Spinal Cord Compression Caused By Solid Malignant Tumors in Children

Çocuklarda Solid Malignan Tümörler Nedeniyle Oluşan Spinal Kord Kompresyonu

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Abstract: The medical records of 154 children with solid malignant primary tumors outside the central nervous system were retrospectively reviewed to achieve a better understanding of the incidence, presentation, outcome and treatment options for metastatic spinal cord disease. Of the 154 total, 12 children had symptomatic and 5 had asymptomatic spinal metastases (total 17 cases; 11%). In eight cases, the spinal epidural space had been invaded by the primary malignancy. Four of these eight tumors were sarcomas, and the other four were neuroblastomas. Eight of the 12 symptomatic patients underwent laminectomy, and gross total or subtotal tumor resection and/or spinal fusion. Six of the 12 individuals were alive during their last follow-up visit. The study revealed that biological behavior of malignant tumors that produce spinal cord compression in children differs from the behavior of similar tumors in adults. In the children with neuroblastoma who have reasonably good motor function, chemotherapy works rapidly and neurologic improvement can be achieved without surgery. Surgical decompression is recommended for neuroblastoma cases that show rapid neurologic deterioration or complete loss of motor function despite chemotherapy. Compared to neuroblastomas, sarcomas of soft tissue and bone, do not respond as rapidly or dramatically to chemotherapy and radiation. The neurologic outcome in sarcoma cases treated with surgical decompression was significantly better than the outcome in the group that was treated non-surgically. A combined approach with chemotherapy, radiotherapy and surgery should be the treatment of choice for both primary and metastatic spinal sarcoma.

Key words: Chemotherapy, Children, Laminectomy, Radiotherapy, Spinal metastasis.

Özet: Çocukluk çağında görülen metastatik spinal tümörlerin sıklığı, klinik seyri, tedavisi, prognozu hakkında yorum yapabilmek ve değerlendirmek için, 154 pediyatrik solid malign tümör olgusu retrospektif olarak gözden geçirildi. Toplam 17 vakada (%11) spinal metastaz teşhis edildi. Bunlardan 12 (%7.7) vakanın semptomatik 5 (%3.3) vakanın ise asemptomatik spinal metastazı vardı. Sekiz vakada primer tümör spinal epidural kanalı invaze etmişti. Bu vakaların 4'ü primer spinal kolon sarkomu, 4'ü ise neuroblastoma idi. Sekiz vakaya laminektomi, total veya subtotal tümör rezeksiyonu ve posterior veya anterior vertebral füzyon uygulandı. Son kontrollerinde altı vaka hayatta idi. Çocukluk çağında görülen malign tümörlerin biyolojik davranışlarından dolayı, çocukluk çağı spinal kord metastazları, erişkinlerde görülen spinal kord metastazlarından farklıdır. Eğer primer tümör nöroblastomsa ve hastada motor fonksiyon varsa kemoterapi ilk etapta önerilen tedavi yöntemi olup cerrahi dekompresyona gerek kalmadan nörolojik tabloda düzelme görülür. Bu tümörlerde eğer kemoterapiye rağmen ilerleyen nörolojik arazlar varsa veya hastada tam motor kayıp varsa acil cerrahi dekompresyon önerilir. Ancak kemik veya yumuşak doku sarkomları kemoterapi ve radyoterapiye dramatik olarak ve çabuk cevap vermezler. Bu nedenle sarkomlarda cerrahi dekompresyon ve tümör rezeksiyonu ile kombine olarak kemoterapi ve radyoterapi tercih edilen tedavi yöntemidir.

Anahtar kelimeler: Çocuk hasta, Kemoterapi, Laminektomi, Radyoterapi, Spinal metastaz.

INTRODUCTION

Spinal cord compression is a rare but serious complication of malignant disease in children. Acute spinal cord dysfunction in children with systemic malignancy is a neurosurgical emergency and is usually due to metastatic spinal cord compression.

Although, some series consider neuroblastoma (NB) the most common cause of metastatic spinal cord disease [6,18], of all the solid malignant tumors, that occur in children, sarcomas are the most common cause of spinal cord or nerve root compression [11,12]. Spinal cord compression due to NB may occur either as metastatic osteolytic lesion of the vertebral bodies, or by tumor growth in a dumbbell configuration that extends through the vertebral foramina(e) into the epidural space [17].

