โรคมะเร็งขององคชาต ผลการรักษาผู้ป่วยที่ไม่พบก้อนโตของต่อมน้ำเหลืองขาหนีบและการนำไปใช้ในการวางแผนการรักษาในโรงพยาบาลสุรินทร์

Squamous cell carcinoma of the penis : Management of patients with clinically negative inguinal nodes and implications for management at Surin Hospital

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ABSTRACT

Introduction : Early or delayed inguinal lymph node dissection, in patients with squamous cell carcinoma of the penis and clinically negative inguinal nodes, are controversial. But risk of surgical complications of lymph node dissection are reported. Urologists in Surin Hospital use surveillance policy for management of patients with clinically negative inguinal nodes. Results are evaluated and implications for management are concluded.

Objective : To study the results of management of patients with clinically negative inguinal nodes at Surin Hospital That were treated initially with surveillance policy.

Patients and methods : Between 2001 and 2006, 40 patients with squamous cell carcinoma of the penis were reviewed. Two were high staged tumor and were referred to other hospital. Six with clinically palpable inguinal nodes were managed by lymph node dissection. Thirty two patients with clinically negative nodes, Tis to T3, were evaluated after definitive treatment of the primary tumor.

Results : Thirty-two patients with clinically negative nodes, Tis to T3, were managed by surveillance policy. Twenty-one patients (65.6%) were known to have no metastatic nodes at least 12 months. Status of lymph nodes of ten patients (31.3%) were not known. One patient died of the disease, with metastatic groin node dissection, in 17 months later.

Conclusion : Follow-up of patients with carcinoma of the penis should be systematically approached and medical team should educate them how importance of node metastasis for their survival. Although status of lymph nodes in one-thirds of the patients were not known, we imply that they had no palpable nodes because they did not present with enlarged groin nodes or ulcerative nodes. Thus the surveillance policy is still be used as management policy for SCCP patients with clinically negative nodes at Surin Hospital.

Key words : Carcinoma, Penis Lymph nodes

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บทคัดย่อ

เหตุผลของการวิจัย : ในผู้ป่วยมะเร็งองคชาตการผ่าตัดเลาะต่อมน้ำเหลืองขาหนีบในผู้ป่วยที่ไม่พบก้อนโตของต่อมน้ำเหลืองขาหนีบอาจมีบางส่วนที่มีการแพร่กระจายแล้ว แต่ยังตรวจไม่พบก้อน ช่วยให้อัตราการรอดชีวิตของผู้ป่วยสูงขึ้น แต่อาจพบภาวะแทรกซ้อนจากการผ่าตัดโดยไม่จำเป็นเพิ่มขึ้น เนื่องจากมีรายงานการพบการแพร่กระจายของมะเร็งสู่ต่อมน้ำเหลืองขาหนีบเพียงประมาณ 20% เท่านั้น การผ่าตัดเลาะเอาต่อมน้ำเหลืองขาหนีบอาจทำให้เกิดภาวะแทรกซ้อนโดยไม่จำเป็นในผู้ป่วยอีก 80% การเฝ้าติดตามการเกิดต่อมน้ำเหลืองขาหนีบโตขึ้นภายหลังการผ่าตัดมะเร็งองคชาตและทำผ่าตัดเลาะต่อมน้ำเหลืองขาหนีบออกจะช่วยลดการผ่าตัดและภาวะแทรกซ้อนที่ไม่จำเป็นลงได้มาก

วัตถุประสงค์ของการศึกษา : เพื่อศึกษาผลของการรักษาผู้ป่วยมะเร็งองคชาตที่ต่อมน้ำเหลืองขาหนีบไม่โตด้วยการเฝ้าติดตามในโรงพยาบาลสุรินทร์และการนำผลการรักษาไปใช้ต่อเนื่อง

ผู้ป่วยและวิธีการ : ระหว่างปี พ.ศ. 2545 ถึงปี พ.ศ. 2549 การศึกษาข้อมูลผู้ป่วยมะเร็งองคชาตที่ต่อมน้ำเหลืองไม่โต ระยะ Tis ถึง T3 จำนวน 32 ราย ที่ได้รับการรักษาด้วยการเฝ้าติดตามต่อมน้ำเหลืองขาหนีบภายหลังได้รับการผ่าตัดมะเร็งที่องคชาตออก

