

Prostate adenocarcinoma with negative immunohistochemical stain of prostate-specific antigen presenting with cervical mass: A case report

Liming Zhu, Cong Luo, Wei Wu¹, Jier Ying, Haijun Zhong

Departments of Chemotherapy, ¹Pathology, Zhejiang Cancer Hospital, Hangzhou 310022, China

Cervical regional nodal involvement, as the first manifestation of prostatic cancer, has been rarely reported. Prostate cancer metastasis to the supraclavicular lymph nodes with negative immunohistochemical stain of PSA is even rarer. We report a case of prostate cancer with negative immunohistochemical stain of prostate-specific antigen presenting with left supraclavicular node enlargement. A 63-year-old man was referred to our hospital for a left supraclavicular mass. He had a family history of gastric cancer (two brothers had died of gastric cancer). Enhanced computed tomography of the abdomen revealed retroperitoneal lymph node enlargement. Gastroscopy revealed no evidence of any gastric tumor. Biopsy of the left-sided supraclavicular lymph nodes revealed metastatic adenocarcinoma with a negative prostate-specific antigen (PSA) stain. The serum tumor markers were examined, revealing PSA levels of 21.820 ng/ml. Biopsy of the prostate disclosed poorly-to-moderately differentiated adenocarcinoma (Gleason 4 + 4 = 8). Although rare, prostate cancer should be considered in the differential diagnoses of elderly men with undetermined original adenocarcinoma, metastatic to the supraclavicular lymph nodes. Rectal examination, serum PSA and pelvic image can be helpful to lead the diagnosis. PSA stain may be weak or negative in some poorly differentiated patients, however, it is still a sensitive and specific marker of prostatic differentiation and must be routinely applied.

Key words: Metastasis, prostate cancer, prostate-specific antigen, supraclavicular lymph node

How to cite this article: Zhu L, Luo C, Wu W, Ying J, Zhong H. Prostate Adenocarcinoma with Negative Immunohistochemical Stain of Prostate-specific Antigen Presenting with Cervical Mass: A Case Report. *J Res Med Sci* 2013;18:814-7.

INTRODUCTION

Malignancies metastatic to the cervical lymph nodes are commonly seen in primary malignancies in the mucosal surfaces of the upper aerodigestive tract. Most of the remaining metastatic cancers to the cervical chain are from the nonmucosal head and neck primary sites, such as, the salivary glands, thyroid gland or skin.^[1]

As we know, lymph nodes are the single most common metastatic sites for prostate carcinoma, and the most frequently involved regions are the pelvis and retroperitoneum lymph nodes.^[2] However, cervical regional nodal involvement, as the first manifestation of prostatic cancer, has been rarely reported.^[3,4]

We report a case of prostate cancer presenting with left supraclavicular node enlargement. The patient has a family history of gastric cancer. The medical approach is also described. Immunohistochemical staining in the biopsied node specimen and the increased serum PSA

level suggested the diagnosis of prostate carcinoma, allowing the clinicians to start the appropriate treatment.

CASE REPORT

A 63-year-old male was referred to our hospital for a left supraclavicular mass. The patient complained of an asymptomatic swelling on the left side of his neck for approximately one month. He denied any other subjective complaints, including difficulty in swallowing or breathing. However, he had a family history of gastric cancer (two brothers died of gastric cancer). Physical examination of the patient's neck revealed a hard left-sided neck mass, approximately 4 cm in diameter. Subsequent computerized tomography (CT) scan of the head and neck showed a 5 cm, solid, left supraclavicular mass, with extension from the clavicles to the true vocal cords [Figure 1a]. The abdominal CT scan showed multiple enlarged retroperitoneal lymph nodes [Figure 1b]. Percutaneous fine needle aspiration (FNA) was performed and interpreted as poorly differentiated adenocarcinoma.

Address for correspondence: Dr. Liming Zhu, Department of Chemotherapy, Zhejiang Cancer Hospital, 38 Guangji Road, 310022, Hangzhou, P.R. of China. E-mail: hzhazlm@163.com

Received: 20-08-2012; **Revised:** 28-04-2013; **Accepted:** 06-05-2013

Laryngoscopy, bronchoscopy, colonoscopy, and gastroscopy were performed on the patient, and no evidence of any tumor was found. Biopsy of the left supraclavicular mass showed metastatic adenocarcinoma and the immunohistochemistry tests showed up with a negative PSA stain [Figure 2a] and positive P504s stain [Figure 2b]. A digital rectal examination revealed an enlarged prostate with an uneven surface. In the absence of other signs or symptoms, serum tumor markers were measured and the PSA level was found to be increased to 21.820 ng/mL. Although the PSA stain was negative, metastatic adenocarcinoma from the prostate was greatly suspected, considering the morphology, P504s stain, and PSA level. The patient underwent a transrectal ultrasound-guided biopsy and the histopathological diagnosis was poorly differentiated invasive acinar adenocarcinoma (Gleason score 8 = 4 + 4; cT2aNxM1) with a negative PSA stain [Figure 2c] and positive P504s stain [Figure 2d]. Finally, a whole-body bone scan was performed with a normal result.

