An epidural neuroblastoma causing spinal cord compression in a 67-year-old woman

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Abstract

We report a case of disseminated neuroblastoma (NB) causing epidural spinal cord compression in a 67-year-old woman. Because NB is primarily a tumor of infancy and childhood, less is known about its clinical course and optimal treatment in adults. This patient was treated with a thoracic laminectomy and tumor resection; polychemotherapy with one cycle of vindesine, cisplatin, and etoposide; one cycle of vincristine, dacarbazine, ifosfamide, and doxorubicin; and radiotherapy to the spine. She remained able to walk but died 8.5 months later of diffuse systemic tumor progression.

Introduction

Neuroblastoma (NB) is a very rare tumor in adults: fewer than 0.5% of cases are diagnosed in persons over the age of 20 years,[1] while 34.4% of cases are diagnosed in infants and 55% in children aged 1 to 10 years.[2] Treatment algorithms have been established for children and adolescents, but optimal therapeutic strategies for the rare adult patients are not as well founded. We report on a 67-year-old woman who presented with paraparesis owing to an epidural metastasis of NB in the thoracic spine. Signs and symptoms, magnetic resonance imaging (MRI), treatment, follow-up to death, and autopsy findings are covered and discussed in view of the current literature.

Case Report

Clinical manifestations and surgical treatment

A 67-year-old woman was admitted to the hospital with acute weakness and paresthesia in both legs, and intermittent urinary retention, after having suffered thoracolumbar back pain for two months. Physical examination revealed a spastic paraparesis affecting the proximal more than the distal musculature, hyperreflexia in the lower limbs, an ataxic gait, and a T8 sensory level. The residual bladder volume after micturition was 700 mL. MRI of the spine revealed multifocal contrast-enhancing lesions in the vertebral body and prevertebral tissue of T4 and in the laminae and paravertebral soft tissues of T6, T7, and T8 (Figure 1); at T7 and T8 the spinal cord was compressed by the epidural extension of the tumor. Emergency decompressive surgery was performed; the muscle-infiltrating paravertebral component of this soft tumor was removed from T6 to T8 and the infiltrated T7 and T8 laminae were removed to expose the epidural part of the tumor, which was lifted off the dura *en bloc*. After surgery the patient's paraparesis improved substantially, and she was able to walk with a walking frame.

Pathology

Neuropathological analysis revealed a highly cellular, mitotically active mass featuring a lobular histoarchitecture (Figure 2A). Small undifferentiated round cells corresponding to neuroblasts were dominant, whereas isolated intermingled cells showed features of ganglion-cell differentiation (Figure 2B). No prominent Schwannian stroma component was identified. The tumor focally invaded adjacent skeletal muscle (Figure 2C). Most of the tumor cells were immunoreactive for synaptophysin, neuron-specific enolase, and chromogranin A, confirming neuronal histogenesis (Figure 2D and E). In addition, some cells with ganglion-cell differentiation had neurofilament immunoreactivity (Figure 2F). Based on these findings, a NB (Schwannian stroma-poor, undifferentiated subtype) was diagnosed. The *MYCN* oncogene was not amplified.

Further clinical investigations and treatment

Postoperative thoraco-abdominal computed tomography (CT) and single photon emission computed tomography (SPECT) revealed a small primary lesion in the left adrenal gland, paravertebral soft tissue metastases at T4 and T10, and multiple osseous metastases in the left proximal humerus, left femur, and pelvis.

Metaiodobenzylguanidine (^{131}I-MIBG) was not a treatment option, because scintigraphy showed no uptake. The patient therefore underwent an intensive polychemotherapy with curative intention, performed according to the protocol of the NB-2004 Study of the German Neuroblastoma Group (one cycle of vindesine, cisplatin, and etoposide and one cycle of vincristine, dacarbazine, ifosfamide, and doxorubicin). Unfortunately, the tumor progressed systemically thereafter. Palliative locoregional radiotherapy with a total of 30 Gy was directed at T2 to T11. A follow-up MRI after four months showed that the vertebral metastases had not progressed. Eight months after surgery, the patient suffered from rapidly progressive dyspnea and a chest X-ray revealed multiple pulmonary metastases. She died a few days later.