ผลการศึกษา : ในจำนวนผู้ป่วย 32 ราย ที่ต่อมน้ำเหลืองขาหนีบไม่โต พบว่าผู้ป่วย 21 ราย (65.6%) สามารถติดตามผลการรักษาได้ไม่พบว่ามีการแพร่กระจายสู่ต่อมน้ำเหลืองขาหนีบตั้งแต่ 12 เดือนขึ้นไปจนถึง 69 เดือน มีผู้ป่วยที่ไม่มาตามนัดและไม่ทราบผล 10 ราย (31.3%) มีผู้ป่วย 1 ราย ที่พบการแพร่กระจายสู่ต่อมน้ำเหลืองขาหนีบ 2 ข้าง ใน 3 เดือน และได้รับการผ่าตัดเลาะต่อมน้ำเหลือง แต่ผู้ป่วยเสียชีวิตจากโรคโดยมีชีวิตอยู่ได้ 17 เดือน

สรุป : การเฝ้าติดตามการแพร่กระจายของมะเร็งองคชาตสู่ต่อมน้ำเหลืองขาหนีบยังเป็นปัญหาที่ไม่สามารถติดตามได้ครบถ้วนและตามระยะเวลา ซึ่งต้องมีการติดตามอย่างเป็นระบบและให้การศึกษาแก่ผู้ป่วยให้เห็นความสำคัญของการตรวจต่อมน้ำเหลืองขาหนีบด้วยตนเอง เพื่อมารับการรักษาได้รวดเร็วและทันท่วงที แม้ว่าประมาณ 1 ใน 3 ของผู้ป่วยจะไม่สามารถทราบได้ว่ามีการแพร่กระจายของมะเร็งสู่ต่อมน้ำเหลืองขาหนีบหรือไม่ แต่สามารถคาดได้ว่าผู้ป่วยน่าจะไม่มีต่อมน้ำเหลืองโต เพราะหากผู้ป่วยมีความผิดปกติของต่อมน้ำเหลืองขาหนีบคงต้องมาพบแพทย์เพื่อการรักษา ดังนั้นการรักษาผู้ป่วยมะเร็งองคชาตที่ต่อมน้ำเหลืองขาหนีบไม่โตด้วยการเฝ้าติดตามยังเป็นวิธีการรักษาที่ได้ผลดี

Introduction

Squamous cell carcinoma of the penis (SCCP) is an uncommon disease, accounting for less than 1% of all male malignancies in the Western countries, the reported incidence is 0.5 to 1.5 per 100,000 population[1]. But in developing countries it is more common, in South India the incidence is 2.9 per 100,000 population[2]. Penectomy is the standard treatment although some institutes try to treat primary tumor with conservative surgical techniques in selected patients[3]. Other modalities for treatment SCCP such as laser therapy, radiation or chemotherapy are of limited to a small series with inconclusive results and not suitable for treatment of SCCP patients at Surin Hospital.

Regional lymph node metastasis to inguinal nodes may be found concomitantly with primary tumor, or may be palpable later after penectomy was done. Early regional lymph node dissection in patients with negative nodes on physical examination are controversial, as these patients have been found occult lymph node metastasis about 20% of cases[1,4]. About 50% of palpable inguinal nodes at diagnosis are reactive nodes, but nearly all of enlarged nodes that appearing during follow-up are metastatic[5]. The reported incidence of inguinal node metastases is 35-60% and determine the outcome of this disease[6-8].

However, because of reported risk of surgical complications of lymph node dissection[9,10], we use surveillance policy in patients with clinically negative nodes. Antibiotics was given to penectomized patients on discharge day from Surin Hospital and an appointment of 4 to 6 week follow-up was planned. If groin node, unilateral or bilateral, was palpable during the follow-up period, inguinal node dissection was planned.

Objectives

This retrospective study was designed to evaluate the results of management of patients with clinically negative groin nodes.

Patients and methods

Between 2001 and 2006, the medical records of 47 patients with carcinoma of the penis admitted in Surin Hospital were reviewed. Seven patients (mean age 74.7 years, median 73) were excluded from this study for denying surgical treatment. Forty patients, whom histopathology of the primary tumor were reported, were enrolled in this study.

