Penile cancer is an uncommon tumor with a significantly higher incidence in some areas of underdeveloped countries. Unfortunately, delay on the part of the physician in initiating diagnosis may be considerable and many patients are referred to treatment after developing advanced disease. There is a large volume of data on penile cancer in Brazil. Losing patients to follow-up is common and in some areas of the country, penile cancer accounts for 17% of all malignancies in men. In these less developed areas, penile carcinoma represents one of the most important health problems. A recent epidemiological study sponsored by the Brazilian Society of Urology (SBU) gave us an idea about the complexity of the problem [1]. For example, the highest incidence rates of penile carcinoma were found in Maranhão and São Paulo. Maranhão is situated in an underdeveloped area and São Paulo is the richest state of the country. An explanation for this contradiction is the large migration of the poor from underdeveloped areas to São Paulo. The SBU and the federal government are now waging a campaign to increase early diagnosis and improve health measures in order to eradicate the disease in the future.

Most tumors of the penis are of lower grades. Lack of correlation between grade and survival has been noted by a number of investigators. Other series report reduced survival among patients with anaplastic tumors. Several studies have also emphasized the association of high-grade disease with regional nodal metastases.

At the Brazilian National Cancer Institute we adopt the 1978 TNM staging classification system for penile carcinoma. The problem with the current TNM version is the difficulty of assigning nodal status before definitive therapy. We favor the 1978 TNM version because we believe that clinical stage must be assigned before definitive therapy and that such a staging system has prognostic significance. Unfortunately, the 1978 TNM version did not provide a designation for pelvic nodal status, a known indicator of poor prognosis.

Before the administration of therapy, a biopsy is required to provide histologic confirmation of the diagnosis of penile cancer and staging information by assessing the depth of microscopic invasion. Adjacent normal tissue should be included to evaluate invasion, a critical differential point with regard to planning definitive surgery.

Primary treatment of penile cancer depends on the size and location of the tumor. Actually, surgery is the gold standard method used to treat penile carcinoma although radiation therapy has yielded local control rates similar to surgical resection. The scope of surgery varies from wide excision to total penectomy and amputation. Circumcision is performed in selected patients whose lesions were limited to the foreskin. Successful local control by partial penectomy depends on division of the penis at least 2 cm proximal to the gross tumor extent, leaving tumor-free margins. Total penectomy is indicated in lesions whose size or location precludes adequate excision with a functional residual remnant by partial penectomy.

Mohs micrographic surgery is used for the treatment of selected patients with small, superficial penile cancers. The Mohs technique involves excision of the penile lesion and microscopic examination of the underside of each layer for systematic inspection of serial sections. Laser ablation using a neodymium:yttrium-aluminum garnet (Nd:YAG) or carbon dioxide (CO₂) laser have also been used in selected patients with small superficial or superficially invasive penile cancers. The risk of local recurrence after this penis-conserving therapy is significantly related to category T, with 10% local recurrences in stage T1 tumors in contrast to 32% and 100% in stages T2 and T3 tumors, respectively.

Radiation therapy techniques include external-beam irradiation, iridium molds or wires, and interstitial brachytherapy. Using external-beam radiation therapy, a control rate of 39–65% can be achieved. For T1–T2 penile carcinoma, an overall local control rate of 74–86% can be achieved with 192Ir interstitial implants and of 80% with brachytherapy.

Metastases to the regional inguinal nodes are the earliest route of dissemination from penile carcinoma. Due to inflammatory factors, it is difficult to clinically detect metastatic involvement of these inguinal lymph nodes. Other potential reasons for false-negative examinations include obesity, preexisting edema, and changes from prior therapy (radiation, inguinal surgery).

