

Case Report

Primary Non-Hodgkin Lymphoma of the Urethra

Somchai Insiripong¹, Surachai Sripiyasothorn² and Sunya Prabripootalung³

¹Department of Medicine; ²Department of Surgery; ³Department of Obstetrics and Gynecology, Maharat Nakhon Ratchasima Hospital, Nakhon Ratchasima

Abstract: A 73-year old lady presented with a painless mass originating from the introitus, without fever or weight loss. The tumor grew over a few months, obstructing urethra. She also had diabetes mellitus, well controlled with glibenclamide. Physical examination revealed a fungating mass, size 8x4 cm originating from the urethral meatus, no other node, no hepatosplenomegaly. The pathological diagnosis was diffuse large B-cell non-Hodgkin's lymphoma (NHL), stage IEA. The HIV antibody was negative and serum LDH was normal. Primary NHL of the urethra among patients without HIV infection is rare and has not been reported in Thai patients. The patient had partially surgical resection, followed by local irradiation and 6 cycles of CHOP regimen respectively. She tolerated treatment well, was alive and free from the disease at 2.5-year follow-up visit.

Key Words : ● Non-Hodgkin lymphoma ● Extranodal ● Urethra

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Introduction

Non-Hodgkin's lymphoma (NHL) is a malignant neoplasm of lymphoid tissue which is pathologically lack of Reed-Sternberg cell. It usually originates from lymphatic organs. However around 25-40% of lymphomas occur in non-lymphoid tissues, so called extra-nodal lymphoma¹. Common extranodal sites are gastro-intestinal tract, especially the stomach, whereas other areas such as skin, orbit, uterus, testis² including the urethra³ are unusual sites.

The NHL involving the urethra has two forms. In the primary form, NHL originates and confines solely within the urethra, whereas in the secondary form, the urethra is involved by the NHL as a part of multiple extranodal sites, mainly as extension from the urinary bladder.⁴ Urethral NHL had been first reported in 1972,⁵ then the sporadic cases have been occasionally reported,⁶⁻⁸

with primary urethral NHL first reported in 1987. Up to 2009, only 25 cases of primary urethral NHL have been reviewed with 1 case additionally reported from Japan.⁹

In Thailand, two nationwide surveys of NHL identified extranodal lymphoma between 30%¹⁰ and 55%.¹¹ The most common sites were aero-digestive and gastrointestinal tracts, particularly the stomach.¹² The other sites of extranodal NHL¹³⁻¹⁹ included skin and soft tissue, liver, cervix, cerebellum, head and neck, oral cavity, but not from urethra. We hereby report a case of primary NHL of the female who sought medical attention due to a urethral mass.

Case report

The married Thai female, of 73 years of age, presented with a painless fungating mass at the urethral orifice protruding into the introitus for a few months. The mass had gradually enlarged until the micturition was hardly possible due to the obstruction of the urethral orifice, without constitutional symptoms such as fever or weight loss. She had diabetes mellitus, well controlled with glibenclamide

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Requests for reprints should be addressed to Somchai Insiripong, Department of Medicine, Maharat Nakhon Ratchasima Hospital, Nakhon Ratchasima 30000 e-mail: chaikorat@gmail.com

for many years. On physical examination, she had no pallor, no hepatosplenomegaly and no lymphadenopathy. Pelvic examination showed a solitary fungating mass, 8x4 cm, with firm consistency, apparently normal covering mucosa, originating from the urethral meatus, partially protruding into the introitus. The vaginal mucosa had whitish discharge with the excoriation of both labia later proved to be vaginal candidiasis, and the uterus as well as the adnexae appeared normal.

A complete blood count revealed hematocrit of 30.7%, normal white cell count (9,000/ μ L with normal differential), and normal platelet count (243,000/ μ L). Serum chemistry revealed direct bilirubin 0.0 mg/dL, total bilirubin 0.4 mg/dL, AST 13 U/L, ALT 8 U/L, alkaline phosphatase 63 U/L, albumin 3.9 g/dL, globulin 2.7 g/dL, BUN 11 mg/dL, creatinine 1.24 mg/dL, fasting blood glucose 92 mg/dL, cholesterol 172 mg/dL, triglyceride 209 mg/dL, LDH 339 U/L, uric acid 7.5 mg/dL, Ca 7.9 mg/dL, PO_4 3.1 mg/dL, Mg 1.6 mg/dL. HIV antibody was negative. Urinalysis revealed 10-20 red cells/high power field (HPF), 5-10 white cells/HPF, ketone 2+, blood 3+, protein trace, sugar-negative.

The chest radiograph and the ultrasonography of the whole abdomen confirmed absence of lymphadenopathy or hepatosplenomegaly. Cystoscopy revealed single mass at the urethral meatus as previously described.

