Case Report

Ominous Occurrence of Spinal Intradural Primary Malignant Peripheral Nerve Sheath Tumor Four Decades following Radiation Therapy for Testicular Seminoma

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Received 16 August 2019; Accepted 27 November 2019; Published 28 January 2020

Academic Editor: Dominic B. Fee

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Primary intradural malignant peripheral nerve sheath tumor (MPNST) is an extremely rare diagnosis and is associated with an extremely poor prognosis. A 77-year-old man diagnosed with an intradural MPNST, more than 40 years after radiation for a testicular seminoma, is reported. Intradural MPNSTs of the spine outside the setting of neurofibromatosis is extremely rare and can masquerade as common benign nerve sheath tumors, on imaging. An older age at presentation with short duration of symptoms and prior regional radiation treatment encompassing the spine in the treatment field regardless of remoteness should alert the oncologists and neurosurgeons to the possible existence of this rare and aggressive tumor, as the management, and overall prognosis of this tumor is distinctly different compared to the usual intradural spinal tumors.

1. Introduction

Malignant peripheral nerve sheath tumors (MPNSTs) are aggressive, locally invasive rare soft tissue sarcomas arising from peripheral nerves that originate from Schwann cells or pluripotent cells of neural crest origin [1, 2]. MPNSTs represent 3–10% of all soft tissue sarcomas, with an overall incidence of 0.001% in the general population that peaks in the seventh decade [2–4]. In patients with neurofibromatosis type 1 (NF1), the annual incidence is 1.6 per 1000 with a lifetime risk of 8–13% [5]. Prior radiation exposure is another important risk factor, with a reported incidence of radiation induced MPNST ranging from 5.5–11% of patients [6]. MPNSTs are usually located in the extremities, trunk, and head, and neck. Spinal MPNSTs, however, are exceedingly rare. Table 1 comprises a list of the spinal MPNSTs in the literature. While there are a few instances of spinal and paraspinal MPNST following radiation for testicular seminomas, all the cases reported occurred within 7–10 years following radiation and were mainly extradural in location [7–10]. An intradural spinal MPNST with subsequent intracranial leptomeningeal metastasis diagnosed forty years after radiation is presented in this report with a pertinent review of the literature.

2. Case Report

2.1. History and Presentation. A 77-year-old man with past medical history significant for esophageal adenocarcinoma as well as testicular seminoma that was treated with conventional external beam radiation therapy (EBRT) almost 40 years back presented with three months of left hip and buttock pain in addition to left foot weakness. He had no history or clinical stigmata of neurofibromatosis.

A magnetic resonance imaging (MRI) of the lumbar spine with and without gadolinium demonstrated a homogenously enhancing, well demarcated intradural extramedullary neoplasm (Figure 1). An initial MRI of the cervical and thoracic spine with and without gadolinium was negative for additional lesions. While a diagnosis of benign nerve sheath tumor was suspected given typical radiological appearance, a metastatic lesion was also considered in the differential because of prior
Table 1: Primary spinal malignant peripheral nerve sheath tumors (MPNST) reported in the literature.

