Clinical Research Paper

**Diagnosis and therapy for penile cancer**

A report of 46 cases with literature review

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**Background and Objective:** Penile cancer is an uncommon malignant tumor, which is mainly treated by surgery, radiation and chemotherapy. This study was to investigate reasonable curative methods for penile cancer.

**Methods:** Medical records of 46 patients with penile cancer in the Department of Urology, The First Affiliated Hospital of Sun Yat-sen University from January 1996 to January 2005 were analyzed retrospectively. Forty-four patients had squamous cell carcinoma, one had Paget disease, and one had verrucous carcinoma.

**Results:** Thirty-nine patients received partial penectomy, four received total penectomy and perineal urethrostomy, one Paget disease patient received lesion resection and skin grafting, and two did not receive surgery. Nine out of 10 patients with positive lymph nodes received ilioinguinal lymphadenectomy, and five received pelvic lymphadenectomy. Forty-one cases were regularly followed up for one to 10 years. The one-, two-, five- and 10-year survival rates were 95.1%, 95.1%, 82.9% and 31.7%, respectively. Prognosis of patients with pelvic lymph node metastasis was poor. Two patients who had pelvic lymph node metastasis died of lung metastasis within two years after surgery.

**Conclusions:** Partial penectomy is an appropriate and effective management for penile cancer. Lymph node metastasis is an important prognostic factor for penile cancer. Patients with ilioinguinal lymph node metastasis should receive lymphadenectomy as early as possible to improve the therapeutic effect. The prognosis is poor for patients with pelvic lymph node metastases.

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Penile cancer is an uncommon malignant tumor. With the improvement of life quality and healthy conditions in China, the occurrence rate of penile cancer has been decreased noticeably in recent years, which accounts for less than 1.0% of all male malignant cancers in China. The genesis of penile cancer has been thought to be related to long-term irritation of smegma, and the majority of penile cancers are squamous epithelial carcinoma. Till now, surgery is still the most common therapy for penile cancer. This paper reported retrospective analysis on 46 cases with penile cancer, in order to explore reasonable curative methods.

**Data and Methods**

**General information.** Forty-six cases of penile cancer, aged 22–83 years old, with a median age of 56 years were included into the study. Thirteen cases were aged ≤ 40 years (28.3%). The disease course lasted from one week to 60 months, with a medium duration of 11.6 ± 3.7 months. Twenty-one cases had phimosis or redundant prepuce, eleven cases had the history of smoking, and one case had the history of acuminate warts. There were 22 peasants, 16 workers, and eight other occupations.

**Clinical manifestations.** Twenty-two cases had indurations or cauliflower-like lumps on the glans penis; nice cases had ulcers on the glans penis, sulcus coronarius, and prepuce; two cases had dysuria and hematuria due to tumor invasion into the urethra; 10 cases had redundant prepuce accompanied by itching and stabbing pain of the glans penis, purulent and bloody discharge from the prepuce orifice and palpable masses; five cases had only purulent and bloody discharge from the prepuce orifice which was detected during phimosectomy. Twenty-four cases were found swollen inguinal glands, including 14 bilateral cases and 10 unilateral cases.

**Diagnosis.** Diagnosis was confirmed by clinical manifestations and pathological biopsy. B-mode ultrasonography and CT examination were used to determine metastasis to the inguinal glands and pelvic lymph nodes. Thirty-two cases were subject to CT scans of the pelvic cavity, among which eight cases were found metastasis to the inguinal glands and two cases were found metastasis to pelvic lymph nodes. Pulmonary metastasis was found in one case by chest X-rays.

**Therapy.** Operation. All except two cases who refused to be treated by operation underwent surgery. Thirty-nine cases underwent partial penectomy, four cases underwent total penectomy and perineal urethrostomy, one Paget disease patient received lesion resection and skin grafting. Twenty-three cases underwent inguinal gland biopsy. Nine out of 10 patients with positive lymph nodes received ilioinguinal lymphadenectomy, and five received pelvic lymphadenectomy.

