Spinal Tumors

18

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Contents

Abstract

Spinal cord tumors are very rare in children. They present unique clinical challenges, and their treatment should be individualized based on the histologic type. The use of postoperative irradiation for spinal cord tumors has been controversial, and largely inconsistent. Radical surgery is the aim for low-grade astrocytic

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A. Mahajan, A. Paulino (eds.), *Radiation Oncology for Pediatric CNS Tumors*,
https://doi.org/10.1007/978-3-319-55430-3_18

tumors and ependymomas. The need for adjuvant therapy most often depends on the extent of resection as well as the tumor type. While the role of postoperative radiotherapy in high-grade spinal cord tumors is widely accepted, its role in low-grade intramedullary tumors is debatable. Patients with disseminated low-grade glial tumors and ependymomas of the spinal cord may achieve long-term progression-free survival with craniospinal irradiation. The potential role of chemotherapy in the management of spinal cord astrocytoma remains to be defined.

18.1 Epidemiology

Primary spinal cord neoplasms constitute about 5% of central nervous system (CNS) tumors in children, and are usually intradural in origin. They need to be distinguished from extradural tumors (neuroblastoma, peripheral PNET, etc.), which are outside the scope of this chapter. Thirty-five percent of pediatric spinal tumors are intramedullary, higher than the 20% cited for adults (Constantini et al. 1996). The cervical spinal cord is affected slightly more frequently than the thoracic. The average lesion spans multiple segments (Reimer and Onofrio 1985) and can also result in holocord tumors as well (Epstein and Epstein 1981).

The median age at diagnosis of intramedullary spinal cord tumors (IMSCT) in children is around 10 years, with a slight male predominance (DeSousa et al. 1979, Reimer and Onofrio 1985, Zileli et al. 1996, Goh et al. 1997). Astrocytic tumors account for nearly 60% of primary spinal cord tumors in children; of which, low-grade astrocytomas, such as fibrillary or pilocytic astrocytomas (PA), constitute more than two-thirds of the cases. There are a handful of very rare cases of oligodendroglia-like and neuroepithelial tumors of spinal cord, presenting as disseminated tumors (Schniederjan et al. 2013). Another rare entity is a gliofibroma of spinal cord, which also has a propensity for leptomeningeal spread (Prayson 2013). High-grade neoplasms, including anaplastic astrocytoma and glioblastoma, represent less than 20% of the cases, are more commonly diagnosed at younger ages, and have a high propensity for leptomeningeal dissemination (Hardison et al. 1987, Cohen et al. 1989). Ependymoma is the second most common pediatric spinal cord neoplasm, yet it represents less than 5% of all ependymomas diagnosed in children. Other gliomas, like ganglioglioma and oligodendroglioma, comprise less than 10% of spinal cord tumors.

18.2 Predisposing Factors

18.2.1 Etiology

Histologically, primary spinal cord tumors are mostly indistinguishable from their brain counterparts, and likely share a common etiology. With regard to environmental risk factors, ionizing radiation has been most commonly linked with CNS tumors,

but data on its association with primary spinal cord tumors is sparse. There is no evidence of any association between chemical environmental exposures and spinal cord tumors.

18.2.2 Genetic Issues

As with brain tumors, only a very small proportion of newly diagnosed spinal cord tumors can be linked with genetic syndromes. Patients with neurofibromatosis type 1 (NF-1) have a higher incidence of developing both low- and high-grade astrocytomas in the spinal cord. Neurofibromatosis type 2 can be associated with meningiomas within the spine, as well as with intramedullary gliomas and ependymomas. Hemangioblastoma's association with von Hippel–Lindau syndrome sometimes can be manifested in the spinal cord, particularly with multifocal presentation. Of note, patients with retinoblastoma, NF-1, Li–Fraumeni syndrome, or nevoid basal cell carcinoma syndrome are at substantial risk for developing radiation-related cancers, and can be diagnosed with primary spinal tumors within the radiation field.