| Author & year            | Age (yrs), sex | Location       | Presentation                                      | NF history | Radiation history | Extent of resection | Radiation therapy | Chemotherapy | Recurrence | Metastasis | Outcome       |
|--------------------------|----------------|----------------|---------------------------------------------------|------------|-------------------|---------------------|-------------------|--------------|------------|------------|---------------|
| Thomeer et al., 1981 [12]| 42, M          | Cauda equina   | Low back pain for 9 yrs with occasional L radiculopathy, impotence for 4 wks, leg weakness for 3 wks | Not specified | Total             | T11 - S4 2.5 Gy 4x/wk for 6 wks | Yes, 3 yrs   | T9-11       | No         | Alive at 3 yrs |
| Valdueza et al., 1991 [13]| 40, F          | Thoracic       | Thoracic pain, R leg weakness                      | Not specified | Partial           | Total 12 Gy after initial operation, total 40 Gy after spinal metastasis | No           | Yes, 2 mo   | Chest, pelvis, spine | Alive at 4 yrs |
| Valdueza et al., 1991 [13]| 43, F          | Thoracic       | Low back pain for 1 mo, leg weakness for 2 wks     | Not specified | Partial           | Total 24 Gy after first operation, total 32 Gy after second operation for recurrence | No           | Yes, 8 yrs   | No         | Alive at 10 yrs |
| Valdueza et al., 1991 [13]| 47, M          | Cervical       | Neck pain radiating to R shoulder for 9 mo, R arm weakness for 1 mo | NF1        | Not specified     | Total 10 Gy         | No               | Yes, 3 mos   | Brain, lumbar | Dead at 18 mos |
| Valdueza et al., 1991 [13]| 18, M          | Cervical       | L shoulder and arm pain for 4 mos                  | Not specified | Total             | No                  | No               | No          | No         | Alive at 8 mos |
| Valdueza et al., 1991 [13]| 70, F          | Cervical       | Neck pain radiating to R shoulder for 6 mos        | Not specified | Total             | No                  | No               | No          | No         | Alive at 7 mos |
| Valdueza et al., 1991 [13]| 13, M          | Lumbar         | Paraparesis                                       | NF1        | 12 yrs ago for Wilms tumor | Partial             | Not specified | Not specified | Yes         | Brain, systemic | Dead at 2 mos |
| Valdueza et al., 1991 [13]| 13, M          | Lumbar         | Paraparesis                                       | Not specified | Total             | Not specified | Not specified | Not specified | Yes         | Systemic       | Dead at 7 mos |
| Valdueza et al., 1991 [13]| 45, F          | Sacral         | Not specified                                     | NF1        | Not specified     | Total             | Not specified | Not specified | Yes         | Systemic       | Dead at 2 mos |
| Valdueza et al., 1991 [13]| 35, M          | Lumbar         | Radiculopathy                                     | NF2        | Not specified     | Total             | Not specified | Not specified | Yes         | Systemic       | Dead at 18 mos |
| Valdueza et al., 1991 [13]| 23, F          | Thoracic       | Not specified                                     | Total      | Yes               | No                | Yes, 2 yrs     | Dead at 6 yrs |
| Valdueza et al., 1991 [13]| 37, F          | Cervical       | Radiculopathy                                     | Total      | No                | Yes               | Dead at 8 mos   | Dead at 8 mos |
| Valdueza et al., 1991 [13]| 47, M          | Cervical       | Neck pain radiating to R shoulder for 9 mo, R arm weakness for 1 mo | Not specified | Total             | No                  | No               | No          | No         | Alive at 10 yrs |
| Valdueza et al., 1991 [13]| 35, M          | Lumbar         | Radiculopathy                                     | NF1        | Not specified     | Total             | Not specified | Not specified | Yes         | Systemic       | Dead at 18 mos |
| Valdueza et al., 1991 [13]| 23, F          | Thoracic       | Not specified                                     | NF2        | Not specified     | Total             | Not specified | Not specified | Yes         | Systemic       | Dead at 8 mos |
| Valdueza et al., 1991 [13]| 37, F          | Cervical       | Radiculopathy                                     | Not specified | Total             | Yes               | Dead at 6 yrs   | Dead at 6 yrs |