The patient started treatment for the neoplasm with an androgen blockade (oral flutamide and a GnRH agonist) in August 2011. Eight months later, the serum PSA level declined to 1.360 ng/ml and a cervical ultrasound examination showed a significant response in terms of the number and size of the nodal involvement.

DISCUSSION

The most common spread of prostate cancer is via direct invasion to the pelvic organs or vertebral bodies. Lymphatic spread typically occurs in the regional lymph nodes, such as, obturator, internal iliac, external iliac, and sacral lymph nodes. Further spread occurs via the iliac and para-aortic nodes to the cisterna chyli, the thoracic duct, and from there to the systemic blood circulation, via the left subclavian vein.^[5]

The incidence of cervical lymph node involvement in patients with prostate cancer has been rarely reported. In an extensive review of all urogenital malignancies, Flocks and Boatman^[6] found that only six out of 1,500 (0.4%) prostate cancer patients had evidence of cervical node metastases

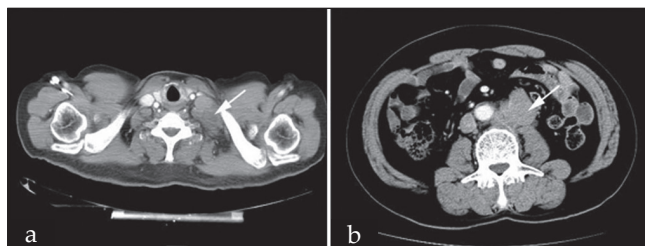


Figure 1: (a) Computer tomography scan of the neck showing an enlarged left supraclavicular lymph node measuring 5 cm. (b) Abdominal computer tomography scan showing multiple enlarged retroperitoneal lymph nodes

on postmortem examination. Hematpour *et al.*,^[7] reviewed 1,400 biopsies between 1997 and 2005, at the Greater Los Angeles VA Healthcare System, and only found four (0.3%) metastatic prostate cancers of the supraclavicular lymph nodes. However, these patients almost uniformly presented with a widespread metastatic disease.

As mentioned previously, cervical node enlargement as the only initial presenting finding for disseminated cancer of the prostate is extremely rare. In a review of the English language literature in Medline, we found 10 such cases reported previously [Table 1]. The mean age of these patients was 70.8 years (range, 42-84). Eight patients were referred for left side masses, one patient for a right side mass, and one patient for masses on both sides. The PSA was measured in seven patients, and it was markedly increased in all, with a mean of 1332.3 ng/mL (range, 14.6-4537.5). Seven patients had biopsies performed from cervical lymph nodes and the PSA stainings were all positive. Six patients underwent prostate biopsies and the mean Gleason score was 7.8 (range, 4-10). Of the-eight patients who underwent a bone scan, five had evidence of metastasis.

This case is unique because the patient had a family history of gastric cancer (two brothers died of gastric cancer). It is easy to be misled to a gastrointestinal malignancy. 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 a high sensitivity and specificity and can be easily performed. If doubt remains about the origin of the tumor, lymph node biopsy using the immunohistochemistry stain is of some benefit in making

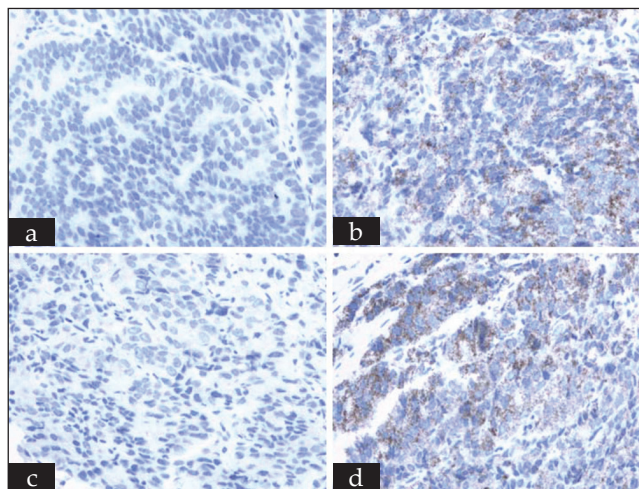


Figure 2: Biopsy of the left supraclavicular lymph node demonstrating metastatic adenocarcinoma with the PSA stain negative (a) and the P504s stain positive (b) (original magnification $\times 200$). Transrectal ultrasound-guided needle biopsy of the prostate demonstrating adenocarcinoma (Gleason score 4 + 4 = 8) with the PSA stain negative (c) and the P504s stain positive (d) (original magnification $\times 200$)