Patients were staged clinically according to TNM classification for penile cancer AJCC (Table 1). The primary tumor histological grade was classified as well (grade I), moderately (grade II) and poorly differentiated (grade III). Penectomy (partial or total) was undertaken according to the extent of clinical involvement in each case.

Table 1 American Joint Committee on Cancer (AJCC) 1997 Staging of Penile Cancer

Tumor (T)	
Tx	Primary tumor cannot be assessed
T0	No evidence of cancer
Tis	Carcinoma in situ
Ta	Noninvasive verrucous carcinoma
T1	Tumor invades subepithelial connective tissue
T2	Tumor invades corpus spongiosum or carvernosum
T3	Tumor invades urethra or prostate
T4	Tumor invades other adjacent structure
Nodes (N)	
Nx	Regional lymph nodes cannot be assessed
N0	No region node metastasis
N1	metastasis to a single, superficial inguinal lymph node
N2	Metastasis in multiple or bilateral superficial inguinal lymph nodes
N3	Metastasis in deep inguinal or pelvic lymph nodes, unilateral or bilateral
Metastasis (M)	
Mx	Presence of distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

Results

Statistics used in this study are mean, standard deviation, median, and percentage.

All of the forty-seven patients were in the poor socio-economic conditions and low educated. Their occupations were farmers and workers, living in the rural area. Forty-five patients were Surin Provincial residents, the other two were not. The peak incidence occurred in the fifth, sixth and seventh decades, with a mean age of 61.5 years (sd, range 11.9,37- 92). The mean duration of disease development was 8.3 months (sd,range 10.9,1-48). The median follow-up was 12 months (mean 10.5, range 1-46). Most of them were lost to follow-up after surgery for primary tumor.

Of the forty patients that were enrolled in this study, 35(87.5%) had grade I disease, 5 (12.5%) had grade II disease (Table 3). None of the patients had grade III disease. The penis was totally penectomied in 4 patients, partially penectomied in 32, circumcised in 2, and biopsied only in 2 of

whom were referred for radiation therapy at higher center for high stage tumor (T4N1 and T3N1).

Clinically positive nodes were found in 8 patients (20%) at initial physical examination, the rest of the patients (80%) were found to have negative nodes. Pathological T and clinical N stage were described in Table 2. Clinical N stage and tumor grade were described in Table 3.

Table 2 Pathological T-stage and clinical N-stage.

Pathological T-stage	Number	Clinical N-stage	Number
Tis	1	N0	1
Ta	2	N0	2
T1	25	N0	22
		N1	2
		N2	1
T2	5	N0	3
		N1	1
		N2	1
T3	5	N0	3
		N1	2
T4	2	N0	1
		N1	1

Table 3

Clinical N-stage	Number	Grade	Number
N0	32	I	27
		II	5
N1	6	I	6
N2	2	I	2

Penectomy with unilateral inguinal node dissection in the single operation was done in 3 patients. Among the three, one was found to have negative node metastasis and two were found to have positive node 1 in 2 nodes and 2 in 3 nodes respectively. One patient had contralateral groin node dissection done in 12 months later and positive node metastasis was reported. During the follow-up period, bilateral groin node dissection was done in two patients who have T2N2 and T1N0 with grade 1 tumor, 1 and 3 months after penectomy respectively. The latter died of the disease in 17 moths. (Table 4)

Table 4 Results of lymph node dissection (LND)

Case	Age	TNM	Grade	Surgical procedure	Results
1	54	T1N1	I	partial penectomy with Lt. inguinal LND	reactive lymph nodes, no metastasis follow up for 3 months then lost.
2	72	T3N1	I	partial penectomy with Rt. inguinal LND	metastasis to 1 node. Referred for adjuvant radiotherapy.
3	42	T1N1	I	prepuce resection with Rt. Inguinal LND	Rt. Inguinal LND ; metastasis in 2 of 3 nodes, Lt. inguinal LND done 15 months later ; tumor growth 2 cm. at skin of Lt. groin, negative all 7 nodes. Alive without disease for 43 months.
4	60	T1N2	I	Partial penectomy with bilat. inguinal LND	Rt. ; metastasis in 1 of 8 nodes. Lt. ; metastasis in 2 of 7 nodes.
5	58	T2N2	I	Partial penectomy	Bilateral inguinal LND 1 month later and found metastatic nodes bilaterally. Alive without disease for 48 months.
6	43	T1N0	I	Partial penectomy	Bilateral inguinal LND 3 months later and found metastatic nodes bilaterally. Died of the disease in 17 months.