Table 1: Primary spinal malignant peripheral nerve sheath tumors (MPNST) reported in the literature.
| Author & year | Age (yrs), sex | Location | Presentation | NF history | Radiation history | Extent of resection | Radiation therapy | Chemotherapy | Recurrence | Metastasis | Outcome |
|---------------|----------------|----------|--------------|------------|------------------|-------------------|------------------|--------------|------------|-----------|---------|
| Celli et al., 1995 [15] | 52, F | Thoracic | Pain for 8 mos, weakness | Not specified | Total | No | No | No | No | Alive at 6 yrs |
| | 68, F | Lumbar | Pain for 9 mos, weakness | Not specified | Total | No | No | No | No | Alive at 2 yrs |
| | 43, M | Lumbar | Pain for 3 mos | Not specified | Total | No | No | No | No | Alive at 6 yrs |
| | 36, F | Thoracic | Pain for 5 mos | Not specified | Total | Yes | No | Yes | No | Alive at 4 yrs |
| | 22, F | Cervical | Pain for 2 yrs, weakness, incontinence | NF1 | Total | Yes | No | Yes | Lung | Dead at 6 mos |
| | 30, M | Thoracic | Pain for 3 yrs, weakness | Not specified | Total | Yes | No | Yes | Lung | Dead at 14 mos |
| West et al., 1997 [7] | 40, M | Sacral | Radiculopathy | 8 yrs ago for testicular seminoma, 30.6 Gy | Total | No | No | Yes, 7 mos | No | Not specified |
| | 11, F | Lumbar, sacral | Not specified | NF1 | Not specified | Partial | Yes | Yes | Yes, 0.5 mos | No, location not specified | Dead at 5 mos |
| | 25, F | Lumbar | Not specified | NF1 | Not specified | Partial | Yes | Yes | No | No, location not specified | Alive at 18 yrs |
| | 33, F | Lumbar | Not specified | NF1 | Not specified | Partial | No | No | No | No, location not specified | Dead at 2 mos |
| | 33, M | Lumbar | Not specified | NF1 | Not specified | Partial | Yes | Yes | Yes, 3 mos | No, location not specified | Dead at 22 mos |
| | 31, F | Lumbar | Not specified | NF1 | Not specified | Partial | Yes | Yes | Yes, 6 mos | No, location not specified | Dead at 10 mos |
| | 37, F | Lumbar | Incidental | Not specified | Partial | No | Yes | Yes, 3 mos | No | No, location not specified | Dead at 4 mos |
| | 40, M | Sacral | Not specified | For testicular seminoma | Total | No | No | Yes, 9 mos | Yes, location not specified | Alive at 14 mos |
| | 17, M | Thoracic | Not specified | NF1 | Not specified | Partial | No | Yes | Yes | No, location not specified | Dead at 11 mos |
| | 19, F | Thoracic | Incidental | NF1 | Not specified | Total | No | No | No | No, location not specified | Alive at 35 mos |
| | 53, F | Thoracic | Not specified | For breast carcinoma | Partial | No | No | Yes, 6 mos | No, location not specified | Dead at 7 mo |
| | 26, M | Thoracic | Not specified | For Hodgkin's lymphoma | Partial | Yes | No | Yes, 13 mos | No, location not specified | Dead at 27 mo |
| Author & year | Age (yrs), sex | Location    | Presentation                                                                 | NF history | Radiation history | Extent of resection | Radiation therapy | Chemotherapy | Recurrence | Metastasis | Outcome      |
|--------------|---------------|-------------|------------------------------------------------------------------------------|------------|-------------------|---------------------|-------------------|--------------|------------|------------|-------------|
| Acharya et al., 2001 [20] | 32, M          | Cauda equina | Back pain, leg weakness, bowel and bladder dysfunction, Low back pain        | Not specified | Partial            | Yes                 | No                | No           | No         | No      | Alive at 18 mos |
| Yone et al., 2004 [16] | 4, M           | Cauda equina | Not specified, Radioculopathy, bladder dysfunction                           | Not specified | Total              | Yes                 | Yes               | Yes          | Brain, spine | Dead at 21 mos |
| Adamson et al., 2004 [17] | 37, M          | Cervical    | L C6 radiculopathy                                                           | 6 yrs ago for Hodgkin's lymphoma | Partial            | Yes                 | No               | Not specified | No         | Dead after 1 yr |
| Amin et al., 2004 [9] | 38, M          | Cauda equina | Back pain, leg weakness, bowel and bladder dysfunction                       | 10 yrs ago for testicular seminoma, 30 Gy/15 fractions over 3 wks | Biopsy             | No                  | Yes, palliative | Yes, 7 mos | Not specified | Not specified |
| Albayrak et al., 2006 [18] | 25, M          | Thoracic    | Paraparesis, bladder dysfunction                                              | NF1        | Not specified      | Total               | No                | No           | Yes, 7 wks | Lung       | Alive at 7 wks |
| Chamoun et al., 2009 [14] | 5, F           | Cervical    | Pain, gait disturbance                                                        | Not specified | Partial            | Yes                 | Yes               | Yes          | Brain, thoracic and lumbar spine | Alive at 4 mos |
| Xu et al., 2012 | 8, M           | Lumbar      | Pain                                                                          | Not specified | Total              | Yes                 | No                | Yes          | Brain      | Dead at 16 mos |
| Mitsuhara et al., 2013 | 47, F          | Cauda equina | Back pain, leg weakness, bowel and bladder dysfunction, altered mental status | NF2        | Partial            | Yes, 36 Gy brain and spine, additional 14.4 Gy to lumbosacral lesion/28 fractions | No             | Not specified | No         | Not specified |
| Author & year | Age (yrs), sex | Location | Presentation | NF history | Radiation history | Extent of resection | Radiation therapy | Chemotherapy | Recurrence | Metastasis | Outcome |
|---------------|----------------|----------|--------------|------------|-----------------|-------------------|------------------|--------------|-----------|-----------|---------|
| Stark et al., 2013 | 56, F | Sacral | L leg radiculopathy, L foot paresis | 15 yrs ago for non-Hodgkin's lymphoma | Not specified | No | Yes | Yes | Brainstem, spine | Dead at 24 mos |
| Wu et al., 2014 | 9, F | Thoracic, lumbar, sacral | R hip pain, bilateral leg weakness Low back pain, R leg radiculopathy, hydrocephalus | NF2 | Not specified | Partial | No | No | Yes | Brain | Dead at 9 mos |
| Li et al., 2014 | 33, F | Low thoracic, upper lumbar | Low back pain, L leg radiculopathy for 5 mos | Not specified | Partial | Yes, 28 Gy/19 fractions | No | Yes | Brain, diffuse spine | Dead at 29 mos |
| Lau et al., 2014 [10] | 43, M | Cauda equina | Low back pain, L leg radiculopathy for 5 mos | 10 yrs ago for testicular seminoma | Total | No | | Yes, alternating between ifosfamide/doxorubicin and ifosfamide/etoposide | Brainstem, cervical spine, renal | Dead at 5 yrs |
| Thomas et al., 2014 | 49, M | Cauda equina | Low back pain, paraparesis Paraplegia, bladder and bowel dysfunction | Not specified | Partial | No | No | No | Brain and spine | Not specified |
| Baharvahdat et al., 2016 | 3, F | Cervical, upper thoracic | Hydrocephalus | Not specified | Partial | No | No | No | Brain and spine | Dead shortly after surgery |
| Chou et al., 2017 | 5–74 (mean 40) | Cervical, upper thoracic | Hydrocephalus | Not specified | Partial | Yes | Yes | No | No | Intracranial leptomeningeal disease | Dead at 2 mos |
| Samancia et al., 2017 | 27, M | Cervical, upper thoracic | Hydrocephalus | Not specified | Partial | Yes | Yes | No | No | Intracranial leptomeningeal disease | Dead at 2 mos |

