Multiple Primary Primitive Neuroectodermal Tumours within the Spinal Epidural Space with Non-concurrent Onset

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A case of multiple primary primitive neuroectodermal tumours (PNETs), which occurred at different levels of the spinal epidural space successively over a period of 8 months, is reported. A 24-year-old male, presenting with rapidly progressive paralysis, hyperesthesia and a posterior epidural mass extending from T8 to T10 revealed by magnetic resonance imaging (MRI), exhibited a good recovery after initial emergency surgery. Lower back pain, chest pain and paralysis were subsequently reported. Spinal MRI in month 7 revealed a mass extending from T12 to L1 and another mass extending from T4 to T5 was detected epidurally in month 8. Additional operations were performed and radiotherapy was given. Pathological findings were consistent with PNETs and symptoms improved with treatment, particularly following each surgical excision.

KEY WORDS: SPINAL EPIDURAL SPACE; INTRASPINAL TUMOUR; PRIMITIVE NEUROECTODERMAL TUMOUR (PNET); MULTIPLE PRIMARY TUMOURS

Introduction

Primitive neuroectodermal tumours (PNETs) are malignant and highly cellular neoplasms which occur predominantly in the cerebellum (medulloblastomas) in children. A few arise in the pineal gland, cerebrum, spinal cord, brain stem and peripheral nerves.1 Primary intraspinal PNET is a rare condition and always carries a poor prognosis. Epidural location of primary intraspinal PNET is extremely rare; only five cases have been reported in the English literature to date and these have presented as a single mass lesion.2 - 6 Here we report the case of primary multiple PNETs, occurring intermittently at different levels of the spinal epidural space (T8 – T10, T12 – L1 and T4 – T5).

Case report

A previously healthy 24-year-old man presented with a 1-month history of thoracal back pain. Rapidly progressive weakness and numbness in the lower extremities and the sensation of incomplete bladder emptying occurred 5 days before admission. On the first day of hospitalization he was unable to walk unassisted and urethral catheterization yielded 1100 ml of urine. Neurological
examination revealed paraparesis (2/5) in the lower extremities and hypoaesthesia below the T10 level. Vital signs were normal and his familial medical history was unremarkable.

Spinal magnetic resonance imaging (MRI) revealed a posterior epidural mass extending from T8 to T10, causing compression of the cord (Fig. 1A). In the sagittal T1- and T2-weighted image, the mass exhibited a similar MRI signal intensity as the spinal cord. After use of contrast agents, the mass demonstrated a uniformly high signal intensity. Cranial MRI and thoraco-abdominal computerized tomography (CT) showed no other lesions.

An emergency laminectomy from T8 – T10 was performed and the epidurally located mass was totally excised microscopically. Intra-operatively, the tumour appeared soft and was grey-reddish in colour; it did not adhere to the adjacent structures and had a diameter of 1.5 cm sagittally and 4.0 cm axially. Paraffin sections of a specimen of the neoplasm revealed a highly cellular tumour, mainly composed of small round cells with hyperchromatic nuclei and a small cytoplasmatic wall (Fig. 2A). Immunohistochemically there was a strong positive expression of the CD99 (Fig. 2B) cell surface glycoprotein. In some cells Ki-67, vimentin, neuron-specific enolase (NSE) and S-100 proteins were present. No positive reaction was found for chromogranin A, synaptophysin, leucocyte common antigen, glial fibrillary acidic protein and myeloperoxidase. Histological and immunohistochemical features of this round-cell tumour were both consistent with the diagnosis of PNET.

Two weeks after the laminectomy, the patient received hyperfractionated focal radiation therapy to the T8 to T10 region, with a total dose of 45 Gy delivered over 21 days. This was well tolerated without any complications. Five weeks after the operation, the patient was able to walk with crutches and had normal bladder function. Six months later he was able to walk unassisted with full neurological recovery.

**FIGURE 1**: Sagittal magnetic resonance imaging (T1-weighted image) shows posterior epidural mass lesions in a 24-year-old man: (A) at T8 – T10 before the first operation; (B) at T12 – L1 before the second operation; (C) at T4 – T5 before the third operation. In (C) the spinal cord is smooth at the level of T8 – T10 and T12 – L1, where no tumour recurrence is found. The lesions are indicated by arrows.
Seven months after the first operation, he was readmitted for investigation of lower back pain; there was no weakness or numbness in the lower extremities. Spinal MRI revealed an epidural tumour at the level of T12 – L1 and the corresponding spinal cord segment was slightly compressed (Fig. 1B). There was no tumour recurrence at the original site. A laminectomy was performed from T12 to L1 and an epidurally located, uncapsulated mass was totally excised. No new neurological deficits occurred after this second laminectomy.

