Clinical Study

Primary intraspinal primitive neuroectodermal tumor: report of two cases and review of the literature

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Summary

Background. Primary intraspinal primitive neuroectodermal tumor (PNET) is a very rare tumor entity. The optimal therapeutic approach is not known yet. We report on two women with primary intraspinal PNETs and review the literature. We describe the typical course of the disease, compare our patients to the other 17 cases reported until today, and discuss therapeutic options.

Patients and method. Case A: In a 49-year-old woman with an intraspinal PNET at L2, laminectomy and a gross tumor removal was accomplished. Postoperative radiation was performed from T12 to L3 to a dose of 50.4 Gy. Subsequently she was treated with chemotherapy containing vincristine, cisplatinum and lomustine. Case B: A 29-year-old woman presented with intramedullary PNET lesions at T1–3 and T10–11. Due to the multifocal location, she received a primary craniocaudal axis irradiation to a dose of 35.2 Gy plus a boost to the tumor region to a total dose of 53.2 Gy.

Results. Both patients developed multilocular intraspinal relapses with meningeosis neoplastica 17 and 6 months from radiation therapy and underwent palliative chemotherapy. Case A died 23 months, case B 17 months after primary diagnosis.

Conclusion. Despite modern treatment with microsurgery, irradiation and chemotherapy in primary intraspinal PNETs, local relapse or dissemination in most cases lead to death within a few months. An improvement of treatment outcome can only be achieved by intensification through multidisciplinary treatment.

Introduction

Primitive neuroectodermal tumors (PNETs) are malignant small, highly cellular neoplasms, which occur predominantly in children. The most common localization of the disease is in the cerebellum (medulloblastomas), which accounts for 20–25% of all childhood brain tumors. PNETs, however, can also arise in the pineal gland, in the cortex, brain stem and peripheral nerves [1,2]. An intraspinal location of PNETs has to date been reported in only 17 patients.

Multidisciplinary treatment has been well established as the standard therapy for PNETs. The mainstay of therapy is a surgical tumor resection whenever feasible [3]. There is general consensus that patients with PNETs of the cerebrum should receive postoperative radiation therapy. Because of their propensity to spread throughout the subarachnoidal space, both supratentorial and cerebellar PNETs are treated with craniospinal axis irradiation [4–6]. The efficacy of chemotherapy in a multimodal therapeutic setting has been shown in randomized studies and is part of several currently ongoing studies [5–7].

It has become obvious that outcome depends on the primary tumor location: compared to infratentorial PNETs, supratentorial tumor locations are associated with significantly decreased survival rates [8,9].
In contrast to these two intracranial locations, for intraspinal PNETs little is known about the optimum treatment strategy and therapeutic results.

We compare therapy and outcome of two patients suffering from intraspinal PNETs treated in our hospital with other cases reported in literature, describe the typical course of the disease and discuss currently available therapeutic options.

Case report A

A previously healthy 49-year-old woman presented with lower back pain projecting down to the right leg. She had repeatedly experienced paresthesias in the lower extremities, right more than left. The neurological and general physical examination at presentation revealed no specific findings.

Magnetic resonance imaging (MRI) revealed an isointense lesion with a diameter of 1.3 cm in the sagittal and 2.0 cm in the axial direction. The tumor was localized at level L2. The fibers of the cauda equina were markedly shifted to the left, consistent with an intraspinal lesion. Following the application of contrast medium, the tumor showed a homogeneous enhancement.

A laminectomy of L2 was performed. Intraoperatively, the tumor appeared soft with diffuse bleeding upon touching. Gross total removal of the tumor was performed under microsurgical conditions. Because of relationship of the tumor to the nerve root L1 and the MRI findings a neurinoma was most likely; thus, the histologic diagnosis was surprising.

The paraffin sections of the tumor specimen revealed a highly cellular tumor, consisting of mainly small round cells with hyperchromatic nuclei and a small cytoplasmatic wall (Figure 1). No well-defined Homer–Wright and only a few ependymal rosettes were found. Numerous mitotic figures and necroses were present. Of all cells, 30–40% revealed an expression of neurofilaments, approximately 10% expressed vimentin. No positive reaction was found for the S-100 protein. There was a strong immunoreactivity for MIC-2 and neuron-specific enolase (NSE). The diagnosis of a PNET was made by the typical histological picture and immuno-histochemical detectability, in particular, of the positive expression of the MIC-2 antigen, which is only positive in peripheral PNETs. A restaging MRI showed no further tumor localizations, especially not intracerebral. Eight weeks after the initial operation, the patient was scheduled only for a local spinal irradiation to pay regard to the diagnosis of peripheral PNET. She received a radiation dose of 50.4 Gy in 1.8 Gy single fractions to the spine from T12 to L3 using 6 MV photons from a linear accelerator. The patient tolerated the radiation therapy without complications.

After irradiation, a multidrug chemotherapy was started. The patient received 6 cycles of vincristine, lomustine (CCNU) and cisplatinum given 6 weeks apart. Vincristine was administered on days 1, 8 and 15; CCNU and cisplatinum on day 1. The dosage was 1.5, 75 and 70 mg/m², respectively. Due to the vincristine application, the patient developed signs of an intestinal affection with symptoms of subileus. Furthermore, she experienced a hyporeflexia from vincristine-induced neuropathy. Thus vincristine was stopped after the second cycle.

Seventeen months from primary diagnosis, the patient developed multiple intraspinal metastases at S1/S2 and another microsurgical resection was performed with the identical histologic and cytologic (cerebrospinal fluid) findings. A salvage radiation to the lower spine (L4–S5) was planned to a total dose of 45 Gy. She received radiation in conventionally fractionated doses (5 × 1.8 Gy/week) to a total dose of 32.4 Gy using 20 MV photons. Radiation was stopped because of progressive neurological symptoms, especially a rapid progression of leg weakness. A restaging MRI was carried out and showed a meningeosis neoplastica and multiple intraspinal metastases 'T6–11 cranial of the previous radiation portal (Figure 3). A final neurosurgical procedure only by decompression was performed.