Nearly 70% of all primary spinal bone tumors in children are benign [23], and it is relatively rare to observe primary involvement of the vertebral column in cases of osteosarcoma or chondrosarcoma.

Ewing's sarcoma is the most common sarcomatous tumor, that causes metastatic spinal cord compression [11].

The aim of this study was to achieve a better understanding of the incidence, presentation, outcome and treatment options for metastatic spinal cord disease in children with solid malignant tumors. We reviewed our experience with 12 consecutive cases seen at the University of Kentucky Medical Center during the 12 year period.

PATIENTS AND METHODS

From Jan. 1982 to Jun. 1994, 242 children with solid malignant neoplasia (leukemia and lymphoma excluded), were admitted and treated at the UKMC. Of these 242 children, 88 (36.4%) had primary tumors of the central nervous system (CNS), and 154 (63.6%) had non-CNS malignancies. Of the latter 154 cases, 12 were symptomatic and 5 were asymptomatic spinal metastases (17 cases total; 11%). Twelve of these 17 cases had NB, 4 had sarcomas, and one child was diagnosed with Wilm's tumor. Eight of the 12 NB cases, had symptomatic spinal cord compression due to spinal metastasis or invasion, of the spinal canal. In the remaining four cases, spinal metastasis was asymptomatic, and was diagnosed incidentally during a radiological survey for tumor spread. Thoracic spinal column metastasis was also detected during the survey step in the patient with Wilm's tumor. All the diagnoses were established through tissue examination/bone marrow biopsy, and with radiological studies including abdominal and pelvic ultrasound, whole body bone scans, axial computed tomograpy (CT) scans and magnetic resonance imaging (MRI). Spinal column metastasis and/or invasion of the epidural space were detected on axial CT, whole body bone scan, MRI and/or myelography. We used the system described by Evans et al [5] to stage the 12 NB cases (Table 1).

Table 1: Evans Staging for Neuroblastoma

Stage I: Tumor confined to the organ or structure of origin.
Stage II: Tumor extending in continuity beyond the organ or structure of origin but not crossing the midline. Regional lymph nodes on the ipsilateral side may be involved.
Stage III: Tumor extending in continuity beyond the midline, regional lymph nodes may be involved bilaterally.
Stage IV: Remote disease involving skeleton, organs, soft tissues, or distant lymph node groups.
Stage IV-S: Otherwise classified as having stage I or II but with remote disease confined to one or more of the following sites; skin, liver, or bone marrow (without radiographic evidence of bone metastases). Most patients with this stage are under one year of age.
For tumors arising in midline structures, penetration beyond the capsule and involvement of the lymph nodes on the same side is considered stage II. Bilateral extension of any sort is considered stage III.

RESULTS

As noted above, of the 154 children with primary solid malignant tumors outside the CNS, 12 had symptomatic, and 5 had asymptomatic spinal metastasis (total 17 cases; 11%). Three of the 154 children had nerve plexus metastasis and these individuals were excluded from the study.

In all five asymptomatic cases, spinal metastases were detected during routine radiological surveys after the primary tumor was diagnosed. Four of these 5 children had NB. Metastasis to the thoracic

spine was detected on bone scans, and two of the four patients had also skull metastases. These four NB patients underwent chemotherapy, and follow-up bone scans at the completion of treatment were negative. Three of the four asymptomatic children with NB were alive and in remission at 2-40 months after the metastasis was diagnosed. The other patient died due to progression of primary disease. The fifth asymptomatic child had Wilm's tumor. This patient also had parenchymal brain metastasis and died 3 months after this was diagnosed.

Of the symptomatic children, eight had forms of NB, and the other four were diagnosed with sarcoma. The eight NB cases showed spinal metastasis or invasion of the epidural space. The histological diagnoses in these patients were NB in three cases, and ganglioneuroblastoma (GNB) in the other five individuals. Seven of the eight NB patients had dumbbell neuroblastomas (DNB), and 2 of these were congenital tumors. The clinical findings ranged from paraparesis to complete paraplegia with or without sphincter disturbances. In one of the paraplegic patients, the left lumbosacral plexus had also been invaded by the tumor. Four of the 8 patients underwent laminectomy and epidural tumor removal, with or without chemotherapy and/or radiation therapy. The other four received chemotherapy and/or radiation therapy, but did not undergo surgery.