18.3 Presenting Symptoms

Most patients present with insidious symptoms, evolving over several months or even years (Innocenzi et al. 1996; Rossitch et al. 1990). The short duration of presenting symptoms is associated with aggressive high-grade neoplasms and poor survival (Bouffet et al. 1998). Pain is the most frequent presenting symptom, and complaints of worsened pain at night may result from venous congestion and dural tube distention caused by the recumbent position. The pain may or may not be localized to the level of the lesion; however, search for local tenderness of the spine is still important during a physical examination. The most common localizing symptoms and signs are hemiparesis, hemisensory loss, and hyperreflexia which will often correspond to the level of involved lesion (Houten and Weiner 2000). Although rare, dissemination of disease may cause neurologic dysfunction, which can make localization of tumor more challenging. Upper motor neuron signs are usually evident at presentation, and include mild spasticity and increased deep tendon reflexes. Since these tumors are usually located in the central portion of the spinal cord, cervical tumors can produce weakness and muscle wasting in the upper extremities, prior to the development of lower extremities' sensory disturbances such as dysesthesias. Dorsal column dysfunction is less common because of the central location of these masses. A partial Horner syndrome (ipsilateral ptosis, miosis, and anhidrosis) may also be present in some patients with upper cervical cord disease as a result of compromise of the descending sympathetic tracts. Torticollis commonly appears in tumors of the cervical spine prior to the development of objective neurological dysfunction. Spinal cord and cauda equina involvement may cause bowel or bladder dysfunction. Kyphoscoliosis may be seen in tumors of the thoracic spine. Hydrocephalus can be associated with intramedullary spinal cord tumors and can occur with greater frequency in pediatric than adult patients (Rifkinson-Mann et al. 1990).

18.4 Radiographic Findings

Spinal tumors should be imaged preoperatively; however when this cannot be accomplished, it is recommended to perform a baseline imaging examination at approximately 3 weeks in the postoperative period to avoid difficulty with interpretation of findings caused by postsurgical subdural blood. MRI has a significant advantage as an imaging modality for visualization of anatomical details of spinal cord tumors. It can help to readily distinguish intramedullary from extramedullary lesions and to appreciate the full extent of the tumor. Typically, sagittal T1 images of the entire spine with gadolinium are obtained with axial T1 images obtained as needed. Tumors such as pilocytic astrocytoma, high-grade gliomas, and ependymomas are typically contrast enhancing lesions (Fig. 18.1). T2 sequences can better delineate nonenhancing tumors, like fibrillary astrocytomas and gangliogliomas; however, high-grade lesions sometimes do not enhance after contrast administration (Fig. 18.2). Intramedullary astrocytomas and hemangioblastomas are sometimes associated with multiple cysts or larger confluent rostral and/or caudal cysts, which typically are lined with nonneoplastic, gliotic tissue.

In evaluating spinal cord tumors, it is important to image the entire length of the spinal canal. It is important not to miss rare, but clinically important "skip" lesions

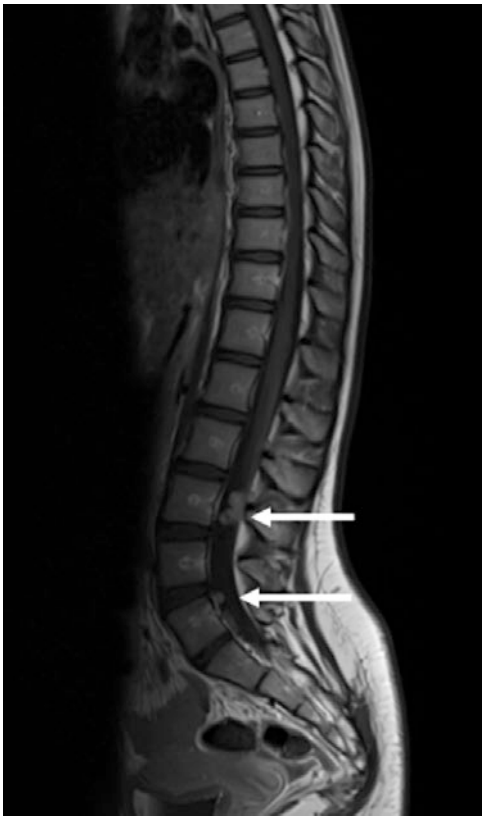

Fig. 18.1 Fifteen-year-old girl with known diagnosis of neurofibromatosis type I was incidentally found to have lesions in distal thecal sac during surveillance imaging (sagittal T1 sequence post-gadolinium administration demonstrated several enhancing masses (*arrows*)). Pathology after resection was consistent with grade II ependymoma