There were thirty-two patients with clinically negative nodes, Tis to T3, to be evaluated in this study. Because of the long period of follow-up time and poor socio-economic conditions, tendency of the patients to be lost to follow-up was highly possible. All patients were advised to observe their groin node for early detection for abnormal enlargement of groin lymph nodes which means metastatic disease may occur and they had to meet the doctor as soon as possible. During the follow-up period only one patient with negative nodes needed to have bilateral groin node dissection done and died of the disease in 17 months.

To know the status of the disease of the patients with clinically negative nodes who were lost to follow-up, questionnaires were mailed to the patients or their relatives asking for conditions of recurrences and their groin node status. Of the 28 questionnaires, 17 were received back and all were alive without recurrence or abnormal enlargement of groin nodes. Four patients can be followed (62, 26, 13 and 12 months) and were doing well. Ten patients did not response to questionnaires; 4 patients were lost to follow-up within 6 months and 6 patients can not be accessed because of lost of out patient medical records.

Thirty-two patients with stage Tis to T3N0 (clinically negative node) who were managed by surveillance policy can be evaluated as in Table 5. Twenty-one patients (65.6%) were known to have no metastaic nodes at least 12 months by follow-up or by questionnaire. Ten patients (31.3%) cannot be evaluated because of incomplete data and lost to follow up less than 12 months. One patient was found to have bilateral inguinal nodes metastasis 3 months later and bilateral inguinal node dissection was done, he died of the disease 17 months later.

Table 5 Results of management of patients with negative nodes.

patient	Stage	Tumor grade	Results
1	T1N0	I	na
2	TaN0	I	Alive, neg. node, 62 months by questionnaire.
3	T1N0	II	Alive, neg. node, 62 months by follow-up.
4	T1N0	I	Alive, neg. node, 69 months by questionnaire.
5	T1N0	I	Alive, neg. node, 68 months by questionnaire.
6	T1N0	I	Alive, neg. node, 68 months by questionnaire.
7	T1N0	I	Alive, neg. node, 64 months by questionnaire.
8	T3N0	I	na
9	T1N0	I	Follow-up 3 months, then lost to follow-up.
10	T1N0	I	Alive, neg. node, 54 months by questionnaire.
11	T1N0	I	na
12	T1N0	I	Alive, neg. node, 54 months by questionnaire.
13	T1N0	II	Follow-up 3 months, then lost to follow-up.
14	T3N0	I	Alive, neg. node, 51 months by questionnaire.
15	T2N0	I	Alive, neg. node, 50 months by questionnaire.
16	T1N0	II	Alive, neg. node, 50 months by questionnaire.
17	T1N0	II	Follow-up 26 months, then lost to follow-up.
18	TisN0	I	Alive, neg. node, 42 months by questionnaire.
19	T1N0	I	Alive, neg. node, 42 months by questionnaire.
20	T2N0	I	Follow-up 6 months, then lost to follow-up.
21	T2N0	I	na
22	T1N0	I	Bilateral inguinal LND 3 months later, found metastatic nodes bilaterally. Died of the disease in 17 months.
23	TaN0	I	Alive, neg. node, 38 months by questionnaire.
24	T3N0	I	na
25	T1N0	II	Follow-up 1 month, then lost to follow-up.
26	T1N0	I	Alive, neg. node, 31 months by questionnaire.
27	T1N0	I	Alive, neg. node, 27 months by questionnaire.
28	T1N0	I	na
29	T1N0	I	Alive, neg. node, 21 months by questionnaire.
30	T1N0	I	Follow-up 13 months, neg. node.
31	T1N0	I	Alive, neg. node, 24 months by questionnaire.
32	T3N0	I	Follow-up 12 months, neg. node.

Discussion

For the period of five years, 45 patients with SCCP were found in Surin Province (the other two patients were not Surin provincial residents), it is estimated that the incidence of SCCP is about 0.65 per 100,000 population (calculated on population of 1,371,429 in 2003[11]), lower than South India (2.9) as mentioned earlier and may be in the range like Western country.

