Presentation of Prostate Carcinoma with Cervical Lymphadenopathy: Report of Three Cases

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The most common method of spreading of prostate cancer is via direct invasion to the pelvic organs or vertebral bodies. Supraclavicular lymph node metastasis is uncommon in patients with prostate cancer. Previously researchers have shown that the prognosis after such a presentation is generally poor. We herein present three patients with prostate carcinoma presenting with supraclavicular lymph node enlargement at the initial diagnosis. Abdominal computed tomography showed multiple enlarged lymph nodes in retroperitoneal space. All of our patients had hormone therapy and the prostate specific antigen (PSA) level declined. The mean follow up time was 16 months (range, 6-24 months). None of our patients experienced progression during follow up. Prostate carcinoma should always be considered in the differential diagnosis of elderly men with cervical lymphadenopathy, even in the absence of lower urinary tract symptoms. Evaluation of the PSA level and lymph node biopsy with PSA immunohistochemistry stain can lead to the final diagnosis. In addition, hormone treatment has been shown to be of benefit even in patients in the advanced stages. *(Chang Gung Med J 2004;27:840-4)*

Key words: prostate neoplasm, metastases, cervical lymphadenopathy.

Prostate cancer presents in various ways, including in-growth, local invasion and regional lymph node or skeletal system metastasis. Metastases in non-regional supradiaphragmatic lymph nodes are uncommon. Of the few cases reported, the left supraclavicular group was the most commonly affected.[1] We present three patients with prostate carcinoma metastases to the lymph nodes at the initial diagnosis and we remind clinicians of this possibility.

CASE REPORTS

Case 1

A 78-year-old man presented with left multiple neck masses for about 4 months. The physical examination showed a 3-cm supraclavicular soft nodule on the left side and a 4-cm supraclavicular soft nodule on the right side. Head and neck computed tomography (CT) images showed bilateral neck multiple enlarged lymph nodes over the right internal jugular, left spinal assessory chain and right para-tracheal region (Fig. 1). CT scans of chest showed multiple enlarged lymph nodes in the retrocaval, paratracheal, and tracheobronchial regions. Sonography guided fine needle aspiration for bilateral neck masses showed malignant cells. Nasal mucosa and tonsil biopsies were negative for malignancy. Bronchoscopic examination was then performed and showed multiple endobronchial nodules in bilateral bronchial tree. Biopsy on the bronchial nodule showed adenocarcinoma that was strongly positive for prostate specific antigen (PSA) in immunohistochemical study. Digital rectal examination revealed enlarged prostate with a firm and uneven surface.

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Fig. 1 Neck computer tomography showed an enlarged lymph node (arrow) on right supraclavical region.

The initial serum PSA was 45375 ng/ml (reference range, 0-4 ng/ml) and alkaline phosphate was 389U/L (reference range, 28-94U/L). The Tc-99m whole body bone scan revealed multiple bone metastases. Hormone treatment was started, initially with cyproterone acetate then leuprorelin acetate. Six months after the treatment his serum PSA declined to 201.7 ng/ml and the neck lymph node enlargement disappeared. He has been progression-free for the last 24 months.

Case 2

A 69-year-old man presented with a supraclavical mass on the left side for about 6 months. Biopsy of the mass revealed adenocarcinoma with positive PSA stain. Therefore, he was referred to our urological clinic for further evaluation. Physical examination showed supraclavical soft nodule on the left side and digital rectal examination revealed an enlarged prostate with a firm and uneven surface on the left lobe. The serum PSA was 563.88 ng/ml. Transrectal ultrasonography guided prostate biopsy revealed bilateral lobe adenocarcinoma with a Gleason score of 4+5. Abdominal CT showed multiple enlarged lymph nodes in the retroperitoneal space, encasing the aorta and vena cava, and extending to the left pelvic and inguinal region (Fig. 2A). The Tc-99m whole body bone scan revealed an active bone lesion on L5. Hormone treatment was started with bicalutamide and goserelin acetate. Six months after treatment, the serum PSA declined to 0.04 ng/ml. Follow-up abdominal CT scans showed total regression of retroperitoneal lymphadenopathy (Fig. 2B). The hormone therapy remained and the PSA was in the nadir status and the patient has been symptom-free for the last 18 months.

