

Paraneoplastic sensorimotor polyneuropathy in prostatic adenocarcinoma

A case report

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Abstract

Rationale: Paraneoplastic syndrome is a very rare syndrome among prostate cancer patients. In particular, paraneoplastic sensorimotor neuropathy has never been reported as a complication of prostatic adenocarcinoma.

Patient concerns: A 75-year-old man who was diagnosed with prostatic adenocarcinoma with multiple metastases received cancer treatment. But, numbness and tingling sensations in both sides of the upper and lower limbs got progressively worse.

Diagnoses: He was diagnosed with positive anti-Hu antibodies paraneoplastic sensorimotor polyneuropathy caused by prostatic adenocarcinoma.

Interventions: The patient received physical therapy, occupational therapy, and opioid medication during 3 weeks at cancer rehabilitation department during 3 weeks.

Outcomes: There was no improvement in functional outcome in this patient. But, the patient's neuropathic pain was improved by the use of opioid agents.

Lessons: This case report is the first to report anti-Hu antibody-positive paraneoplastic sensorimotor neuropathy in a patient with adenocarcinoma of the prostate.

Abbreviations: EMG = electromyography, PNS = paraneoplastic neurological syndrome.

Keywords: neurologic manifestations, paraneoplastic polyneuropathy, prostatic neoplasm

1. Introduction

Paraneoplastic syndrome is a rare syndrome that occurs in less than 1% of cancer patients.^[1] Paraneoplastic syndrome is often associated with small cell lung cancer^[2] and can be largely divided into neurologic paraneoplastic syndrome and non-neurologic paraneoplastic syndrome. Although paraneoplastic neurological syndrome (PNS) is a rare immune-mediated disorder, it presents with various neurologic symptoms that are hard to distinguish from the other neurologic symptoms that cancer patients experience. Therefore, to properly diagnose PNS, additional examinations designed to detect specific antineuronal antibodies in serum or cerebrospinal fluid are required.^[1,3,4]

Prostate cancer is the 2nd most common cancer and the 6th leading cause of cancer deaths around the world.^[5,6] The clinical

features of PNS in prostate cancer are manifold, and only a limited number of case reports or studies have reported PNS in prostate cancer.^[5] Antibody-positive paraneoplastic syndrome in prostate cancer occurs at a higher frequency if the pathologic finding is small-cell prostatic cancer than adenocarcinoma of prostate.^[3,7,8] In general, PNS tends to stabilize or improve following cancer treatment.^[2,4] This case report describes for the first time a case of anti-Hu antibody-positive paraneoplastic sensory-motor neuropathy that did not respond well to treatment in a 75-year-old male adenocarcinoma prostate cancer patient.

2. Case report

This study was conducted with approval from Asan Medical Center institutional review board (Approval No. 2017-0267), and consent was obtained from the patient's daughter. This case report was retrospective observations of a patient. So, ethical approval was not needed. The patient is a 75-year-old male patient who was admitted to a hospital with anuria symptoms in November 2013. The patient was diagnosed with adenocarcinoma of the prostate after a transurethral vapor resection of prostate (TURVP) examination. Biopsy results indicated that the tumor had Gleason score 8 (4+4) (about 40% in volume). The patient was placed under hormone therapy after diagnosis. Despite 2 years of hormone therapy, the prostate specific antigen (PSA) level in blood tests was higher than at diagnosis. From June 2015, the patient was treated with 40mg enzalutamide. Bone scans showed bone metastasis to the right scapula and the right ilium after the patient was transferred to our hospital in April 2016 (Fig. 1). Whole spine MRI results indicated metastases to the cervical spine involving the C4-T7 vertebrae and to the Rt

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Figure 1. Bone metastases to the right scapula and the right ilium in 99mTc-3,3-diphosphono-1,2-propanodicarboxylic acid (DPD) whole body bone scan.

scapular bone and Rt Iliac bone. In addition, diffuse leptomeningeal seeding was observed. The patient underwent radiation therapy for bone metastasis lesions 10 times in May 2016. Numbness and tingling sensations in both sides of the upper and lower limbs got progressively worse as numerical rating scale 8. The results of cerebellar function tests, such as Romberg and the heel-to-shin coordination tests, were positive. However, there was no evidence of brain metastasis or other brain diseases besides mild leukoariosis in both periventricular white matters on conventional brain MRI. The pinprick test revealed sensory impairment below the C4 dermatome as well as light touch and loss of tendon reflexes. The manual muscle test showed that muscle strengths at both extremities were grade 4 on manual

muscle test. The berg balance test could not be performed due to severe ataxia. Electrodiagnostic studies were performed to examine the motor and sensory nerves of the extremities bilaterally. Electromyography (EMG) results indicated that sensory nerve action potentials (SNAPs) were not detected on both sides of the upper and lower limbs. Also, the motor nerve conduction study showed decreased amplitude and conduction velocity. Needle EMG revealed unusual findings that reduced recruitment of the distal muscles. We diagnosed the patient with peripheral sensorimotor polyneuropathy on the basis of the EMG results (Table 1).

