Prostate cancer presented with de novo brain metastases as initial manifestation: A case report with review of the literature

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Introduction

Prostate cancer is the most common cancer and among the leading causes of cancer death in men and its clinical symptoms vary a lot. The most common metastatic site is the bones [1], but rarely prostate cancer can metastasize to brain in very advanced stages of the disease. However, brain metastases giving neurological symptoms as first manifestation of prostate cancers have been reported. Research of international literature revealed only seventeen patients (including our own) that were diagnosed with prostate cancer presented with neurological symptoms (Tables 1, 2).

| Case number | Gender | Duration of symptoms | Presenting symptoms | MRI findings | PSA | Recurrence | Symptoms | Ref. |
|-------------|--------|----------------------|---------------------|--------------|-----|------------|----------|------|
| 1           | 70     | 2y                   | headache, loss of balance | Cystic lesion in the left cerebellum | 3.3 | N/A        | N/A      | (15) |
| 2           | 56     | N/A                  | mild expressive apraxia and right-sided weakness | Cystic lesion in the left parietal lobe | N/A | N/A        | N/A      | (15) |
| 3           | 76     | 4m                   | personality change, forgetfulness, agitated confusion, difficult with short memory | Cystic mass right frontal horn and midline shift | 2.1 | N/A        | N/A      | (16) |
| 4           | 56     | 6m                   | partial complex symptoms | Large ring-enhancing lesion in the left anterior temporal lobe | > 100 | N/A        | N/A      | (17) |
| 5           | 56     | 9w                   | partial complex symptoms | Contrast enhancing mass | 1.4 | N/A        | N/A      | (18) |
| 6           | 55     | 1m                   | partial complex symptoms | Contrast enhancing mass | 0.5 | N/A        | N/A      | (19) |
| 7           | 71     | concurrent           | progressive leg weakness, headache, poor concentration, lack of coordination of his left arm | Isolated cerebellar space occupying lesion | 5   | N/A        | N/A      | (19) |
| 8           | 62     | 3w                   | headache, acute onset of confusion | Lesion in the right hemisphere | N/A | N/A        | N/A      | (20) |
| 9           | 65     | 2m                   | headache, gait disturbance, intracranial pressure, urinary incontinence | Lesion in the right hemisphere | N/A | N/A        | N/A      | (20) |
| 10          | 55     | concurrent           | headache, incoordination of his left arm | Enhancing mass measuring in the left parietal lobe | 11.5 | N/A        | N/A      | (19) |
| 11          | 70     | 3m                   | weakness, dizziness, left homonymous sensory, vomiting, anosmia, right-sided weakness | Cerebellar mass with central hemispheres | 100 | N/A        | N/A      | (21) |
| 12          | 62     | 2m                   | headache | Right posterior fossa mass | 11.7 | N/A        | N/A      | (21) |
| 13          | 57     | none                 | none | Mass in the right thalamic area | N/A | N/A        | N/A      | (22) |
| 14          | 46     | concurrent           | headache, confusion | Right cerebellar hemisphere | N/A | N/A        | N/A      | (23) |
| 15          | 52     | concurrent           | headache | Lesion in the frontal lobe and hemispheres | N/A | N/A        | N/A      | (24) |
| 16          | 62     | 6d                   | headache | Intracerebral hemispheres of the right temporal lobe | N/A | N/A        | N/A      | (25) |

Table 1: Reported cases of brain metastasis from prostate cancer. d: days, m: months, N/A: Not assessed, w: weeks, y: years * PSA value at diagnosis
### Table 2: Reported cases of brain metastasis from prostate cancer with de novo presentation or after local therapy. N/A: Not assessed, y: years