Case 3

A 73-year-old man had previously suffered from obstructive voiding symptoms for 1 year. He had visited our urological clinic for help and elevated serum PSA was noted at that time. However, he received no active treatment until the voiding symptoms became more severe. Physical examination found a 3-cm supraclavicular lymph node on the left side. Digital rectal examination revealed a hard, enlarged prostate. Serum PSA level was 647.6 ng/ml. Prostate biopsy

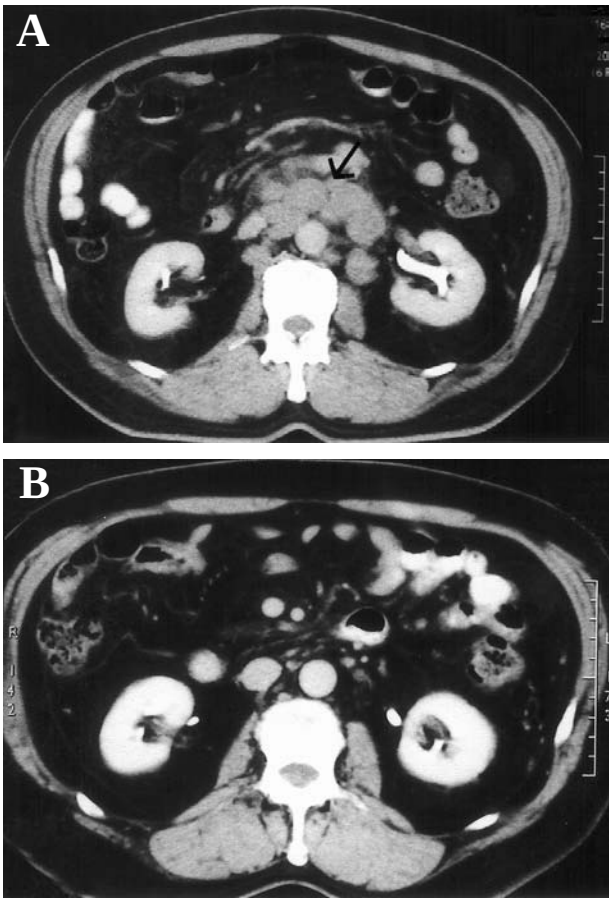

Fig. 2 Abdominal computer tomography showed (A) multiple enlarged lymph nodes (arrow) in retroperitoneal and paraaortic area before treatment and (B) total regression after hormone therapy.

showed adenocarcinoma in the bilateral lobes. The Gleason score was 3+5. Abdominal CT scans showed prostate nodules with left urinary bladder and ureter invasion and multiple enlarged lymph nodes at para-aortic and left iliac chain. The Tc-99m whole body bone scan revealed an active bone lesion on the left sacral-iliac joint. Hormone treatment was started with bicalutamide and leuprorelin acetate. The PSA level declined to 2.11 ng/ml after 6 months of hormone therapy. The enlarged supraclavicular lymph node also disappeared.

DISCUSSION

The growth of prostate cancer may cause symptoms such as obstruction and irritation when voiding. It usually presents with only voiding symptoms. The most common spread of prostate cancer is via direct invasion to the pelvic organs or vertebral bodies.[2] Lymphatic spread typically occurs in the regional lymph nodes, such as obturator-hypogastric or presacral nodes. Further spread occurs via iliac and para-aortic nodes to the cisterna chyli, the thoracic duct and then tumors gain direct entry into the systemic blood circulation via the left subclavian vein.[3] Supraclavicular lymph nodes metastasis is uncommon in patients with prostate cancer. Only a few case reports and a small series of case analyses have been reported.[1,4-6] Saeter et al. reported that the left supraclavicular fossa was the most common site of extraskeletal non-regional lymphatic spread.[7] It may be postulated that tumor cells lodge in these nodes, which are close to the entry of thoracic duct into left subclavian vein, by retrograde spread.[3] Cho and Epstein identified 26 patients with metastatic prostate cancer in the supradiaphragmatic lymph nodes from 1972 through 1987, 15 of which were in the supraclavical nodes.[5] Saitoh et al. found that 0.4% (5 of 1367 patients) of the patients with prostate cancer at autopsy had metastases to the cervical lymph nodes.[8] In our first patient, the supraclavicular node on the right side was also involved. Cervical lymph node metastasis on the right side from prostate has been reported in only three patients and two of these had simultaneous left cervical lymphadenopathy.

