Chinese Journal of Clinical Oncology Apr. 2007, Vol. 4, No. 2 P 129~132 Tong Fang.
[SpringerLink] DOI 10.1007/s11805-007-0129-1

Clinical Analysis of 29 Cases with Primary Malignant Lymphoma of the Prostate

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OBJECTIVE To summarize the clinical characteristics, pathology，treatment and prognosis of malignant lymphoma of the prostate.
METHODS Clinical data from 29 patients with primary malignant lymphoma of the prostate were reviewed retrospectively. The median age was 66 years. Clinical signs and symptoms were due to lower urinary tract obstruction resulting from a diffusely enlarged prostate. Prostate biopsies revealed diffuse large B-cell non-Hodgkin's lymphoma. The therapeutic modalities included prostatectomy, radiotherapy and chemotherapy.
RESULTS Extraprostatic involvement at various sites became evident in 19 of the 29 patients after diagnosis. Ten patients died from lymphoma with a median survival of 23 months (range, 2-30 months) . Seven patients were alive up to 60 months.
CONCLUSION Malignant lymphoma involving the prostate was rare and has a rather poor prognosis. Prognosis related to the patient age，histologic type, and treatment or clinical stage of the disease at presentation.

KEYWORDS: malignant lymphoma, non-Hodgkin's, prostate

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Received January 15, 2007; accepted March 6, 2007.

Primary malignant lymphoma of the prostate is rare. Less than 100 cases have been reported, mostly as single-case reports. Studies from the M.D Anderson hospital, Mayo Clinic, Stanford University, the University of Chicago, and Johns Hospkins Hospital over 115 years period have documented only 7 primary prostatic lymphomas[1]. In order to understand the disease more fully, we collected 29 cases of primary malignant lymphoma (24 cases overseas, 4 cases in China and 1 case which was treated by us) between 1980 and 2002 and summarized the clinical characteristics.

MATERIALS AND METHODS

General data

Patients with primary prostatic lymphomas ranged in age from 32 to 66 years (mean, 66 years). Symptoms were known for 26 patients of which 24 had clinical symptoms resulting from a lower urinary tract obstruction. These were retention, including urgence, frequency, nocturia, difficulty voiding and retention. Eleven patients had hematuria, including 3 patients without obstruction. Clinical symptoms were absent in 2 patients. On rectal examination 14 patients had a diffusely enlarged prostate. Four patients had a nodular prostate, 5 were hard and enlarged. The prostate specific antigen (PSA) range was 0.38-10.0 ng/ml(mean, 3.5 ng/ml). PSA was elevated ($>$ 4 ng/ml) in 4 patients with prostate carcinoma. The others were lower than 4 ng/ml. The di-

agnosis of prostatic lymphoma was made by radical prostatectomy in 4 patients, transurethral resection in 17 patients, and transrectal needle biopsy in 8 patients. The therapeutic modalities of the 29 patients were as follows: 4 received operation, chemotherapy and radiotherapy, 8 radiotherapy, 6 chemotherapy, 5 both treatments, 2 patients received no treatment, and therapy for 2 patients was known. (Table 1).

Table 1. Clinical findings from prostatic lymphoma patients.

Items	Cases (%)
Age	66
PSA(ng/ml)	3.55
Needle biopsy	8 (27)
Transurethral resection	17 (59)
Prostatectomy	4 (14)
Pathologic type	
B-cell chronic lymphocytic leukemia	4
Follicular center cell, follicular, Grade1(small cell)	2
Follicular center cell, follicular, Grade2(mixed small and large cell)	1
Follicular center cell, diffuse,small cell	5
Diffuse large B-cell lymphoma	15
High grade B-cell lymphoma, Burkitt-like	2
Treatment	
Operation+chemotherapy+radiation	4 (14)
Chemotherapy	6 (20)
Radiation	8 (28)
Chemotherapy+radiation	5 (17)
None	4 (14)
Unknown	2 (7)
Outcome	
Died of tumor	10 (35)
Died of unknown causes	2 (7)
Died of other causes	2 (7)
Alive with tumor	1 (4)
Alive with no tumor	6 (21)
Lost to follow-up	8 (28)

Diagnositic certeria

Three criteria for primary prostatic lymphoma included: (1) tumor limited to the prostate and adjacent tissues; (2) the absence of lymphoma node involvement; and (3) lymphoma-free interval of at least month[1].

