imaging modalities, might improve the quality of life of penile carcinoma patients. The main problem of imaging modalities to detect occult metastases, however, is a low sensitivity. Computerized tomography and magnetic resonance imaging have a very low sensitivity and specificity in the detection of occult lymph node metastases in the groin. Ultrasound with fine-needle aspiration cytology is more accurate. However, as a staging tool, it is inadequate with a sensitivity and specificity of 39 and 100%, respectively, as reported in this chapter. The main problem is the detection of small metastases, i.e., smaller than approximately 3 mm. Positron emission tomography with ^{18}F -fluorodeoxyglucose (FDG-PET) has been advocated to detect occult lymph node metastases in several types of cancer. This technique relies not solely on anatomic identification but largely on physiological characterization of cells. However, the visualization by FDG-PET requires a minimum diameter of about 3 mm, and this technique is therefore not a good alternative for dynamic sentinel node biopsy in staging patients with clinically node-negative penile carcinoma. Magnetic resonance lymphangiography is a promising technique in the detection of occult lymph node metastases. Metastases as small as 1 mm have been detected by using this technique. Preliminary results of this technique in penile carcinoma are promising. Improvement of this technique could possibly replace dynamic sentinel node biopsy in the future.

References

- Liegl B, Regauer S. Penile clear cell carcinoma. a report of 5 cases of a distinct entity. *Am J Surg Pathol*. 2004;28:1513.
- Sanchez-Ortiz R, Huang SF, Tamboli P, et al. Melanoma of the penis, scrotum and male urethra. a 40-year single institution experience. *J Urol*. 2005;173:1958.
- Stancik I, Holth W. Penile cancer. review of the recent literature. *Curr Opin Urol*. 2003;13:467.
- Horenblas S, van Tinteren H, Delemarre JF, et al. Squamous cell carcinoma of the penis. III. Treatment of regional lymph nodes. *J Urol*. 1993;149:492.
- Ornellas AA, Seixas AL, Marota A, et al. Surgical treatment of invasive squamous cell carcinoma of the penis. retrospective analysis of 350 cases. *J Urol*. 1994;151:1244.
- Kroon BK, Horenblas S, Lont AP, et al. Patients with penile carcinoma benefit from immediate resection of clinically occult lymph node metastases. *J Urol*. 2005;173:816.
- Harmer MH. TNM classification of malignant tumors. UICC. 3rd ed. Geneva; 1978.
- International Union Against Cancer. Penis. In: Hermanek P, Sobin LH, editors. TNM classification of malignant tumours. 4th ed. Berlin Heidelberg: Springer Verlag; 1987.
- Mohs FE, Snow SN, Messing EM, et al. Microscopically controlled surgery in the treatment of carcinoma of the penis. *J Urol*. 1985;133:961.
- Windahl T, Hellsten S. Laser treatment of localized squamous cell carcinoma of the penis. *J Urol*. 1995;154:1020.
- Horenblas S, van Tinteren H, Delemarre JF, et al. Squamous cell carcinoma of the penis: accuracy of tumor, nodes and metastasis classification system, and role of lymphangiography, computerized tomography scan and fine needle aspiration cytology. *J Urol*. 1991;146:1279.
- Maiche AG, Pyrhonen S. Clinical staging of cancer of the penis. By size? By localization? or By depth of infiltration? *Eur Urol*. 1990;18:16.
- de Kerviler E, Ollier P, Desgrandchamps F, et al. Magnetic resonance imaging in patients with penile carcinoma. *Br J Radiol*. 1990;68:704.
- Hricak H, Marotti M, Gilbert TJ, et al. Normal penile anatomy and abnormal penile conditions. evaluation with MR imaging. *Radiology*. 1988;169:683.