Most metastases of cancers to the cervical lymph nodes are from the head and neck primary cancers involving the mucosa of the upper aerodigestive tract, while others are from non-mucosal head and neck primary sites such as salivary or thyroid glands.[9] Cancers metastatic to the cervical chain from non-head and neck origin are rare. This occurs more frequently in patients with lung, kidney, and breast cancer.[9] The current assessment of cervical lymphadenopathy presumed to be metastatic in nature involves careful history taking and physical examination. To search for the primary site, examinations including panendoscopy with random biopsies and CT scans of the head and neck and chest are advocated. Fine needle-aspiration is recommended to determine the diagnosis because it has high sensitivity and specificity and can be easily performed.[9] If doubt remains about the origin of the tumor, lymph node biopsy using a some special immunohistochemistry stain has of some benefit in making final diagnosis.[5] In our first patient , the malignant cells were only found using fine needle-aspiration, and further biopsy with PSA stain found the tumor was of prostate origin.

Extensive data derived from large-scale prospective studies involving patients with stage D2 (bone metastases) disease treated with any combination of androgen-deprivation maneuvers indicated that the medians in time to progression and survival ranged from 12 to 18 months and 2 to 3 years, respectively.[10] Though all of our patients had good responses to hormone therapy, the times of follow up were only 24 months, 18 months and 6 months, respectively. Furthermore, the Gleason scores were high in all of our patients, so it is too early to draw the conclusions as to whether the cervical lymphadenopathy in the prostate cancer patients had any impact on progression. A previous report on the prognosis after such a presentation was generally poor, with a mean survival of 19.8 months (range, 1-46 months).[5] Jones and Anthony reported 11 patients with prostate cancer presenting with cervical lymphadenopathy. Six patients survived for 1-101 months (average, 25.8 months) and five died at 7-66 months (average, 34.4 months) with a combined survival of 29.7 months.[1] However, Chitale et al. presented a patient with prostate cancer presenting with cervical lymphadenopathy who received regular hormone therapy and remained symptom-free for 9 years.[4]

We herein emphasize that prostate carcinoma should always be considered in the differential diag-

nosis of elderly men with cervical lymphadenopathy, even in the absence of lower urinary tract symptoms. Evaluation of the PSA level and skeletal X-ray may be helpful, but immunohistochemical stain of PSA can lead to the final diagnosis. Once the diagnosis is established, hormone treatment has been shown to be of benefit even in patients in the advanced stages of the disease.

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前列腺癌以頸部淋巴腺腫大爲表現：三病例報告

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前列腺癌通常會轉移到骨盆腔的淋巴結及脊椎骨，很少會有頸部淋巴腺的轉移。以前的一些病例報告指出前列腺癌若是有頸部的淋巴腺轉移，預後通常比較差。我們報告3例前列腺癌以頸部淋巴腺腫大爲初始表現的治療經驗。3位病患在就醫時均表現出頸部淋巴腺病變，經由荷爾蒙治療後頸部的淋巴腺腫大消失，攝護腺特異抗原的值在追蹤期間也有明顯的下降，疾病本身也表現出良好的控制而無再進一步的擴散。3位病患的平均追蹤時間爲16個月 (6到24個月)。我們的經驗顯示對於這類病患以荷爾蒙治療依然有不錯的結果。在接觸年紀較大的男性病患發現有頸部淋巴腺病變時。我們建議需要將前列腺癌合併淋巴腺轉移的可能列入鑑別診斷，而切片作攝護腺特異抗原免疫組織染色及血液攝護腺特異抗原測量能做出正確診斷並可以儘早給予病人適當的治療。(長庚醫誌2004;27:840-4)

關鍵字：前列腺癌，轉移，頸部淋巴腺病變。

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