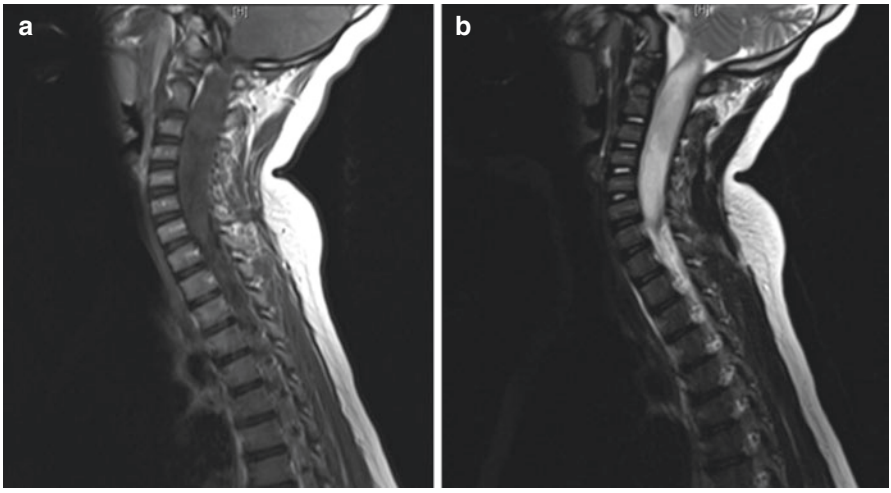

Fig. 18.2 Expansile cervical cord lesion in a 7-year-old child, nonenhancing on T1 post-contrast sagittal image (**a**) and hyperintense on T2 sagittal sequence (**b**), pathology from biopsy was consistent with anaplastic astrocytoma

sometimes seen in astrocytomas and ependymomas, and/or subarachnoid dissemination, more commonly found in malignant gliomas and ependymomas (Hardison et al. 1987; Cohen et al. 1989). Brain imaging should be performed in multifocal and disseminated cases, as there is a risk of rostral disease spread. The presence of multiple discrete tumors, along with other stigmata, is commonly associated with neurofibromatosis.

18.5 Workup

Medical history should focus on details of presenting symptoms including duration. Long-standing symptoms are more indicative of low-grade tumors while rapidly evolving ones raise concern for a more aggressive neoplasm. Additional history, including pre-existing genetic conditions and history of ionizing radiation exposure, cannot be overlooked. Inheritable genetic syndromes should be recognized in the family history. Attention during the physical examination should be directed to both upper and lower motor neuron signs, as well as sensory function. The constellation of neurological signs, such as Brown-Séquard syndrome, can help to localize the lesion. Imaging evaluation gives the best delineation of tumor process, and should include the entire neuraxis. As discussed above, MRI has become a gold standard in imaging of spinal tumors and should be considered first, when available. Cerebrospinal fluid (CSF) examination for protein levels, cytology, and infectious cultures, among other factors, can help diagnostic workup, particularly when nonneoplastic processes are still considered in diagnosis. Cytological detection of tumor cells can confirm the presence of disseminated tumor and can be complementary to spinal imaging. Ultimately, biopsy or resection, when feasible, can establish the most accurate diagnosis.

18.6 Acute Management

Spinal cord tumors commonly grow contiguously across the spinal cord and can result in significant mass effect on neurons and lead to a functional loss (Peschel et al. 1983; Reimer and Onofrio 1985; Hardison et al. 1987). Steroids are commonly prescribed to patients exhibiting symptoms from tumor mass effect, but laminectomy with or without tumor decompression is a very important intervention. Steroids should be administered carefully, as it could alter diagnosis in certain histologies such as lymphoma or other infectious agents.

18.7 Treatment

The benefit from postoperative radiotherapy in low-grade intramedullary spinal cord tumors is debatable. Data is limited to institutional case series, and there is no randomized study that has evaluated the use of postoperative radiotherapy (Nadkarni and Rekate 1999). While the extent of resection has more consistently been shown to be a significant prognostic factor in tumor control probability for low-grade lesions, tumor histology is the most important predictor of a patient's outcome (Whitaker et al. 1991, Innocenzi et al. 1996, Goh et al. 1997, Ahmed et al. 2014). A handful of studies demonstrated a trend toward improved tumor local control with the use of adjuvant radiotherapy when compared with surgical resection alone (Nadkarni and Rekate 1999, Guss et al. 2013). With regard to grade II ependymomas in children, radiotherapy is most commonly given after subtotal versus gross-total resection; this practice trend in North America has not significantly changed over the past three decades (Lin et al. 2014). There is also limited, but convincing evidence on radiation treatment achieving durable local control in patients without any surgical resection (O'Sullivan et al. 1994, Guss et al. 2013).