RESULTS

All patients were non-Hodgkin's lymphoma of a B-cell type. A major histologic subtype was diffuse large B-cell lymphoma. Ten patients died from lymphoma with a median survival of 23 months (range, 2-30 months). Seven patients were alive more than 60 months after diagnosis of prostatic lymphoma. There were 19 patients who died from involvements at other locations after diagnosis over 1-59 months. Involvements were as follows: 11 lymphoma nodes, 3 spleen, 1 liver, 3 bladder and ureter, 1 bone and 2 gastrointestinal tract.

DISCUSSION

Primary lymphoma of the male urinary tract and reproductive system is rare. Testicular primary lymphoma is more common. According to reports from different medical centers, about 7%-62% of malignant lymphoma may involve uropoiesis and the male reproductive system. The order of involvement is the kidney, testis, bladder and prostate. Involvement of the adrenal, ureter, epididymis and urethra were the most rare[2]. Bostwick et al.[3] reported that autopsies of six thounsand cases, who died from malignant carcinoma, showed only 49 cases (0.82 %) were non-Hodgkin's lymphoma. According to a report from the Connecticut Tumor Registry[4] the incidence of non-Hodgkin's lymphoma has risen steadily since the 1930s, especially in men. The average annual age-standardized rate of non-Hodgkin's lymphoma in men rose from 3.5 per 100,000 in 1935-1939 to 20 per 100,000 in 1990-1994. The majority of this increase may reflect improvements in detection and pathologic diagnosis rather than incidence.

As noted previously malignant lymphoma involving the prostate is rare. Secondary involvement is more common than primary involvement (65% vs.35%). The diagnosis of most patients depends on autopsy[3]. Patel et al.[5] reported a frequency of $<$10% of urinary tract involvement with non-Hodgkin's lymphoma, with $<$1% involving the prostate. Since the 1985 study of Bostwick and Mann[1], at least 19 additional cases of non-Hodgkin's lymphoma have been reported. These correspond to 0.09 % of all prostatic malignancies.

Clinical symptoms

The age of onset for primary prostatic lymphoma was 32-89 years (mean, 66 years), whereas the mean age for secondary prostatic lymphoma involvement was six years earlyer than primary lymphoma[6]. The clinical presentation of prostatic malignant lymphoma is difficult to distinguish from other prostatic diseases that cause lower urinary tract obstructive symptoms. Urgency, frequency, nocturia, difficulty voiding and acute retention were the most commom presenting symptoms, with occasional hematuria and acute retention. These obstructive symptoms were always attributed to nodular hyperplasia or prostatic carcinoma. Systemic symptoms (including fever , nightsweats and weight loss) were rare, unless there was

associated systemic lymphoma .

Clinical examination

Rectal touch was the most simple and direct examination method. The majority of patients showed a diffuse enlargement of the prostate on rectal touch. When the examination of the prostate was nontender, firm or rubbery and obliteration of the median furrow, they were nodular. Upon cystoscopically examination, malignant lymphoma was indistinguishable from hyperplasia of the prostate gland. Both clinical situations were changed to long and narrow in the urethra of the prostate. Patients with advanced lymphoma showed transfiguration of the bladder neck and triangular area. Lymphoma should be considered in the differential diagnosis of a lower urinary tract obstruction and abnormality with rectal touch, particularly in patients with diffuse rubbery prostatic enlargement and a prior history of lymphoma.