**Auxiliary treatments.** Four cases underwent external radiotherapy with a total dose of 5,500–6,000 cGy for six weeks combined...
with chemotherapy (bleomycin + cisplatin + vincristine). Among the four cases, two were pathologically confirmed after pelvic lymphadenectomy; one case with positive inguinal glands did not undergo lymphadenectomy; and one case had metastasis to inguinal glands and lung.

Results

Pathological types. There were 44 cases of squamous cell carcinoma, including 36 cases at G1, eight cases at G2, one case of Paget disease, and one case of warty carcinoma.

Results of TNM staging. Patients were classified according to the TNM staging based on the UICC staging system proposed in 1997. There were one case at T1a, 18 cases at T1, 23 cases at T2, and four cases at T3. There were 20 cases at N0, nine cases at N1, 16 cases at N2, and one case at N3. Pulmonary metastasis occurred in one case.

Postoperative complications. Necrosis of skin flaps occurred in four cases after lymphadenectomy, three of which underwent skin grafting; infection of incision occurred in two cases, which were healed after conservative therapy; lymphocyst occurred in one case.

Follow-up and prognosis. Of the 46 patients, 41 received regular follow-up for 1–10 years. Five cases were lost during follow-up, yielding a follow-up rate of 89.1%. Among those followed cases, two died within one year after operation, and five died within 2–5 years; the one-, two-, five- and 10-year survival rates were 95.1%, 95.1%, 82.9% and 31.7%, respectively.

Discussion

The incidence of penile cancer tends to decrease in recent years. The average onset age of penile cancer is approximately 60 years in Europe and US, while it is about 50 years in China. Data collected from this study show that the median age of patients with penile cancer is 56 years; patients under the age of 40 account for 28.3%; the youngest patient was 22 years old at the time of diagnosis, indicating that penile cancer may occur at any age. It is not easy to establish the diagnosis for penile cancer, because patients may feel ashamed of visiting doctors or the cancer is covered by phimosis or the redundant prepuce. Therefore, the disease course of penile cancer is often long. The medium time from the occurrence of penile cancer to the diagnosis in this study is 18 months. If a young patient is suspected of having penile cancer, he should undergo pathological biopsy timely to avoid delayed treatments.

Etiology and clinical manifestations of penile cancer. Some risk factors, such as phimosis and redundant prepuce are considered to be related to the onset of penile cancer. Research shows that early phimosis may significantly lower the occurrence of penile cancer. We find that patients with phimosis and redundant prepuce account for 45.7% of all penile cancer patients in this study.

The major clinical manifestations of penile cancer include single or multiple small indentations on the prepuce or glans penis, which would eventually develop into typical cauliflower-like masses with the growth of the tumor. Their tumor surface may fester to produce purulent and bloody discharge, and emit a foul smell when it is infected, or form refractory ulcers. A total of 47.8% patients in this study had indurations or cauliflower-like lumps on the glans penis, and 19.6% had ulcers on the glans penis, sulcus coronarius, and prepuce. Cauliflower-like masses are less malignant and have less potential of lymph node metastasis compared with ulcer-like masses. For patients with metastasis to inguinal glands, the swollen inguinal glands may be palpable. About 52.1% of the patients in this study were found swollen inguinal glands on diagnosis.

Diagnosis of penile cancer. It is not difficult to establish the diagnosis of penile cancer based on the medical history, clinical manifestations and physical examination. Timely pathological biopsy is the major method to confirm the disease. Sometimes the diagnosis is delayed at the early stage of penile cancer because of phimosis, redundant prepuce, difficulty in turning the prepuce inside out, or being ashamed of seeing doctors. In this study, two patients had been previously diagnosed as acuminate wart and underwent electrocautery for many times; one case presented with an unhealed ulcer seven months after phimosisectomy; another Paget disease patient with an unhealed superficial ulcer on the radix penis went undiagnosed for five years. Therefore, we suggest that patients with phimosis should undergo phimosisectomy as early as possible and accept routine pathological examination, in order to detect malignant lesions at an early stage.