F: Female, Gy: gray, L: left, M: male, mos: months, NF1: neurofibromatosis type 1, NF2: neurofibromatosis type 2, R: right, wks: weeks, yrs: years. Multicenter series (N = 29), individual patient data not available.
arising from the left L3 nerve root with obvious enlargement and involvement of the nerve root. A frozen specimen was sent early for pathological evaluation that was diagnosed as MPNST. The nerve root of interest was clearly identified both proximally and distally, which on stimulation resulted in robust electrophysiological response suggestive of origin.

2.2. Operative Course. A partial L2 and complete L3 laminectomy was performed and a midline durotomy was made. A greyish mass was found in the intradural space arising from the left L3 nerve root with obvious enlargement and involvement of the nerve root. A frozen specimen was sent early for pathological evaluation that was diagnosed as MPNST. The nerve root of interest was clearly identified both proximally and distally, which on stimulation resulted in robust electrophysiological response suggestive of origin.

**Figure 1:** (a) Magnetic resonance imaging (MRI) T1-weighted sagittal image of the lumbar spine with gadolinium demonstrates a well demarcated intradural extramedullary mass. (b) Corresponding axial image.

**Figure 2:** (a) Hematoxylin and eosin (H&E) staining showed high cellular density with marked pleomorphism and spindle cells arranged in fascicles (200x). (b) Immunohistochemistry was positive for SOX 10 (100x) and (c) S-100 (100x). (d) Ki-67 labeling revealed a high proliferative index (100x).
period and in an extradural location, with a purely intradural occurrence being exceptionally rare [7–10]. The present case developed almost four decades after being treated with EBRT for testicular seminoma, which is a significantly longer latency period as compared to other cases previously reported. Also, the imaging features were fairly characteristic of a benign intradural extramedullary neoplasm unlike a MPNST, which is typically an irregularly-bordered heterogeneously enhancing mass often with destruction of surrounding osseous structures. Similarly, the presence of leptomeningeal spread is also rare in primary intradural MPNSTs and as illustrated in this case, portends an ominous prognosis [11]. Unique to this case, however, is the rapid development of disseminated disease two weeks after surgery. Patients in other reported cases of intradural MPNSTs with leptomeningeal spread were diagnosed with dissemination ranging from present on presentation to 24 months following initial surgery [10–19]. The authors advocate that regardless of imaging characteristics or the duration since radiation, surgeons should retain a high index of suspicion for a MPSNT. Lumbar puncture may be considered to obtain CSF to identify potential malignant cells.