In two of the symptomatic NB cases histopathological evaluation during the second and third operations, respectively revealed that the tumor had matured into a ganglioneuroma (GN). One of these patients had a congenital tumor in the posterior mediastinum. The mass had invaded the spinal canal at T5-6, but had not associated with any neurologic symptoms. Initially, the patient received chemotherapy only. Three years later, she developed progressive bilateral lower extremity weakness. An axial CT scan of the chest at this stage showed that the same thoracic tumor was now extending into the spinal canal. After total laminectomies at T3-T7 and complete removal of the extradural tumor, her neurologic exam returned to normal. The mass was a DNB and was histopathologically diagnosed as GN. A left-sided thoracotomy and partial tumor resection were performed 3 months after the spinal surgery. The portion of tumor was also histopathologically diagnosed as GN.

The other with congenital tumor was a stage III NB that recurred 40 months after the child had been treated with chemotherapy, and laminectomy with gross tumor removal. Twenty months after the laminectomy, she underwent two thoracotomies to debulk a mediastinal tumor. The histopathological diagnosis for this mass was GN. Forty months post-laminectomy she presented with a complaint of progressive bilateral lower extremity weakness. MRI of the thoracic spine showed a mass located in the posterior mediastinum extending into the spinal canal. After total laminectomies at T3-T10 and gross tumor removal, her neurological condition improved. This was also a DNB and the histopathological diagnosis was GN.

One of the eight children with symptomatic NB died during chemotherapy, and another died during follow-up. The causes of death were progression of primary disease and relapse, respectively. One of the eight was lost to follow-up, and the other five patients were followed for 34-96 months (mean, 53.4 months) . One patient developed the neurologic sequela of neurogenic bladder.

The other four children with symptomatic spinal cord compression all had sarcomas. One was diagnosed with mesenchymal chondrosarcoma (MCS), originating from the L1-2 pedicles, one had osteosarcoma (OS) of the C4 vertebral body, and two patients had Ewing's Sarcoma (ES) originating form L5-S1 laminae and L4-L5 pedicles, respectively. All patients presented with pain and progressive neurological deficits in the extremities. The interval between the onset of symptoms and diagnosis ranged from 1 to 5 months. All cases were treated with chemotherapy, radiotherapy and subtotal tumor resection, with a combined approach that achieved spinal canal decompression. The child with osteosarcoma of C4 body underwent spinal fusion. Two of the four sarcoma patients died during follow-up due to progression of the primary disease. In both cases, there was progressive neurological deterioration during the terminal stage of the disease.

The third patient had ES, originating from the posterior elements of L4-5 vertebrae. In this case, laminectomy and decompression of cauda equina was successful, but he returned with neck pain due to C6 vertebral body metastasis. This individual died at 8 months post-surgery due to progression of the disease.

The fourth patient first presented with neck stiffness and shoulder pain. Plain x-rays of the cervical spine showed a C4 compression fracture.

He eventually underwent C4 corpectomy, and C3-5 anterior fusion, and the pathology report revealed osteoblastoma. Four months after the first operation, he presented with right upper extremity weakness. At this stage, he underwent right hemilaminectomies at C3-5, resection of the osteoblastic lesion and posterior fusion. At this stage, the histopathologic diagnosis of the osteoblastic lesion was osteosarcoma (OS). During follow-up, extensive paraspinal growth of the tumor led to severe cervical spinal cord compression. Although he underwent chemotherapy and radiotherapy, the patient's neurologic condition deteriorated and he died at 24 months post-surgery.

As detailed above, two of the four children with sarcoma died during treatment. The patient with MCS was still alive and receiving chemotherapy 2 months after surgery. Only the child with ES of the L5 pedicle was well and neurologically intact at 98 months post-surgery.

DISCUSSION

In our study, 17 (11%) of 154 children with newly diagnosed primary malignancies external to the CNS, had spinal column metastases, but only 12 (7.8%) had symptomatic metastatic cord compression. None of the patients developed spinal cord dysfunction secondary to non-metastatic causes such as, infection, radiation-related myelopathy, spinal cord ischemia, spinal epidural-subdural hematoma or epidural abscess.