The mass was almost totally resected by the urologist under the general anesthesia and the pathological diagnosis of the tissue, confirmed by the immunophenotyping, was non-Hodgkin's Lymphoma, large B cell type. A bone marrow biopsy showed normal cellularity of 30%, without lymphoma involvement. Clinical stage was IEA.²⁰

She was treated with the cobalt-60 teleradiotherapy for the residual lymphoma at the tumor bed followed by 6 cycles of chemotherapy with vincristine, doxorubicin, cyclophosphamide, and prednisolone (CHOP regimen). The supportive treatments comprised the insulin therapy and oral ketoconazole for the vaginal candidiasis. She could tolerate the sequential therapy well. She was

alive and well, without evidence of disease two and a half years later at the time of this report.

Discussion

The incidence of NHL showed bimodal pattern; with peak incidence between 24-54 years and after 65 years.²¹ For DLBCL cases, the median age is in the seventh decade and it is the most common immunophenotype of extranodal lymphoma.²² All case reports of primary NHL of the urethra were in older people and affect females more often than males.²³⁻²⁶ Our case also fit these descriptions.

DLBCL is known to be associated with immunocompromised conditions including HIV, organ transplantation, or autoimmunity. Similar to other extranodal lymphoma, the primary urethral NHL can be found in cases of either non-HIV³⁴ or in HIV infection.^{35,36} Our case is not associated with HIV. The association between DM and NHL is inconclusive. Some authors found the rate ratio between type 2 DM and NHL to be 1.41 (95% CI 1.07-1.88)³ and 1.79 (95% CI: 1.30-2.47). In a recent meta-analysis, the odd ratio for NHL among the diabetics was increased at 1.22 (95% CI 1.07-1.39; $p < 0.01$)³² whereas others found that there was no association between DM and NHL.³³ Primary NHL of the urethra was reported to be either low grade or high grade histology³⁷ while our case was DLBC.

Anyway, because of limitation of our laboratory facilities, the nature of immunological markers of lymphoma in our patient was not demonstrated.

After nearly total excision of the urethral mass, she was successfully treated with the radiation and followed by the CHOP regimen for 6 cycles. This sequential therapy has been previously reported to be effective for urethral NHL³⁴. Except for her advanced age (> 60 years), international prognostic index score for our case was low: only one extranodal site, the low serum LDH, the clinical stage IEA, and the good performance,³⁸ which predicts prolonged survival.

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Primary non-Hodgkin Lymphoma of Urethra: รายงานผู้ป่วย

สมชาย อินทศิริพงษ์¹ สุระชัย ศรีปิยะโสทร² และ สัญญา ปราบริบูรณ์³

¹กลุ่มงานอายุรกรรม, ²กลุ่มงานศัลยกรรม, กลุ่มงานสูติ-นรีเวชกรรม โรงพยาบาลมหาราชนครราชสีมา นครราชสีมา

บทคัดย่อ ผู้ป่วยหญิงไทย อายุ 73 ปี มาพบแพทย์ด้วยอาการมีก้อนยื่นออกมาจากช่องคลอดเป็นเวลา 2-3 เดือน ไม่เจ็บ ไม่มีไข้หรือ น้ำหนักลด ก่อนโตช้าๆ มีอาการปัสสาวะขัด ผู้ป่วยมีประวัติเป็นเบาหวานควบคุมได้ด้วย glibenclamide ตรวจร่างกายพบก้อนเนื้อยื่นออกมาจาก ปากช่องคลอดขนาด 8x4 ซม. ไม่พบต่อมน้ำเหลืองที่อื่นๆ ตับม้ามไม่โต ผลการตรวจทางพยาธิวิทยาเป็นมะเร็งต่อมน้ำเหลืองชนิด diffuse large B cell non-Hodgkin's lymphoma ระยะที่หนึ่งไอเอ ผลตรวจเลือดไม่พบแอนติบอดีต่อเอชไอวี และมีระดับซีรัมแอลดีเอชปกติ มะเร็งต่อมน้ำเหลืองที่พบเฉพาะปากช่องคลอดในผู้ป่วยที่ไม่ติดเชื้อไวรัสเอดส์ยังถือว่าพบน้อยมาก และยังไม่เคยมีรายงานในคนไทย ผู้ป่วยได้รับการรักษาด้วยการผ่าตัดก้อนเนื้อออกเกือบหมด ตามด้วยการฉายรังสีเฉพาะที่ และเคมีบำบัด สูตร CHOP ทั้งหมด 6 รอบ ผู้ป่วยทนการรักษาได้ดี และ ยังคงสบายดี โดยไม่พบว่ามีมะเร็งกลับเป็นซ้ำภายใน 2 ปีครึ่ง

Key Words : ● Non-Hodgkin lymphoma ● Extranodal ● Urethra

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