| Case number | First Diagnosis of Prostate cancer | Treatment of first diagnosis | Time to brain metastases | Ref. |
|-------------|----------------------------------|-----------------------------|--------------------------|------|
| 1           | NO                               | RT                          | 12y                      | (15) |
| 2           | NO                               | radical prostatectomy AND RT| 4y                       | (15) |
| 3           | NO                               | RT                          | 9y                       | (16) |
| 4           | YES                              | de novo                     | de novo                  |      |
| 5           | NO                               | N/A                         | N/A                      | (17) |
| 6           | YES                              | de novo                     | de novo                  | (18) |
| 7           | YES                              | de novo                     | de novo                  | (19) |
| 8           | YES                              | de novo                     | de novo                  | (20) |
| 9           | YES                              | de novo                     | de novo                  | (21) |
| 10          | NO                               | radical prostatectomy AND RT| 2y                       | (13) |
| 11          | YES                              | de novo                     | de novo                  | (21) |
| 12          | YES                              | de novo                     | de novo                  | (21) |
| 13          | NO                               | prostatectomy               | 3y                       | (22) |
| 14          | YES                              | de novo                     | de novo                  | (23) |
| 15          | YES                              | de novo                     | de novo                  | (24) |
| 16          | YES                              | de novo                     | de novo                  | (25) |

### Case report

A 61-years-old man, ex-smoker of 25 pack-years, with free personal history and positive family history, presented with headache and tingled right hand. From the physical examination there was reduced muscular strength of the right hand. A brain CT demonstrated multiple secondary metastases (Fig. 1) and the patient started WBRT.

For the finding of the primary site we did lung and abdomen CT, bronchoscopy, endoscopy of larynx, upper GI endoscopy and colonoscopy which did not show something pathological. From the tumor markers of the patient we had CEA 44.6ng/ml (<4.7), PSA 12.94ng/ml (<4), NSE 15.9 (<16.3). Due to the raised PSA we did a prostate U/S, which showed hypertrophy of the gland. In the figure-rectal examination we found a tough prostate and the biopsy of the gland showed a prostate adenocarcinoma (Fig. 2). Then we did a bone scanning which revealed one secondary lesion on the 4th thoracic vertebra.

Unfortunately his neurological symptoms got worse before the start of the hormonotherapy and, finally, the patient died.

![Figure 1: Brain computed tomography (CT) showing multiple secondary metastases](image-url)
Discussion
Prostate cancer is the most common cancer among men and it is the second leading cause of death due to cancer [2]. It represents 26% of all new diagnosed cancers in men and 9% cancer-related deaths [3]. The risk for prostate cancer increases steeply with age. The rise in incidence is basically explained by improved detection capability, using prostate-specific antigen (PSA) and transrectal ultrasound [4–6].

The disease spreads by local extension through the capsule and seminal vesicles, the lymphatic system to regional nodes or hematogenously to bone and visceral sites. Bone is the most common site of prostate cancer metastases, producing predominantly osteoblastic lesions rather than osteolytic, although both types may coexist [6].

Brain metastases are present, especially in advanced stages of the disease. Adenocarcinomas of the prostate can metastasize to the brain from either metastases in the lungs and the bones (multistep or cascade theory) [7], or primarily to the central nervous system (single step theory) [8]. The most common intracranial sites of prostate cancer metastases are the dura (67%), cerebrum (25%) and cerebellum (8%) [9].

Almost always, intracranial metastases develop after the diagnosis of the prostatic adenocarcinoma is established; however, intracranial metastases are often difficult to detect, clinically silent and primarily diagnosed at autopsy. The mean time interval between initial diagnosis of prostatic cancer and diagnosis of intracranial metastases is 5.1 years [10].

Interestingly, the literature contains only 16 patients in which neurological symptoms secondary to intracranial metastases have served as the first sign of prostatic adenocarcinoma [11]. Headache, motor dysfunction and seizure appear to be the most common symptoms associated with metastatic prostate cancer.

Treatment options include radiosurgery, conventional external beam radiotherapy and surgery. Radiotherapy in combination with high doses of dexamethasone may be beneficial [12]. Craniotomy also appear to lengthen survival time[14] and hormonal treatment appear to have some efficacy [13-14].

Conclusion
Although neurological symptoms as a first clinical manifestation of prostate cancer are rare, it should be included in the differential diagnosis of a patient presented with secondary symptoms from intracranial metastases. Clinicians should have an index of suspicion for prostate cancer, check PSA and do prostate ultrasound during the investigation of the primary site in a patient presented with secondary brain metastases. Early detection and treatment should be the primary goal, as they may lengthen the survival for some patients with adenocarcinoma of the prostate.

Conflicts of interest: The authors declare that they have no conflict of interest.

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