After diagnosis of penile cancer, it is critical to determine whether there exists metastasis to the inguinal glands, pelvic lymph nodes, and remote areas. The disease should be staged and classified further, in order to make appropriate treatment regimens and predict the prognosis. For patients with swollen inguinal glands whose diameters are greater than 1.5 cm and whose texture is hard, the short-term anti-inflammatory treatment has no effect. They should undergo puncture biopsy of the swollen lymph nodes or cytological examination. Excision of sentinel lymph nodes is a method to stage penile cancer. The application of lymphadenography and radionuclide imaging may greatly enhance the reliability and accuracy of lymph node biopsy. B-mode ultrasonography, CT scan and MRI scan also help to understand the range and the extent of locally metastatic lymph nodes.

Treatments of penile cancer. Treatment of localized primary penile cancer. (1) Local excision is used to treat localized primary penile cancer. This option is suitable for in situ cancers and small tumors at T1. Primary cancer without deep infiltration or local metastasis to lymph nodes may also be treated by laser, electrocautery or radiotherapy, in order to conserve the function and the appearance of the sex organ. But these patients should be followed up closely due to the high rate of local recurrence. (2) Partial penectomy is suitable for the patients with penile cancer localized at the glans penis and sulcus coronarius, but not involved in the corpus penis. For most of the patients, partial penectomy may achieve a good result. Thirty-nine cases (84.8%) of all patients in this study underwent partial penectomy, none of which were found local recurrence. Partial penectomy greatly improves patient’s quality of life. An investigation made by Romero et al. shows that only 55.6% of the patients who underwent partial penectomy feel satisfactory about erection with the residual penis, and only 33.6% were satisfied with their sex life. The conservation of the sexual function is important, especially for young men. Argarwal et al. reveals that the maximal range of proximal infiltration of penile cancer is 5 mm for grade 1 and 2 penile cancer, and it is 10 mm for grade 3 penile cancer. They suggest that the excision of the proximal penile 10mm away from the cancer focus is sufficient to control the localized cancer focus for grade 1 and 2 patients, and 15 mm is sufficient for grade 3 patients.
Therefore, most patients may be treated by partial penectomy, so that the appearance and the function of the residual penis can be well preserved. In recent years, reconstructive surgery of the penis after partial penectomy has been developed. (3) Total penectomy is suitable for patients with penile cancer infiltrating into large areas and involving the majority of the corpus penis; or for those whose residual penis is too short after partial penectomy; and for those who cannot urinate on standing and complete sexual intercourse. Only four cases in this study underwent total penectomy, because multiple nodules on the penis were found in physical examination, or positive incision margin was found during operation.

**Treatment for patients with swollen lymph nodes.** Approximately 30.0–60.0% patients are found swollen inguinal glands at their first visit. However, about a half of these cases were caused by infections instead of cancer metastasis. We found 52.1% cases had swollen inguinal glands, among whom 23 underwent biopsy of the swollen lymph glands. The swollen inguinal glands were revealed to be associated with cancer metastasis in ten cases (43.5%) out of the 23 cases. All patients in this study were treated with antibiotics after admission, and biopsy of the lymph node was performed for those with non-shrunken lymph nodes. Presence or absence of lymph node metastasis is an important prognostic factor of penile cancer. Timely ilio-inguinal lymphadenectomy is an effective measure to treat metastasis to the inguinal glands and pelvic lymph nodes. Research by Fraley et al. reveals that the five-year tumor-free survival rate is 75.0% for patients with positive lymph nodes who underwent timely lymphadenectomy, and 8.0% for patients who underwent delayed operations. Therefore, patients who are pathologically confirmed with lymph node metastasis should undergo lymphadenectomy promptly to improve their prognosis. Patients with metastasis to pelvic lymph nodes as suggested by imaging examination may undergo neoadjuvant chemotherapy or radiotherapy using the linear accelerator. Those patients may further receive surgery if adverse reactions to the neoadjuvant treatment appear. Leijte et al. claim that eight out of 20 cases with lymph node metastasis or remote metastasis that could not be treated by lymphadenectomy were responsive to the neoadjuvant treatment. They subsequently all underwent surgery and achieved a good five-year survival rate of 56.0%. So far, the majority of researchers consider the neoadjuvant treatment as a good option, especially for young patients. In this study, two cases were found metastasis to pelvic lymph nodes as confirmed pathologically after operation. Both of them died of pulmonary metastasis within two years. Their poor prognosis may be attributed to the old age and increased complications caused by chemotherapy after surgery. Patients who do not sensitively respond to chemotherapy are advised to receive radiotherapy in time to enhance the survival rate.