At autopsy, epidural tumor recurrence was found at T7-T8, as well as disseminated disease in both lungs, tracheal and hilar lymph nodes, liver, kidney, iliac crests, the vertebral bodies of T4, T10, and L2, and the paravertebral tissue adjacent to T10 (Figure 3).

Discussion

NB is primarily a tumor of infancy and childhood. It originates from migrating neural crest cells destined for the adrenal medulla and sympathetic nervous system. Thus, primary lesions usually develop in the adrenal glands, sympathetic paraganglia and paravertebral ganglia.[3] NB was, therefore, a highly unexpected finding in this 67-year-old woman. In fact, the incidence of NB in adults aged 30 to 39

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Key words: spine, epidural, neuroblastoma, adult, paraparesis.

Conflict of interest: the authors report no conflicts of interest.

Contributions: GJ recruited the patient, described the clinical presentation and follow-up, reviewed the literature and wrote most of the article, and coordinated the contributions of co-authors; SF contributed to the description of tumor pathology and diagnosis, and provided pictures of macro- and microscopic specimens; NF wrote and revised the text concerning neurooncology management, including considerations for the particular chemotherapy in this patient; ET revised and edited the text; LM revised the article.

Received for publication: 22 February 2010.
Revision received: 30 March 2010.
Accepted for publication: 13 April 2010.

Rare Tumors 2010; 2:e27
doi:10.4081/rt.2010.e27

years is only about 0.2 cases per million persons per year.[2] Most primary NBs arise in the adrenal glands (40%), followed by the abdomen (25%).[1] Our patient's disseminated disease probably originated in an adrenal tumor. Many older patients, however, have primary NB in extra-abdominal locations: in two single-institution series (16 patients aged 13 to 33 years and 30 patients aged 16 to 75 years), and in a literature review involving 57 patients aged 16 to 75 years, half of the primary NBs were found in extra-abdominal locations such as the thorax, pelvis, and neck.[4,5]

The best treatment of NB in adults is unknown. After surgery, our patient received two cycles of polychemotherapy according to the pediatric protocol. Because of generalized tumor progression, radiotherapy (30 Gy) was given for locoregional tumor control in the spine (resulting in stable disease for four months). In another study, 21 Gy sufficed for good local control without relapses in 10 patients who were followed up for 170+ months.[5]

Many infants and children with NB do well in the long term, but advanced age[6] and disease stage,[7] *MYCN* status (amplified versus non-amplified oncogene),[8] ploidy,[9] loss of chromosome 1p,[10] and unfavorable histopathology[11] predict a poorer outcome. One-third of all adult NB patients have metastases at the time of diagnosis (stage IV).[2] Among adult patients (aged 20 years and older) with metastases in one series, only 19.8% were alive 10 years after diagnosis.[2] In the 60-and-older age group (stages I to IV), the 10-year survival was only 29%.

MYCN amplification is found in 30-40% of children with stage IV NB[12] but is uncommon in adult patients.[4,5,13,14] In the present case, *MYCN* was not amplified. Advanced age also independently predicts a poor outcome, regardless of the *MYCN* amplification status. Although a combination of surgery, radiotherapy, and high-dose chemotherapy[5] might produce the best results, the long-term prognosis for adults with NB is still poor.

MIBG is a guanethidine derivative, structurally similar to norepinephrine, that is expressed in sympathetic nervous tissue and in tumors of neural crest origin. ^{131}I-MIBG has been used with success for radionuclide therapy of neural crest tumors since 1984. When given as part of the multimodal therapy protocol, ^{131}I-MIBG may increase the potential cure rate.[15] Some authors advise the use of *cis*-retinoic acid, although there is no strong evidence for its benefit.[16]

NB is the malignant tumor that most frequently causes spinal cord compression in children,[17] and was found in 5.2% of children with NB aged 0 to 15 years.[18] Franks *et al.*[4] reported two adult patients with primary spinal involvement and three adolescent patients