Blood tests were performed to determine the cause of sensorimotor polyneuropathy. Autoantibodies and paraneoplastic antibodies (anti-CRMP-5, -Hu, -Ri, -Yo, -NMO, and -ANA) were tested. Anti-Hu antibody reactivity was positive. Other radiologic studies showed no evidence of pulmonary or other cancers. He was diagnosed with paraneoplastic syndrome caused by adenocarcinoma of the prostate.

His sensory symptoms improved to numerical rating scale 2 after the doses of the fentanyl patch and gabapentin were adjusted. The patient was discharged from the rehabilitation department 3 weeks after physical therapy and occupational therapy. There was no functional improvement, although slight improvements were observed in the box and block test at the time of discharge. The patient is currently under outpatient observation and enzalutamide chemotherapy. Prostate specific antigen was 1.33 ng/mL and testosterone was 0.06 ng/mL in tests conducted in August 2016. However, performance of daily living activities has gradually deteriorated despite the effectiveness of chemotherapy.

3. Discussion

PNS is a type of paraneoplastic syndrome with a prevalence of about 6% in cancer patients.^[9] It is most frequently reported in small cell lung cancer patients and occurs at relatively high frequencies in lymphoma, breast, and ovarian cancers.^[2]

After renal carcinoma, prostate cancer is the 2nd most frequent cancer among urological malignancies.^[5,10] However, PNSs in patients with prostatic cancer are very rare.^[5,7,8] Although small cell carcinoma is a subtype that only occupies 1% to 2% of prostate cancer cases, the prevalence of paraneoplastic syndrome is higher than in other histologic types.^[5,8] In a literature review by Palmgren et al,^[8] 33 out of 113 cases of small cell carcinoma of the prostate with paraneoplastic syndrome exhibited neurologic

Table 1

Results of nerve conduction studies.

Nerve	Sites	Side	Lat, ms	Amp, mV	CV, m/s	
Motor	Median	Elbow-wrist/APB	Rt	3.49	3.0*	46.4*
			Lt	3.85	4.7*	41.8*
	Ulnar	Elbow-wrist/ADM	Rt	2.60	6.3	53.4
			Lt	3.02	4.6*	47.1*
	Peroneal	Fib head ankle/EDB	Rt	3.96	1.2*	35.7*
			Lt	3.02	1.2*	38.4*
	Tibial	Knee-ankle/AH	Rt	3.33	3.9*	41.9
			Lt	3.33	3.5*	41.0
Sensory	Median	Wrist/3rd finger	Both	No response*		
	Ulnar	Wrist/5th finger	Both	No response*		
	Supr peroneal	Leg/ankle	Both	No response*		
	Sural	Calf/ankle	Both	No response*		

ADM = abductor digiti minimi, AH = abductor hallucis, Amp = amplitude, APB = abductor pollicis brevis, CV = conduction velocity, EDB = extensor digitorum brevis, Fib head = fibular head, Lat = latency.

* Abnormal finding.

symptoms, and 2 cases exhibited paraneoplastic peripheral neuropathy. Previously, there have been 4 case reports of paraneoplastic peripheral neuropathy in prostate cancer patients; 2 cases were small cell carcinoma^[11,12] and 2 cases were adenocarcinoma.^[2,13]

Although the exact cause of paraneoplastic syndrome in prostate cancer is not yet known, most hypotheses suggest that inappropriate release of hormonal peptides, biologic amines, or growth factors from tumors is the main cause. Especially for neurological symptoms, there are reports suggesting a link with onconeural antigens.^[1,5,9] Graus et al^[1] published the diagnostic criteria for PNS, and they reported that there is more than one sensory neuropathy, conditions improve after cancer treatment, and the presence of onconeural antibodies is crucial for diagnosis. However, PNS in prostatic cancers can result in severe neurologic deficits despite cancer treatment, and it can also be debilitating.^[5] Furthermore, a recent case report on paraneoplastic subacute sensory neuronopathy in a prostatic adenocarcinoma patient with anti-Hu antibodies showed that symptoms did not improve after cancer treatment.^[2]

This case report is the first to report anti-Hu antibody-positive paraneoplastic sensorimotor neuropathy in a patient with adenocarcinoma of the prostate, which is the most frequent from a histopathological perspective but the rarest among paraneoplastic syndromes. The patient described in this case report, similar to previous case reports of patients with PNS in prostatic cancer, did not show improvement despite cancer treatment and exhibited rapid progression in PNS symptoms.^[5]

Prostate cancer is a tumor of high prevalence in older male patients (>50 years old), and the 5-year survival rate is relatively higher than that of patients with other tumor types. If the diagnosis is delayed or neurological symptoms persist, the possibility of PNS should be considered. More specifically, the physician should appreciate the possibility that PNS patients can experience sensorimotor neuropathy. Additional studies on the pathogenesis and progression of PNS in prostatic cancer patients should be performed in the future. Further studies should consider the possibility of PNS in all histological subtypes, and also the possibility of not only sensory nerve involvement, but also motor nerve involvement.

Although there was no improvement in functional outcome in this patient, the patient's neuropathic pain was somewhat

attenuated by the use of opioid agents. In addition, studies are required to assess the reason why PNS in prostatic cancer does not respond well to cancer treatment, as well as studies designed to establish new treatment protocols. In conclusion, more research into specific diagnostic criteria and treatment protocols for PNS of prostatic cancer are necessary.

Author contributions

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