Previous studies [4,9] have reported a rate of 2.7-3% for metastatic spinal cord compression in the pediatric population. This is far below the overall 11% spinal column involvement noted in our study, and is also well below our finding of 7.7% symptomatic epidural spinal cord compression. There are reasons for the significant differences between our results and other authors' findings [4,9,11]. First, we included all symptomatic and asymptomatic cases with spinal column involvement; however, even the rate for symptomatic cases alone was markedly higher than other results in literature (7.7% vs approximately 3%, respectively). The five patients with DNB in our study group increased the rate of spinal cord metastasis considerably. The DNB is an extension of the primary tumor into the epidural space through the neural foraminae rather than an actual metastasis. Excluding these five cases, the rate of spinal epidural cord compression in our series is 4.5% (n=7 cases).

The reported incidence of DNB ranges from 6% to 25% in different series [10,14,18,19,22]. Infants and children with demonstrated paraspinal tumors, often develops asymptomatic extension of tumor into the neural canal. In approximately 40-55% of these cases, the intraspinal component may not be clinically apparent [2,13]. Therefore, any child with a paraspinal mass of unknown origin should undergo CT scan and/or MRI of the spinal canal in the involved area.

The biological behavior of solid malignant tumors in the pediatric population is totally different from the behavior of malignant tumors in adult patients. In adults, metastases to spinal region tend to invade the epidural space from vertebral sites. Contrasting this, metastatic spinal cord disease in children develops through direct spread or invasion from paraspinal sites [24]. In contrast to situation with adults, positive outcomes are relatively common with spinal metastases in children. According to Klein et al [11], 50% of the children with complete motor loss became ambulatory after surgical decompression and medical treatment. However Ch'ien et al [4] stated that, even after surgical decompression, outcome was poor in patients who were paraplegic and had complete loss of sensory function for more than 48 hours. In their study, only four of 22 such patients became ambulatory after surgical decompression [4]. The same authors reported a 2.7% incidence of metastatic epidural spinal cord compression in 3000 children with systemic cancer. They also noted that sarcomas were the tumors most frequently associated with metastatic spinal cord disease in children. In their series 10-12% of pediatric patients with sarcoma, 7% of those with NB developed metastatic spinal cord disease.

Regarding management, Bouffet et al [3] recommended against surgical decompression for metastatic spinal cord disease in children. The goals of surgery for pediatric spinal cord tumors, include histologic diagnosis, decompression of neural structures, pain relief, gross total or subtotal tumor resection and the restoration and maintenance of spinal stability. In our series, among the 154 children, four (8.5%) of the 49 sarcomas and 8 (9.5%) of 32 NB caused metastatic spinal cord compression. Although 8 of the NB caused spinal cord compression, only three of these were metastases. The other five cases were DNB that caused the spinal cord compression secondary to local tumor invasion.

Most of the previous publications on metastatic NB have been retrospective reports that have covered diverse treatment approaches for metastatic or DNB cases [2,8,10,14,15,19,22]. Review of these results, had led us to adopt a much more conservative approach to DNB. We now recommend chemotherapy as the first line of treatment for NB, even in recurrence associated with progressive neurologic impairment [21]. Hayes et al [8] has also suggested chemotherapy as an alternative to laminectomy and radiation therapy even for paraplegic patients.

When removal of a DNB is indicated, it is generally recommended that the intraspinal portion should be removed first, and that a marker (a silver clip, for example) be left at the most lateral extent of the dissection boundary. This prevents traction on the tumor tissue and neural structures which can lead to epidural bleeding, if the initial dissection is done in the paraspinal area [2]. In our study, half of the symptomatic children with DNB (n=4) underwent laminectomy and gross tumor resection even though we currently recommend chemotherapy as the first line of treatment. The reason for this is that these cases were managed based on early reports, that suggested laminectomy and gross tumor removal as the treatment of choice [2,10,14].

One of the major problems after laminectomy for DNBs and sarcoma has been spinal column deformity. This complication has been reported 56% of NB cases, who survived more than five years (60 months) post surgery [7,16]. Spinal deformity has also been reported to occur in 70-75% of children after spinal irradiation for NB, even in those who have not had spinal surgery [2]. In addition to this potential problem, it has been reported that radiation therapy may not improve the survival in localized disease [15]. According to Mayfield et al [16], the factors associated with the development of spinal column deformity in patients treated for NB include multi-level laminectomy for tumor removal and decompression, orthovoltage radiation therapy exceeding 3000 rads and asymmetrical radiation of the spine. Fortunately to date we have not observed problems with spinal deformity, in any of our patients, even though many of the children were treated with surgery and radiotherapy. However, our mean follow-up period (53.5 months) may not be long enough to have encountered this complication.