For high-grade spinal cord tumors, outcome overall remains dismal. Therapeutic advances in the management of high-grade gliomas of the spinal cord have been hampered by the rarity of incidence and the lack of uniform treatment. Despite the lack of evidence for improved outcome, trimodality approach including maximum safe resection, adjuvant radiotherapy and chemotherapy is commonly used (Merchant et al. 1999).

18.7.1 Role of Surgery

Surgical management plays a very important role in spinal cord tumors for establishing diagnosis while achieving maximum safe resection for improved local control. Laminectomy or laminoplasty, as appropriate, is typically performed to access the lesion. Extramedullary intradural tumors are more readily accessible and can be completely removed for diagnostic and treatment purposes (Jenkinson et al. 2006). When it comes to intramedullary lesions, intraoperative tumor resection is based on whether

a plane of dissection can be identified, which is often dependent on tumor histology. For instance, ependymomas commonly demonstrate a well-demarcated margin between tumor and spinal cord tissues, while astrocytomas can have infiltrative borders; however, for each histological type, there is considerable variability in the presence or absence of identifiable tumor planes (Garces-Ambrossi et al. 2009). The presence of identifiable tumor planes carries positive prognostic significance regardless of tumor type, suggesting that this may offer valuable prognostic information regarding biological aggressiveness and subsequent recurrence. Low-grade spinal cord astrocytomas, in spite of their infiltrative behavior, are amenable to radical surgical resection. Gross-total resection (GTR) has been associated with improved prognosis for low-grade intramedullary tumors such as ependymoma and hemangioblastoma (McCormick et al. 1990, Hanbali et al. 2002, Stephen et al. 2012, Karikari et al. 2015).

Gross tumor resection can significantly affect tumor control and survival for most types of spinal cord tumors, and should be attempted when deemed safe (Garces-Ambrossi et al. 2009). Typically, gross-total and near-total resection is reported in 6–46% of cases with a trend toward increased radical resection in more recent times (Reimer and Onofrio 1985, Allen et al. 1998, Garces-Ambrossi et al. 2009). Subtotal resection (STR) can be achieved in up to 50% of cases (Kutluk et al. 2015). Surgical complication rates are low in the hands of skilled neurosurgeons; however, preoperative functional status is a predictor of good postoperative function (Jenkinson et al. 2006). It has also been shown that significant intraoperative changes of somatosensory evoked potentials can predict postoperative deficit.

Modern surgical techniques with microscopy, intraoperative ultrasonography, and electrophysiological monitoring (sensory and/or motor evoked potentials) can greatly improve the probability to identify tumor margin and achieve total resection with less functional damage (Zentner 1991, Constantini et al. 1996, 2000, Hoshimaru et al. 1999, Houten and Weiner 2000). Intraoperative ultrasound can be used as a tool to demarcate tumor for resection. The use of electrophysiological monitoring has become common practice and can provide the surgeon with continuous intraoperative information about the integrity of the spinal tracts in order to facilitate an aggressive resection with minimal morbidity and to predict postoperative function. Somatosensory evoked potentials (SSEPs) monitor the function of the posterior columns, and its intraoperative monitoring can affect postoperative outcome (Kearse et al. 1993). Motor evoked potentials (MEPs) are a more recently developed technique using scalp and epidural electrodes to provide “real time” information about the integrity of the motor tracts.

18.7.2 Role of Chemotherapy

Experience using chemotherapy is limited. The rationale for using it is mainly based on extrapolation from similar tumors in the brain.

The standard treatment of spinal cord astrocytomas is surgery, followed by radiotherapy for incompletely resected or high-grade tumors. Owing to the major consequences of radiotherapy on the spine in childhood, alternative therapies have been