Diagnosis

The main diagnostic features of lymphoma were types, involvement situs and limits, which are use for a treatment plan. The diagnosis was difficult as it depended on the clinical situation and more on transurethral resection or prostatectomy. After diagnosis, all patients were evaluated for the extent of their disease with cystoscopy, sonography of the abdomen and pelvis, CT, bone scanning, bone marrow aspiration and PSA.

Whitemore[7] suggested that a definitive diagnosis of lymphoma must be depend on a paracentetic biopsy or excisional biopsy, but percutaneous skin needle biopsy has not routinely been used. Conduction of a biopsy by transrectal sonography is suggested. Then a conservative approach to the surgical problem is strongly recommended unless excisional biopsy can be done with minimal dissection. This would not avoid morbidity from a larger operation but will permit restoration of normal physiologic function as the patient responds to systemic chemotherapy or irradiation. Staging methods include evaluation of involvement of lymph nodes by CT scans. The immunohistochemistry stain LCA, PSA and prostatic acid phosphatase were helpful to diagnosis prostatic lymphoma.

Pathologic characterisitics

The most common types of non-Hodgkin's lymphoma (40%) were diffuse large B-cell lymphomas[3]. Primary prostate lymphoma was similar to other types of lymphoma. Most series have described diffuse large cell and small cleaved cell lymphoma, with few mixed cell types[1]. Lymphoma with a nodular pattern , Burkitt's lymphoma , small noncleaved cell type high grade, non-Burkitt's and Hodgkin's lymphoma involve the prostate only infrequently. The majority of T-cell lymphomas tended to be secondary prostate lymphoma[1,8] Diffuse large B-cell lymphomas constituted 51.7%. Reports from the literature indicate about 20% of patients with leukemia have an involved prostate upon biopsy[9]. Most types are chronic lymphocytic leukemia. Less than 1% of the clinical prostatic symptoms are directly caused by leukemia. Four patients were this type in our study (about 13.8%).

Therapy

At present there is no unified therapy for prostate lymphoma. A variety of treatments have been used, including prostatectomy, radiotherapy, chemotherapy or combinations of chemotherapy and radiotherapy. According to the views of the Mayo Clinic Hospital, patients treated with radiotherapy, chemotherapy or combinations of chemotherapy and radiotherapy showed no significant difference in survival time.

Whitemore[7] advocated the use of prostatectomy in order to remove the urinary obstruction and enhance the survival rate. He consided that the main treatments were chemotherapy and radiotherapy. Sarris et al.[10] treated three patients who had received doxorubicin-based therapy. One patient was rendered disease free over 3 years[10]. Fukutani et al.[11] reviewed 16 patients with primary prostate lymphoma who obtained CR receiving alone chemotherapy or with other therapy. We believe chemotherapy of CHOP to be the main therapeutic modality. A few patients might undergo combinations of radiotherapy in the region.

Follow-up

Inconsideration of the ages, stages, types and therapies, the consensus is that prostatic lymphomas are characterized by poor prognosis. The prognosis is not correlated with patient age , but is correlated with the clinical stage, histologic type and therapeatic modality. The prognosis of the primary prostatic lymphomas is worst compared to the bladder[6] and ovary cancers[7]. In the Mayo Clinic Hospital, 43 patients with prostatic lymphoma had a mean survival time of 34 months (1-276 months), and survival rates at 1,2,5,10,15-years were 64%, 50%, 33%, 33%, 16%, respectively. The mean survival time was 23 months (2-30 months) for the primary prostatic lymphoma patients. In our study, 24 of 29 patients were diagnosed between 1-59 months after presentation at an extraprostatic site. Involvement was most in lymphoid nodes, and then spleen, bladder, ureter, gastrointestinal tract, liver, and bone etc. Nine patients were deceased (the mean survival time 23 months), and 7 patients were alive more than 5 years.

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