Prior to the advent of CT, early radiological diagnosis of primary spinal column sarcomas was difficult, and the treatment of these malignant tumors was mostly palliative, aimed at providing temporary relief from pain and neurological symptoms. Also, multi-drug chemotherapy regimens been developed as the primary tool for cancer treatment. Traditional therapy at that time had not yet consisted of limited tumor excision and radiotherapy Ewing's sarcoma is the second most common primary malignancy of bone in children, adolescents, and young adults. This neoplasm arises from primitive bone marrow elements. Although ES, OS, and MCS commonly metastasize to the spinal column, the primary tumor rarely involves the spine. The reported outcomes associated with combined approach have been poor. Grubb et al. [7] recommended against spinal canal decompression and/or tumor resection if the tumor was extensive and the grade was high. They suggested that surgical treatment gross resection, decompression, and/or fusion was still controversial, and noted that patients undergoing laminectomy must be followed closely for the development of progressive kyphosis.

However, other authors have advocated aggressive surgery for ES, OS, and MCS metastases, and other spinal malignancies [20,23]. Barbieri and associates [1] stated that disease-free survival was significantly related to primary tumor volume, noting 5-year disease-free survival rates of 33.2% and 57.7% for patients with bulky and non-bulky tumors, respectively. The authors speculated that surgery may have yielded better results. We preferred surgical decompression and fusion procedures, particularly for neurologically symptomatic patients, and even in cases with large high-grade tumors.

Two of our pediatric patients had primary spinal column ES. One child was off therapy and had been symptom-free for 98 months at the time of writing. This patient was treated with subtotal tumor resection, chemotherapy, and radiotherapy. Although the same treatment protocol (aggressive surgical tumor removal, chemotherapy, and radiotherapy) was used in the second case, the patient died at 8 months post-surgery with multiple metastases.

OS is the most common primary malignant bone tumor, but, as mentioned, primary spinal involvement is rare. Treatment of spinal column lesions is usually difficult, and outcome with this form of OS tumors has generally been very poor. Our one patient with primary C4 body OS died after combined treatment with surgery, chemotherapy, and radiation.

The fourth sarcoma in this study was an L1-2 MCS, and the patient was still undergoing treatment at the time of writing. The treatment protocol in this case was surgery, chemotherapy, and radiotherapy.

Based on our findings and on information in the literature, we conclude that chemotherapy alone should be used in place of radiotherapy and laminectomy in the management of pediatric DNB. This applies even for cases of recurrence with progressive neurologic impairment. Neurosurgical decompression should be reserved for patients in whom chemotherapy fails to improve neurological status, or who show rapid progressive neurological deterioration in the first 24 to 72 hours. A large proportion of our DNB patients had better prognosis and survival than and were cured with current chemotherapy regimens. This underlines the importance of minimizing the long-term effects of therapy in these children. In using stabilization procedures our intent was not to cure the disease; the aim was to achieve neurological improvement, stabilize the spine, improve quality of life, mobilize the patient early, and achieve cytoreduction through surgical tumor ablation. All of these can potentially extend the affected child's life expectancy.

For primary or metastatic spinal sarcomas, a combined approach including chemotherapy, radiotherapy, and surgery is the treatment of choice. Aggressive surgical intervention, such as total or subtotal removal of the affected vertebra(e) and spinal fusion, should be the approach taken in these cases. Preoperative chemotherapy may lead to better success with delayed surgery for local recurrence. Postoperative adjuvant chemotherapy with or without radiotherapy should be the last step in combined treatment for these neoplasms. In general, more aggressive management of these tumors may result in longer survival.

Finally, regardless of the type of mass causing spinal cord compression or the treatment protocol being used, a limited laminectomy should always be done to obtain tumor tissue for histopathologic diagnosis.

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Almost all children with intramedullary tumors are condidates for surgical treatment, unless they are already paraplegic and have a caudal tumor (below T_4). Most malignant gliomas have an atypical and relatively quick clinical course, compared with benign neoplasms.