It is controversial that whether lymphadenectomy should be preventively performed on patients without swollen inguinal glands detected by clinical examination. McDougal et al. performed a study on 23 patients with non-swollen lymph nodes which were pathologically proven positive. They obtained a five-year survival rate of 83.0% for patients underwent lymphadenectomy at an early stage; a survival rate of 36.0% for patients underwent lymphadenectomy after the occurrence, suggesting that preventive lymphadenectomy at an early stage may significantly improve the prognosis for the patients with lymph node micrometastasis. However, a study on 100 penile cancer patients shows that lymph node metastasis occurred only in six out of 33 cases without swollen lymph nodes, and who underwent preventive lymphadenectomy. Metastasis to pelvic lymph nodes, confirmed by pathological examination, occurred in only two out of 12 cases underwent preventive pelvic lymphadenectomy. Therefore, it is concluded that about 82.0% of the patients accepted unnecessary lymphadenectomy. We found metastasis to inguinal glands in only six cases during close follow-up, among whom two cases had metastasis within two years after the excision of tumor, and four cases had metastasis within five years. The risk of metastasis to lymph nodes relates to the size of the primary tumor, infiltration depth, staging, grading, and the presence or absence of the infiltration into lymphatic ducts and blood vessels. Therefore, patients without swollen lymph nodes and well differentiated primary tumors may only be closely observed and followed up. Lymphadenectomy should be performed as early as possible on patients with poorly differentiated cancer or complicated by infiltration into the lymphatic ducts or into blood vessels or active proliferation.

Iliac lymphadenectomy is accompanied by more complications. Seven out of nine cases in this study underwent iliac lymphadenectomy had complications to different extents, accounting for 77.8% of all patients. These complications occurred mainly in cases who accepted the operation at an early stage. In recent years, the technique of lymphadenectomy has been improved, which significantly lowers the incidence of complications. An important issue is how to determine the occurrence of lymph node micrometastasis. Kroon et al. performed biopsy of sentinel nodes on 140 cases without swollen lymph nodes and found 31 cases with lymph node micrometastasis. These patients were subject to further lymphadenectomy. Follow-up and observations on patients with negative lymph nodes proven by biopsy revealed only six cases subsequently appeared lymph node metastasis. Biopsy of sentinel lymph nodes decreases the complication of conventional lymphadenectomy, so that the occurrence of complications is reduced from 88.0% for the conventional lymphadenectomy to 8.0% for sentinel lymphadenectomy. Thus, the latter one may be used to assess whether the penile cancer patients have lymph node micrometastasis. However, a false negative rate of 15.0 % for sentinel lymphadenectomy is detected by some researchers. Recently, the improvement of sentinel lymphadenectomy reduces the false negative rate. Meanwhile, the application of lymphatic mapping and lymphoscintigraphy have greatly increased the positive detection rate of lymph nodes under biopsy. Therefore, patients without swollen lymph nodes may undergo biopsy of the sentinel lymph node, and then undergo further lymphadenectomy only when lymph node micrometastasis has been found. This not only reduces the risk related to unnecessary lymphadenectomy, but also avoids delayed treatments for patients with micrometastasis.

**References**


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