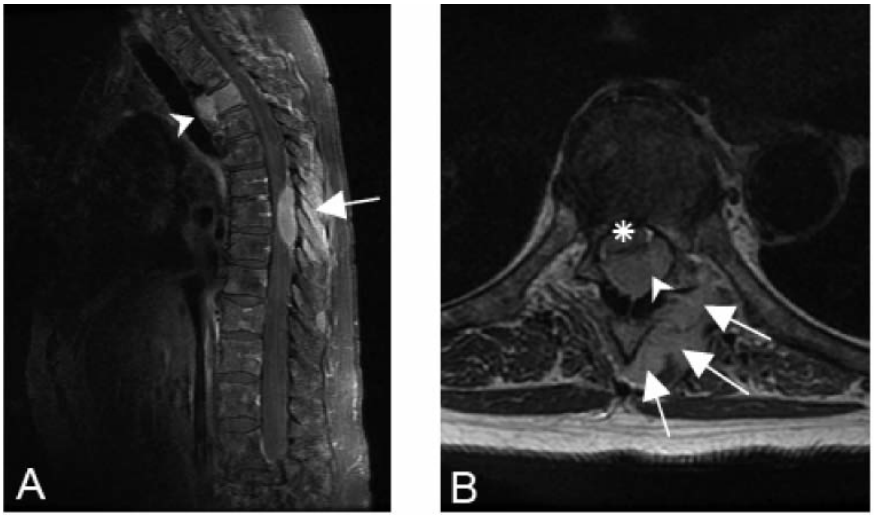

Figure 1. (A) Sagittal T1-weighted MRI with gadolinium reveals a homogeneously enhancing tumor in the posterior elements of T6 to T8 with epidural extension (arrow), and in the T4 vertebral body and prevertebral soft tissue (arrowhead). (B) Axial T1-weighted MRI with gadolinium shows severe compression of the spinal cord (asterisk) by the tumor (arrowhead) and tumor mass in the spinous process and paravertebral musculature (arrows).

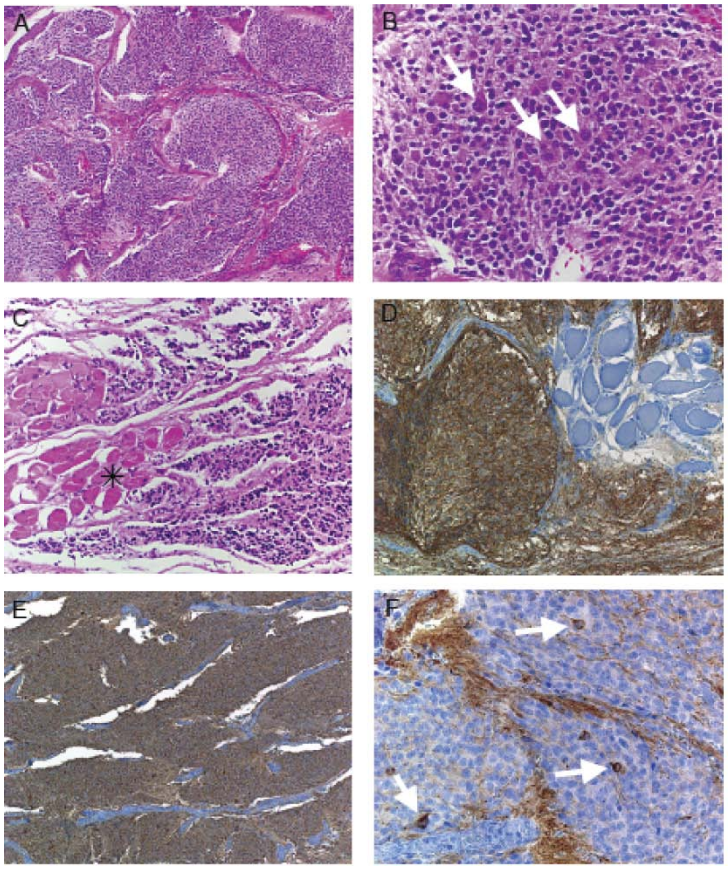

Figure 2. (A) Conventional hematoxylin-eosin staining reveals a cellular mass consisting of small, mostly undifferentiated neuroblastic cells arranged in nests separated by delicate stromal septae (100X magnification). (B) Some neuroblasts differentiating toward ganglion cells are characterized by an eccentrically located nucleus with vesicular chromatin, a single, distinct nucleolus, and an increase of cytoplasm (arrows) (400X magnification). (C) The tumor is seen invading the adjacent skeletal muscle (asterisk) (200X magnification). (D) Immunohistochemical analysis reveals widespread expression of neuronal differentiation markers such as synaptophysin (200X magnification) and (E) chromogranin A (100X magnification). (F) Individual cells with ganglion-cell differentiation express neurofilaments (arrows) (400X magnification).