Dynamic sentinel node biopsy has been used for patients with node negative T2–T3 penile carcinoma. This procedure has also been used for staging the contralateral side in patients with clinically unilateral lymph node involvement. In general, subsequent contralateral inguinal node dissection and ipsilateral pelvic lymph node dissection was carried out if two or more inguinal lymph nodes were involved. However this technique has been associated with a false-negative rate of 16% [2]. The results of the use of isolated gamma probe for sentinel node penile carcinoma detection was recently published by Gonzaga-Silva et al. [3] from the Brazilian Federal University of Ceará. Over the last 5 years at their cancer hospital, 3 new cases of penile carcinoma have been identified per month and 27 newly diagnosed patients (T1, T2, N0) were included in a prospective study. The authors found that the isolated gamma probe technique has a very low sensibility and high false-negative rate concluded that this isolated technique is unreliable. Dr. Simon Horenblas, from the Netherlands Cancer Institute, a pioneer in this field, provided an editorial comment on this article. He believes to be able, with support of refinements, to bring down the false-negative rate of 22% to an acceptable 4.8%. Our group, at the Brazilian National Institute of Cancer is performing a
prospective study using the preoperative lymphoscintigram and the gamma probe detector associated with the injection of patent blue around the tumor to identify the sentinel nodes in patients with stages T1 and T2, N0. After identification of the nodes we are performing a complete inguinal lymphadenectomy in all patients and investigating the histological findings in all excised inguinal nodes to determine the exact false-negative rate when using this technique. We will not be able to cure the patient unless the metastatic disease is diagnosed at the very beginning; therefore, this type of study has to be carefully carried out. It cannot be employed in clinical practice without a precise protocol and without the patients’ awareness of the risks involved.

Due to the low incidence of squamous cell penile carcinoma and lack of well-designed studies, controversies persist over the therapeutic approach in these patients. Inguinal nodal involvement is found in 20–40% of cases at diagnosis and nodal metastasis is an important predictive factor for survival. When confirmed, the presence of inguinal metastases is often devastating for the patient and therapeutically challenging for the urologist. Enlargement of the regional nodes is present in 50% of patients. If an immediate lymphadenectomy was adopted in these patients, an average of 50% of patients could be subjected to the morbidity of inguinal lymphadenectomy with no benefit. On the other hand, if a policy of routine lymphadenectomy were adopted in all patients with clinically negative lymph nodes, the average risk of a false-negative examination (metastasis actually present) would be approximately 20%. Although recent data demonstrated a survival benefit with immediate resection of clinically occult lymph node metastases, surgical morbidity is still high. There are considerable controversies over the extent of lymph node dissection and the proper time of the procedure. Since introduction of the Gibson incision, we observed a drastic decrease in groin dissection morbidity rates [4]. Contemporary series show that refinements of the technique during surgery associated with adequate postoperative care can decrease complication rates to approximately 50%. Recently, Tobias-Machado and associates reported preliminary results suggesting that video endoscopic inguinal lymphadenectomy might decrease postoperative morbidity without compromising oncological control [5]. Future studies should include the bilateral procedure, longer term follow-up and a greater number of patients.

Clinically detectable distant metastatic lesions to the lung, liver, bone, or brain are uncommon and are reported as occurring in 1–10% of cases in most large series. Such metastases usually occur late in the course of the disease after the local lesion has been treated. Distant metastases in the absence of regional node metastases are unusual.

The experience with cytotoxic drugs in penile carcinoma is limited to small series with inconclusive results. Some response has been observed with cisplatin, bleomycin, and methotrexate, as well as with combinations of these agents. Successful surgical resection can be achieved in patients with a fixed inguinal mass after the use of neoadjuvant chemotherapy. Combination chemotherapy in patients with disseminated metastatic disease is associated with excessive toxicity, low response rates, and treatment-related deaths.

Palliative surgical treatment allows, in the short-term, improved quality of life with no surgical complications or mortality. Almost all patients could return home without the infected metastatic lesions. When palliative resection of a large mass must be considered, it is imperative for the surgeon to choose the best method of wound closure. To close a large defect, we generally rotate a tensor fascia lata myocutaneous flap, in which case the muscle, overlying skin and all intervening tissue are transposed as a composite unit, preserving the blood supply. Occasionally, it is possible to obtain a cure for a particular patient. Survival in this patient cohort is related to completely eradicating extensive disease. This task is difficult to achieve with surgery, chemotherapy, or radiotherapy alone. The combination of surgery and chemotherapy has shown some benefit in advanced penile carcinoma.

REFERENCES