Squamous cell carcinoma of the penis is a locoregional disease and lymph node metastasis is the main prognostic factor. This group of SCCP patients should have clinically examination of inguinal node for metastasis during the follow-up period intensively, but the incidence of patients who were lost to follow-up were within 12 months. So the surviellance policy for treatment SCCP in Surin Hospital need a systematic approach and strategy to make sure that these patients will not be lost or they can observe their groin for abnormal enlargement nodes that alert them to the hospital. Therefore the doctor and nurse as a clinical team should educate these patients about the disease and importance of groin nodes in treatment and prognosis before they are discharged.

For patients with negative nodes (as in Table 5), we found that two-thirds of the patients can survive without metastatic nodes, although the results were not complete but we implies that those who were lost to follow up had no metastatic groin nodes and were doing well because none of them presented with enlarged groin nodes or ulcerative nodes. So the surveillance policy can be used in Surin Hospital for patients with grade I and II tumor except grade III which early bilateral inguinal node dissection is recommended because of highly invasive and early metastasis to inguinal nodes[12]. But patients must be followed by any way, such as by mail, by phone call or by nearby Primary Care Unit to make sure that the information of the patients will be followed and surgical lymph node dissection can be done early.

It is accepted that nearly all of enlarged nodes that appearing during follow-up are metastatic[5]. Lymph node dissection should be done bilaterally or unilaterally whenever clinical palpable node was found on follow-up is controversy. The likelihood of bilateral involvement is related to the number of involved nodes in the resected specimen. With two or more metastases the probability of occult contralateral involvement is 30% and warrants an early inguinal lymph node dissection[9]. Therefore bilateral inguinal node dissection should be done whenever palpable groin node was found unilaterally or bilaterally. As we found that three patients with unilateral lymph node dissection were undertaken contraleteral inguinal node dissection later.

In conclusion, for patients with clinically negative inguinal nodes at Surin Hospital can be managed bysurveillance policy, but they must be followed by systematic approach and be educated by medical personel team to assure that the status of the disease and lymph nodes can be assesed early. Palpable nodes during the follow-up period should be done by bilateral inguinal node dissection as early aspossible.

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References

1. Burgers JK, Badalamet RA, Drago JR. Penile cancer : clinical presentation, diagnosis and staging. Urol Clin North Am 1992:19:251-6
2. Hascih K, Ravi R. The role of tobacco in penile carcinoma. Br J Urol 1995;75: 375-7
3. Bissada NK, Yakout HH, Fahmy WE, et al. Multi-institutional long-term experience with conservative surgery for invasive penile carcinoma. J Urol 2003;169:1138-42
4. McDougal WS, Kirshner FK Jr, Edwards RH, Killion LT. Treatment of carcinoma of the penis : the case for primary lymphadenectomy. J Urol 1986;136: 38-41
5. Ornellas AA, Seixas AL, Marota A, Wisnescky A, Campos F, de Moraes JR. Surgical treatment of invasive squamous cell carcinoma of the penis : retrospective analysis of 350 cases. J Urol 1994;151: 1244-9
6. Beggs JH, Spratt JS. Epidermoid carcinoma of the penis. J Urol 1961;91:166-72
7. Hanash KA, Furlow WL, Utz DC, Harrison EG. Carcinoma of the penis : a clinicopathological study. J Urol 1970; 104:291-7
8. Dekernion JB, Tynbery P, Persky L, Fegen JP. Carcinoma of the penis. Cancer 1973; 32:1256-62
9. S. Horenblas. Lymphadenectomy for squamous cell carcinoma of the penis. Part 2 : The role and technique of lymph node dissection. BJU International 2001; 88:473–83
10. C.F. Heyns, Van Vollenhoven, J.W. Steenkamp, F.J. Allen, D.J.J. Van Velden. Carcinoma of the penis-appraisal of modified tumour-staging system. B J Urology 1997; 80: 307-12
11. Department of Provincial Administration, Ministry of Interior, Government of Thailand.
12. Horenblas S, Van Tinteren HV. Squamous cell carcinoma of the penis. IV. Prognostic factors of survival : analysis of tumor, nodes and metastasis classification system. J Urol 1994;151:1239-43.