One month after the second operation, the patient presented with chest pain of 1 week’s duration. There was then rapid progressive weakness in the lower extremities without bladder or bowel dysfunction. MRI revealed a posterior epidural mass at the T4 – T5 spinal level (Fig. 1C). A third laminectomy was performed from T4 to T5 and the tumour was totally removed. Shortly after the operation the patient was able to stand. Neurological recovery was rapid and the patient became able to walk unassisted.

The histological and immunohistochemical phenotypes of the second and third tumours were the same as the first; both were diagnosed pathologically as PNETs. A new course of total spinal radiation therapy, with a total dose of 45 Gy, was completed. Metastatic work-up showed no evidence of an intracranial tumour or metastases outside the neuroaxis. Meanwhile, karyotype analysis of the patient’s peripheral blood and the results from lumbar puncture gave no indication of aetiologypathogenesis. Six months after the third operation, the patient was generally progressing well and there has been no clinical or radiological evidence of tumour recurrence.

**Discussion**

Hart and Earle’ first introduced the term primitive neuroectodermal tumour (PNET) in 1973 to describe predominantly undifferentiated tumours of the cerebrum. In
1993 the World Health Organization (WHO) then recommended that PNET should be used as a generic term for cerebellar medulloblastomas and neoplasms that are histologically indistinguishable from medulloblastoma, but are located in the central nervous system (CNS) at sites other than the cerebellum. PNET was defined in the third edition of the WHO classification of tumours of the CNS as ‘an embryonal tumour composed of undifferentiated or poorly differentiated neuroepithelial cells which have the capacity for or display divergent differentiation along neuronal astrocytic, ependymal, muscular or melanotic lines’. The new, 2007 edition has proposed adding the prefix CNS to PNET, to be used for undifferentiated or poorly differentiated embryonal tumours that occur at any extracerebellar site in the CNS.

A primary intraspinal CNS PNET is a rare lesion and, prior to giving a final diagnosis of primary intraspinal PNET, efforts should be made to exclude primary lesions located in other parts of the body by imaging techniques (X-ray, CT, MRI) or autopsy.

In the English literature, only five cases of primary intraspinal epidural PNET have been described and all have presented as a single mass lesion. It was considered that those located epidurally could not disseminate along the cerebrospinal fluid. In fact, no local recurrence or metastases were found in the five cases in post-operative radiological examinations. Interestingly, our case involved multiple PNETs within the spinal epidural space that occurred successively (T8 – T10 followed by T12 – L1 followed by T4 – T5). Neither of the later lesions were adjacent to the first lesion and all three pathological findings were consistent with PNETs. It was concluded that the second and third tumours could not be metastases from the first tumour via the cerebrospinal fluid because of their epidural location. Furthermore, no intracranial tumour and lesions outside the spinal canal were found with a series of imaging examinations. A diagnosis of multiple primary intraspinal PNETs was, therefore, made.

To the authors’ knowledge, this is the first case of primary multiple PNETs that has occurred successively at different levels of the spinal epidural space. Although the three mass lesions occurred separately, they appeared to be restricted to the thoracic vertebrae canal. Lumbar puncture and karyotype analysis of the patient’s peripheral blood were negative. The aetiopathogenesis is still not clear.

With respect to the therapeutic options for primary intraspinal PNETs, surgery, radiotherapy and chemotherapy are the conventional treatments. Surgical tumour resection is the cornerstone of the therapy and the maximum tumour resection that can be undertaken without causing severe neurological damage is recommended, in general. Some consider radiotherapy to be the best choice for spinal PNETs, especially those located intramedullary. Nearly all the reported patients with primary intraspinal PNETs underwent radiation therapy as part of their primary treatment. Higher doses may achieve better tumour control and hyperfractionation may even enhance local control. The treatment of PNETs by chemotherapy has improved, and the application of maintenance chemotherapy after radiotherapy seems to deliver superior results. Despite these treatments, the prognosis of intraspinal PNETs remains poor. New possible therapeutic alternatives, such as adoptive immunotherapy and peripheral blood stem cell transfusion, are under investigation.

In our case, as for the other five reported cases whose intraspinal PNETs were located
epidurally, gross total resection was performed soon after the initial diagnosis. No lesions were found outside the spinal canal with serial imaging and emergency surgical interventions achieved good outcomes. It appears that early surgical intervention provides a good prognosis for primary intraspinal PNETs located in the epidural space and avoids serious neurological problems.

In conclusion, primary intraspinal epidural PNET is an extremely rare tumour. Further investigations and experience in this rare neoplasm might improve the treatment strategy. Early surgical intervention with gross total resection seems especially important for patients with PNETs located within the spinal epidural space.

Conflicts of interest
The authors had no conflicts of interest to declare in relation to this article.

References

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