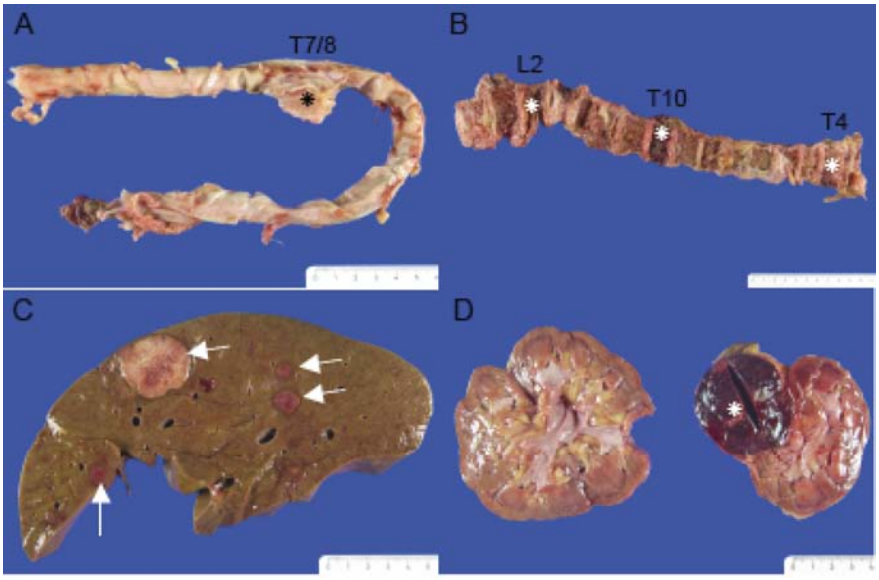

Figure 3. An autopsy revealed a recurrent metastatic epidural tumor at T7/8 (asterisk) (A); multiple spinal metastases at T4, T10, and L2 (asterisks) (B); metastatic disease in the liver (arrows) (C); and hemorrhagic metastatic disease in the left kidney (asterisk) (D). Metastases were also found in the lungs, tracheal and hilar lymph nodes, pelvis, and long bones, but are not shown here.

(aged 15, 17, and 18 years) with spinal metastases. The two patients with primary spinal involvement were diagnosed at stage 2 disease according to the International Neuroblastoma Staging System (INSS stage 2A: localized tumor with incomplete gross resection; stage 2B: localized tumor with complete or incomplete gross resection and positive ipsilateral nonadherent lymph nodes).[19] One patient, aged 20 years, had NB of the thoracic spine, which was treated with surgery, chemotherapy, and radiation. Clinical remission was maintained up to the last reported follow-up 24 months after diagnosis. The second patient, aged 33 years, was treated with surgery and radiation for an epidural NB (level not specified). Disease progressed after two years and five months, and death ensued after just over four years. In our case, acute paraparesis owing to dorsal compression of the spinal cord was treated with emergency laminectomy and tumor resection, a well-tolerated procedure in adults.[20] In children, however, spinal surgery or radiotherapy may cause late spinal deformities.[21] This may be prevented by offering pediatric patients with epidural compression chemotherapy as first-line treatment, which usually results in partial or even full recovery of neurologic deficits. Hence, the role of decompressive surgery as the first therapy step has come under debate.[22] Nevertheless, decompressive surgery can alleviate rapidly evolving paresis in children and adults or improve neurologic functioning of pediatric patients with poor recovery after chemotherapy.[22]

Conclusions

We have presented the case, management, and follow-up of an elderly patient with spinal cord compression by disseminated NB. Our multidisciplinary approach with immediate surgical decompression of the spinal cord, locoregional radiotherapy, and systemic chemotherapy controlled disease progress in the spine so that the patient was able to recover partially from paraparesis and remained able to walk. Despite combined therapy, however, NB in adults still has a poor prognosis for survival.

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