- Kageyama S, Ueda T, Kushima R, et al. Primary adenosquamous cell carcinoma of the male distal urethra. magnetic resonance imaging using a circular surface coil. *J Urol*. 1997;158:1913.
- Kawada T, Hashimoto K, Tokunaga T, et al. Two cases of penile cancer. magnetic resonance imaging in the evaluation of tumor extension. *J Urol*. 1994;152:963.
- Lont AP, Besnard AP, Gallee MP, et al. A comparison of physical examination and imaging in determining the extent of primary penile carcinoma. *BJU Int*. 2003;91:493.
- Horenblas S, van Tinteren H. Squamous cell carcinoma of the penis. IV. Prognostic factors of survival: analysis of tumor, nodes and metastasis classification system. *J Urol*. 1994;151:1239.
- Horenblas S, Kroger R, Gallee MP, et al. Ultrasound in squamous cell carcinoma of the penis; a useful addition to clinical staging? A comparison of ultrasound with histopathology. *Urology*. 1994;43:702.
- Maiche AG. Computer tomography (CT) in the diagnosis and staging of cancer of the penis. *Eur J Cancer*. 1993;29A:779.
- Vapnek JM, Hricak H, Carroll PR. Recent advances in imaging studies for staging of penile and urethral carcinoma. *Urol Clin North Am*. 1992;19:257.
- Scardino E, Villa G, Bonomo G, et al. Magnetic resonance imaging combined with artificial erection for local staging of penile cancer. *Urology*. 2004;63:1158.
- McDougal WS. Carcinoma of the penis. improved survival by early regional lymphadenectomy based on the histological grade and depth of invasion of the primary lesion. *J Urol*. 1995;154:1364.
- Bevan-Thomas R, Slaton JW, Pettaway CA. Contemporary morbidity from lymphadenectomy for penile squamous cell carcinoma. the M.D. Anderson Cancer Center Experience. *J Urol*. 2002;167:1638.
- Horenblas S. Lymphadenectomy for squamous cell carcinoma of the penis. Part 1. diagnosis of lymph node metastasis. *BJU Int*. 2001;88:467.
- Vassallo P, Wernecke K, Roos N, et al. Differentiation of benign from malignant superficial lymphadenopathy. the role of high-resolution US. *Radiology*. 1992;183:215.
- Deurloo EE, Tanis PJ, Gilhuijs KG, et al. Reduction in the number of sentinel lymph node procedures by preoperative ultrasonography of the axilla in breast cancer. *Eur J Cancer*. 2003;39:1068.
- Hall TB, Barton DP, Trott PA, et al. The role of ultrasound-guided cytology of groin lymph nodes in the management of squamous cell carcinoma of the vulva. Five-year experience in 44 patients. *Clin Radiol*. 2003;58:367.
- Kuonen-Boumeester V, Menke-Pluymers M, de Kanter AY, et al. Ultrasound-guided fine needle aspiration cytology of axillary lymph nodes in breast cancer patients. A preoperative staging procedure. *Eur J Cancer*. 2003;39:170.
- Rossi CR, Mocellin S, Scagnet B, et al. The role of preoperative ultrasound scan in detecting lymph node metastasis before sentinel node biopsy in melanoma patients. *J Surg Oncol*. 2003;83:80.

31. Kroon BK, Horenblas S, Estourgie SH, et al. How to avoid false-negative dynamic sentinel node procedures in penile carcinoma. *J Urol*. 2004;171:2191.
32. Harisinghani MG, Barentsz J, Hahn PF, et al. Noninvasive detection of clinically occult lymph-node metastases in prostate cancer. *N Engl J Med*. 2003;348:2491.
33. Wunderbaldinger P, Josephson L, Bremer C, et al. Detection of lymph node metastases by contrast-enhanced MRI in an experimental model. *Magn Reson Med*. 2002;47:292.
34. Tabatabaei S, Harisinghani M, McDougal WS. Regional lymph node staging using lymphotropic nanoparticle enhanced magnetic resonance imaging with ferumoxtran-10 in patients with penile cancer. *J Urol*. 2005;174:923.

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