Table 1: Reported cases of metastatic prostate cancer presenting as cervical lymph nodes enlargement in the English language literature in medline

| References | Published year | No. | Age | Side/size of mass | Bone scan | PSA staining of mass | PSA(ng/ml) | Grade | Treatment | Survival (m) |
|--------------------------------|----------------|-----|-----|----------------------|-----------|----------------------|------------|----------------|---------------------------------|----------------------------------|
| Stein BS ^[8] | 1983 | 1 | 66 | Left/NA | + | Positive | NA | NA | NA | NA |
| Wang HJ ^[9] | 2004 | 3 | 78 | Left/3 cm right/4 cm | + | Positive | 4537.5 | NA | Androgen blockade | 24 (Alive with progression free) |
| | | | 69 | Left/NA | + | Positive | 563.88 | Gleason 4+5=9 | Androgen blockade | 18 (Alive with progression free) |
| | | | 73 | Left/3 cm | + | NA | 647.6 | Gleason 3+5=8 | Androgen blockade | NA |
| Dahm P ^[10] | 2005 | 1 | 84 | Left/4 cm | Normal | Positive | 55.5 | Gleason 2+2=4 | NA | NA |
| Shigeki Kosugi ^[11] | 2007 | 1 | 73 | Left/4 cm | Normal | Positive | 3354.0 | Gleason 3+5=8 | Androgen blockade | NA |
| Bajetta E ^[12] | 2008 | 1 | 72 | Left/3 cm | Normal | Positive | 14.6 | Gleason 4+4=8 | Androgen blockade, chemotherapy | 36 (Alive with bone metastasis) |
| Lin YY ^[13] | 2011 | 1 | 42 | Left/3 cm | + | Positive | 153.0 | Gleason 5+5=10 | Androgen blockade | 15 (Alive with progression free) |
| Copeland B ^[1] | 2001 | 2 | 72 | Left/3 cm | NA | NA | NA | NA | NA | NA |
| | | | 79 | Right/4 cm | NA | NA | NA | NA | NA | NA |
| Current case | | 1 | 63 | Left/4 cm | Normal | Negative | 21.820 | Gleason 4+4=8 | Androgen blockade | 15 (Alive with progression free) |

NA=Not available; +=Bone metastasis; PSA=Prostate-specific antigen

the final diagnosis. This is most often achieved by the PSA stain, which is a sensitive and specific marker of prostatic differentiation and is positive in a large majority of prostatic adenocarcinomas.^[14,15] However, a small subset of metastatic prostate cancers that are usually poorly differentiated show only a weak or negative PSA stain.^[3,16] In recent years, the prostate biomarker Alpha-Methylacyl-CoA-Racemase (P504s) has been used as an adjuvant to morphology in diagnostically challenging cases, with a very high sensitivity and specificity ranging from 82-100%.^[17,18] In our case, the fine needle aspiration only interpreted it as poorly differentiated adenocarcinoma. Thus, a subsequent biopsy of the left supraclavicular node was performed, showing negative immunohistochemical staining for PSA and positive for P504s. It suggested a diagnosis of metastatic prostate adenocarcinoma, which was proved by a transrectal ultrasound-guided biopsy.

Hormonal therapy has been the mainstay of treatment for advanced phases of prostate cancer, for more than 50 years. Jones and Anthony^[19] once reported 11 patients with prostate cancer presenting with cervical lymphadenopathy. Six patients survived for an average of 25.8 months (range: 1~101) and five died at 34.4 months (range: 7~66) with a combined survival of 29.7 months. However, Chitale *et al.*^[20] presented a patient with prostate cancer, who presented with cervical lymphadenopathy, and received regular hormone therapy and remained symptom-free for nine years. As per the literature we reviewed above [Table 1], six patients received hormonal therapies. Three patients were reported to be alive and progression-free and one patient was alive with bone metastasis. Our patient had good response to the hormone

therapy. A cervical ultrasound examination showed a significant response in terms of the number and size of nodal involvement after eight months. However, the patient had a high Gleason score (4 + 4 = 8), was poorly differentiated, and had to be closely followed up.

CONCLUSION

Although rare, prostate cancer should be considered in the differential diagnoses of elderly men with undetermined original adenocarcinoma, metastatic to the supraclavicular lymph nodes. Rectal examination is a convenient and effective method for the initial diagnosis. Serum PSA and pelvic image can be helpful to the patients in the absence of low urinary tract symptoms. Although the PSA stain may be weak or negative in some poorly differentiated patients, it is still a sensitive and specific marker of prostatic differentiation and must be routinely applied.

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Source of Support: Nil, **Conflict of Interest:** None declared.