explored. The potential role of chemotherapy in the management of spinal cord astrocytoma remains to be defined. A small case series demonstrated benefit in both low- and high-grade tumors (Lowis et al. 1998). The Children's Cancer Group (CCG) 945 High-Grade Astrocytoma Committee devised a pilot study to collect natural history information and explore the benefit of an experimental multimodality treatment in children with newly diagnosed high-grade astrocytomas arising within the spinal cord (Allen et al. 1998). Patients were assigned in a nonrandom fashion to the experimental regimen of an 8-drugs-in-1 regimen consisting of vincristine 1.5 mg/m^2, lomustine 100 mg/m^2, procarbazine 75 mg/m^2, hydroxyurea 3000 mg/m^2, cisplatin 90 mg/m^2, mannitol 12 g/m^2, cytarabine 300 mg/m^2, dacarbazine 150 mg/m^2, and methylprednisolone 300 mg/m^2 for three doses (Allen et al. 1998). A centralized neuropathology review was used to confirm the diagnosis of high-grade astrocytoma in 13 of the 18 children: anaplastic astrocytoma (eight patients), glioblastoma multiforme (four patients), and mixed malignant glioma (one patient). Diagnoses were discordant in five patients. There were eight boys and five girls in the group with confirmed diagnoses, with a median age of 7 years (range 1–15 years). The extent of resection was confirmed by computerized tomography or magnetic resonance (MR) evaluation in five of 13 patients. There were six gross-total or near-total resections (>90%), four partial or subtotal resections (10–90%), and three biopsies. Six patients showed evidence of leptomeningeal metastases at diagnosis based on staging MR examinations. Eight of the 13 patients completed at least eight of the prescribed 10 cycles of chemotherapy; five received craniospinal radiotherapy and five had spinal radiotherapy. The 5-year progression-free and overall survival rates for the 13 children were 46 ± 14% and 54 ± 14%, respectively.

Eight children with unresectable or recurrent intramedullary glioma were treated on a French Society of Paediatric Oncology (BB SFOP) protocol of a 16-month chemotherapy regimen with carboplatin, procarbazine, vincristine, cyclophosphamide, etoposide, and cisplatin. Six children had progressive disease following incomplete surgery and two had a postoperative relapse. Three patients had leptomeningeal dissemination at the outset of chemotherapy. Seven of the eight children responded clinically and radiologically while one remained stable. At the end of the BB SFOP protocol, four children were in radiological complete remission. After a median follow-up of 3 years from the beginning of chemotherapy, all children but one (who died from another cause) are alive. Five patients remain progression-free, without radiotherapy, 59, 55, 40, 35, and 16 months after the beginning of chemotherapy. The efficacy of this chemotherapy in patients with intramedullary glial tumors calls for further trials in this setting, especially in young children and patients with metastases. While chemotherapy may delay the need to radiotherapy administration in low-grade glial tumors, most of the patients would need radiotherapy to achieve tumor control (Gajjar et al. 1995, Doireau et al. 1999, Merchant et al. 2000, Bian et al. 2013, Schniederjan et al. 2013). The role of chemotherapy in ependymoma, studied exclusively for intracranial tumors, has proven controversial due to mixed results (Evans et al. 1996, Timmermann et al. 2000, Garvin et al. 2012, Venkatramani et al. 2013, Strother et al. 2014); however, there is renewed interest in investigating its role for WHO grade II and III tumors.

18.7.3 Role of Radiation Therapy

The use of postoperative irradiation for spinal cord tumors has been controversial, and largely inconsistent. There may be an increased trend toward using upfront chemotherapy for low-grade spinal astrocytomas. Radiotherapy is commonly used for progression or recurrence. In some series, radiotherapy was shown to improved progression-free survival while others report no advantage (Bouffet et al. 1998, Ahmed et al. 2014).

For low-grade tumors, surgery and irradiation after incompletely resected spinal astrocytomas can result in survival rates of 50–60% at 5 years (Houten and Weiner 2000, Jenkinson et al. 2006, Ahmed et al. 2014). Although lacking conclusive data, a rational approach includes maximal surgical resection. For incompletely resected tumors, one can support observation for low-grade gliomas (pilocytic histology), especially in prepubertal children where the risk-to-benefit ratio may favor delaying radiation intervention. If one elects to observe a child with suspected or definite residual disease, it is important to commit to a later second surgery when feasible, as well as irradiation, unless the second surgery results in imaging-confirmed total resection, at the time of disease progression.

For spinal cord ependymomas, there is evidence supporting surgery alone for intramedullary tumors and for initial management of cauda equina tumors (McCormick et al. 1990). The indolent nature of myxopapillary tumors may argue for favoring observation after good resection in a young child; however, there is evidence that children with myxopapillary ependymoma experience a shorter time to recurrence and higher rates of dissemination with surgery alone (Bagley et al. 2009, Feldman et al. 2013, Bandopadhayay et al. 2016). Adjuvant radiotherapy can significantly improve local control and progression-free survival and should be considered strongly, especially after STR (Schild et al. 1998, Akyurek et al. 2006, Agbahiwe et al. 2013). Although the impact of histologic grade in ependymomas is apparent in adult studies, higher grade ependymomas of the spinal cord are uncommon in children. Extrapolation from the adult data suggests a role for postoperative irradiation for such lesions. It is evident that patients with grade II ependymoma, especially after subtotal resection, may benefit from postoperative radiotherapy (Lin et al. 2014).