4. Conclusion

A rare case of an intradural MPNST diagnosed more than 40 years after radiation for a testicular seminoma is reported. Intradural MPNSTs of the spine outside the setting of neurofibromatosis are extremely rare and can masquerade common benign nerve sheath tumors on imaging. Short duration of symptoms and prior regional radiation treatment encompassing the spine in the treatment field regardless of remoteness should alert the physician to the possible existence of this rare

from a motor nerve root. No obvious plane was found between the tumor and the nerve root. Given the risk of motor deficit, the nerve root was preserved with partial resection of the tumor. Final pathology confirmed the diagnosis of MPNST (Figure 2).

2.3. Post-Operative Course. Given the initial pathologic diagnosis on frozen section, subsequent management including reoperation with extensive resection was discussed. Given his preoperative status, the patient, and family elected to observe in the short term with consideration of further treatment options following final pathology. The patient did well initially and was discharged to a skilled nursing facility. Two weeks post-operatively, however, the patient was readmitted with encephalopathy. An MRI brain with and without gadolinium demonstrated leptomeningeal metastasis (Figure 3) with cerebral spinal fluid (CSF) cytology positive for malignant cells. Given the extent of disseminated disease and his progressive worsening mental status, the family elected to pursue palliative care, and the patient died two months after his initial surgery.

3. Discussion

MPNSTs are rare entities with an incidence of 0.001%, with 20–50% of cases arising in patients with NF-1. The most common locations include the trunk, extremities, and head, and neck [2]. Primary spinal MPNSTs are extremely rare. Primary MPNSTs of the spine that are exclusively intradural extramedullary without extension into the extradural compartment are exceptionally rare. Outside the setting of NF-1, prior radiation treatment is a risk factor for development of MPNSTs. There have been few reports of MPNST following prior radiation for testicular seminomas. Most occurred after a short latent period and in an extradural location, with a purely intradural occurrence being exceptionally rare [7–10].

The present case developed almost four decades after being treated with EBRT for testicular seminoma, which is a significantly longer latency period as compared to other cases previously reported. Also, the imaging features were fairly characteristic of a benign intradural extramedullary neoplasm unlike a MPNST, which is typically an irregularly-bordered heterogeneously enhancing mass often with destruction of surrounding osseous structures. Similarly, the presence of leptomeningeal spread is also rare in primary intradural MPNSTs and as illustrated in this case, portends an ominous prognosis [11]. Unique to this case, however, is the rapid development of disseminated disease two weeks after surgery. Patients in other reported cases of intradural MPNSTs with leptomeningeal spread were diagnosed with dissemination ranging from present on presentation to 24 months following initial surgery [10–19]. The authors advocate that regardless of imaging characteristics or the duration since radiation, surgeons should retain a high index of suspicion for a MPSNT. Lumbar puncture may be considered to obtain CSF to identify potential malignant cells.

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A rare case of an intradural MPNST diagnosed more than 40 years after radiation for a testicular seminoma is reported. Intradural MPNSTs of the spine outside the setting of neurofibromatosis are extremely rare and can masquerade common benign nerve sheath tumors on imaging. Short duration of symptoms and prior regional radiation treatment encompassing the spine in the treatment field regardless of remoteness should alert the physician to the possible existence of this rare
and aggressive tumor. Being cognizant of this rare pathology can help initiate appropriate work up and evaluation, allow preoperative counselling, and alter overall surgical strategy.

**Abbreviations**

CSF: Cerebral spinal fluid  
CT: Computer tomography  
EBRT: External beam radiation therapy  
H&E: Hematoxylin and eosin  
MPNST: Malignant peripheral nerve sheath tumor  
MRI: Magnetic resonance imaging  
NF1: Neurofibromatosis type I.

**Conflicts of Interest**

The authors declare that they have no conflicts of interest.

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