Glial and ependymal tumor presenting with neuraxis dissemination at diagnosis may also benefit from radiotherapy. There is evidence to support that these patients can potentially achieve long-term progression-free survival with craniospinal irradiation (Gajjar et al. 1995, Merchant et al. 2000).

18.8 Target Delineation

18.8.1 Radiotherapy Volume

Radiation therapy target volume definitions have evolved significantly in the last two decades based on improved imaging technology. Full neuraxis imaging is

warranted, and MRI gives the best anatomical delineation of tumor extent. Tumor extent in the craniocaudal direction can be delineated based on MRI images; image registration should be employed when available to allow accurate delineation of target volumes. Localized intramedullary astrocytomas are generally treated with focal fields targeting the gross tumor and/or tumor bed, based on preoperative and postoperative MRI. Local fields are also indicated for spinal ependymomas (Akyurek et al. 2006, Agbahiwe et al. 2013). Recent studies suggest regional irradiation with a slightly more generous margin and including entire distal thecal sac. In the postoperative setting, target volume definition should start with an analysis of preoperative image sets to appreciate the full extent of disease in the craniocaudal direction; additionally, postsurgical changes should be incorporated in clinical target volume since they may extend beyond original tumor levels and commonly reflect an actual tumor plane. The additional margin for covering microscopic disease extent is created (clinical target volume or CTV); in the longitudinal direction, it is typically 2–3 cm and radially typically includes the entire spinal canal to the body edges of the vertebral body. For astrocytomas, one typically sees decompression or obliteration of the rostral and caudal cystic components after resection of the solid tumor. In such instances, it appears that radiation therapy can be limited to the solid tumor bed. Planning target volume expansion will depend on patient setup, immobilization, and onboard imaging capabilities of treating institution. Typically, the PTV ends up being 0.5–1 cm from the CTV, respecting symmetrical coverage of vertebral bodies in skeletally immature child (Fig. 18.3).

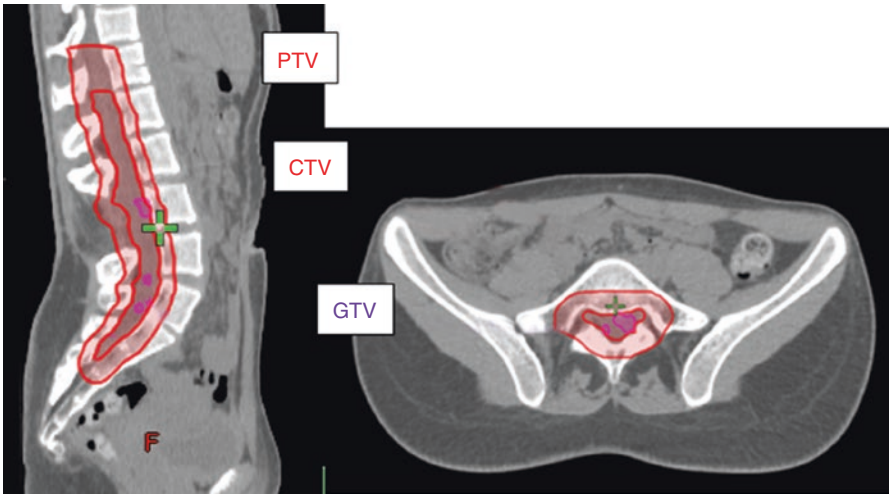

Fig. 18.3 Grade I myxopapillary ependymoma presented with tumor nodules in distal thecal sac: Gross Tumor Volume (*GTV, purple*), Clinical Target Volume (*CTV, inner red*), and Planning Target Volume (*PTV, outer red*)

Comprehensive neuraxis irradiation is given to tumors displaying dissemination (Merchant et al. 2000) and the craniospinal technique is discussed elsewhere in this book. As with brain tumors, age is a very important factor when considering full neuraxis irradiation.

18.8.2 Dose

Radiation dose typically varies from 45 to 54 Gy. These levels were based at least partially on estimated cord tolerance. Radiation dose–response has not been clearly established for spinal cord low-grade astrocytomas, although most patients are treated to a dose ranging from 45 to 50 Gy (O'Sullivan et al. 1994, Guss et al. 2013). There is evidence for better local control acheived with the dose ≥50 Gy in ependymomas (Schild et al. 2002, Pica et al. 2009). The local radiation dose for spinal cord tumors of other glial origin, including high-grade gliomas, has typically been treated to 50–54 Gy, and dose selection is mainly driven by dose constraint to the spinal cord. Daily fractions have ranged from 1.8 to 2 Gy. In cases of the disseminated disease, 36–39.6 Gy is commonly used for the initial dose targeting entire craniospinal axis, followed by focal boosts to a total primary site dose of 45–54 Gy, depending on the level of cord involvement. When prescribing a dose, special attention needs to be given to target volume dosimetry as often there is significant dose buildup from using a single posterior-anterior (PA) field.

18.8.3 Techniques

Historically, single posterior-anterior (PA), or anterior-posterior (AP) and posterior-anterior (PA) opposing fields were used for targeting spinal cord tumors. For PA fields, specific depth of dose prescription was chosen, commonly to the point of the posterior edge of the vertebral body or anterior edge of the spinal canal with the understanding that dose falloff would provide additional dose coverage to take care of setup variability. Particular attention needs to be paid to symmetrical dose coverage to the entire vertebral body in a child with growth potential. Static or dynamic wedges can be used with PA fields to compensate for an uneven body surface, commonly encountered in cervical and lumbar spine (Fig. 18.4). Lateral opposed or posterior oblique fields can be used for a tumor in cervical spine to help to reduce anterior dose exit (Fig. 18.5). Electrons have also been used in some cases; however, because of limited range and surface dose buildup, they are rarely feasible for older age patients. Current techniques have emerged based on the image-guided definition of the target volume, with 3D CRT or IMRT and VMAT approaches to achieve better dose homogeneity and limit the dose exposure to critical visceral organs in proximity to the target, like the kidneys, lung, or heart. Protons provide excellent dosimetry by sparing of tissues anterior to the spinal canal. Homogeneous irradiation of the vertebral bodies for growing children is a very important consideration for treatment planning regardless of techniques.

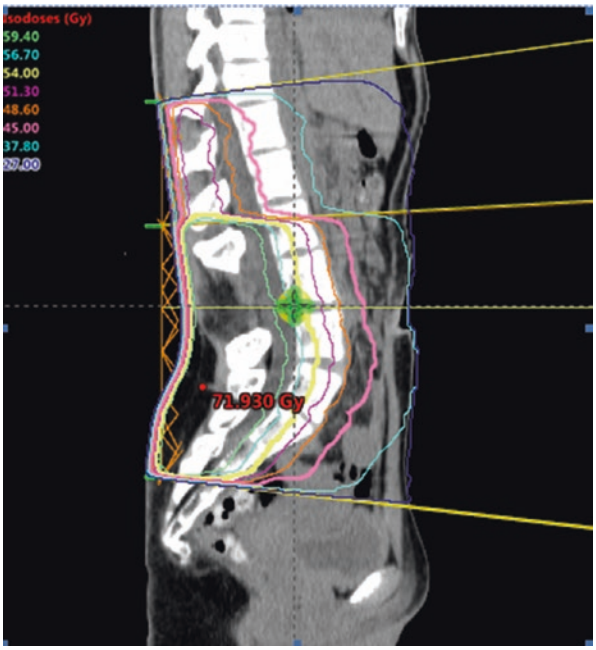

Fig. 18.4 Volumetrically modulated PA field is used to treat grade II ependymoma of a lumbar spine

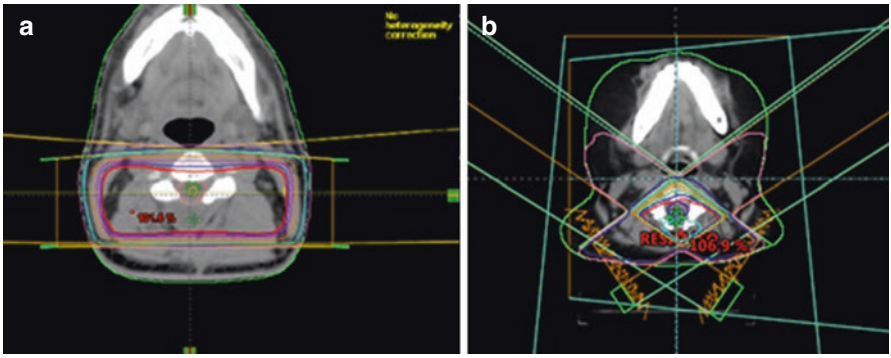

Fig. 18.5 Axial images of planning CT showing field projections and isodose lines for lateral opposed (**a**) and posterior oblique (**b**) field techniques

18.9 Outcomes

Pediatric patients have a good chance of recovery of neurological function over time (Kane, el-Mahdy et al. 1999). For all intramedullary spinal tumors, tumor histology and extent of resection have consistently been shown to be the most significant prognostic factor (DeSousa et al. 1979, Constantini et al. 2000, Houten and Weiner 2000, Ahmed et al. 2014). The histologic grade of astrocytic tumors of the spinal

cord has prognostic implications similar to those found in other central nervous system sites (Kopelson and Linggood 1982). Duration of symptoms can be an additional predictor of disease outcome (Bouffet et al. 1998), whereas the extent of resection may have a less significant effect on spinal cord low-grade astrocytoma outcome compared to ependymoma (Innocenzi et al. 1996). Postoperative radiotherapy can improve the outcome of patients with infiltrative astrocytomas, while no improvement in outcome is seen in patients with completely resected pilocytic astrocytomas (Minehan et al. 2009). Overall, the role of postoperative radiotherapy for low-grade astrocytic tumors of the spinal cord is still controversial, with a median survival time exceeding 6 years (Guidetti et al. 1981, Rossitch et al. 1990).

The prognosis of patients with spinal cord ependymoma is mainly affected by histologic grade and the extent of surgical resection. Grade I ependymoma is associated with good survival outcome; conversely, patients with grade II ependymoma have a significant risk of disease progression and death (Merchant et al. 2000). Recently published population-based study of 64 patients with grade II spinal ependymoma showed that adjuvant radiotherapy was statistically significantly more likely to be administered in cases of STR than in cases of GTR ($p < 0.001$) (Lin et al. 2014). As in other studies, resection was a strong predictor of 10-year survival (93.8% in GTR vs. 87.5% in STR). Survival estimate at 10 years for those who underwent radiation therapy was 87.4%, and for those who did not, it was 75.1%; this difference was not statistically significant. In a multivariate regression model analyzing sex, age at diagnosis, year of diagnosis, radiotherapy, and extent of resection, only female sex was found to be an independent predictor of decreased mortality (HR 0.15 [95% CI 0.02–0.94], $p = 0.04$). Myxopapillary ependymoma originating in the cauda equina has better long-term survival compared with intramedullary tumors, possibly attributable to greater resectability and potentially higher radiotherapy dose that can be applied to the level below the spinal cord.

Children with high-grade tumors of the spinal cord have a median survival time of less than 7 months (Cohen et al. 1989). The prognosis for children with primary high-grade astrocytomas of the spinal cord is dismal despite the use of trimodality therapy (Kopelson and Linggood 1982, Merchant et al. 1999). The majority of patients will either present with or develop leptomeningeal metastases, but the major treatment challenge is still local tumor control (Allen et al. 1998, Merchant et al. 1999). The effect of various clinical, radiographic, and operative factors on progression-free survival remains unknown.

While many patients with low-grade astrocytomas and ependymomas will have good survival and neurological recovery, some will suffer from permanent neurosensory deficits, such as neurogenic bladder, bowel, and scoliosis that can significantly affect quality of life (McGirt et al. 2008, Poretti et al. 2008).

18.10 Follow-up Guidelines

Posttreatment monitoring should be guided by tumor type. Low-grade ependymoma follow-up should include a clinical examination and MRI imaging every 3 months for the initial 2 years, every 6 months for an additional 3 years, annual evaluation

from 5 to 10 years after therapy, and every other year thereafter. High-grade tumors are often monitored more frequently, even though earlier detection of disease progression may not offer effective therapeutic salvage option at this time.

18.11 Future Directions

Better therapy is needed for high-grade intramedullary spinal cord tumors. Long-term damage to spinal cord function precludes significant improvement of local therapy options, such as surgery and radiotherapy. A better understanding of tumor biology may offer the most meaningful improvement in long-term outcomes via development of novel targeted and cytotoxic therapy.

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