CASE REPORT

A case of early extraneural medulloblastoma metastases in a young adult

Slavomir Iliev Kondoff, Milko Dimitrov Milev, Lili Naskova Laleva, Christo Christov Tzekov, Christina Petrova Kostadinova[1], Galina Ivanova Kirova-Nedyalkova[2], Polina Danailova Dakova[3]

Departments of Neurosurgery, [1]Anaesthesiology and Intensive Care, [2]Medical Imaging and [3]Clinical Pathology, Tokuda Hospital, Sofia, Bulgaria

ABSTRACT

Extraneural metastases are a relatively rare manifestation of the primary brain tumors, and a major part of the cases has been associated with initial medulloblastoma. Herein, we present the case of a young female adult diagnosed and operated for medulloblastoma. The patient developed extraneural metastases in the first postoperative year. The condition exhibited an aggressive course of development, and the applied treatment approaches were unable to halt its progression. A short literature review identifies the predictive factors determining both prognosis and treatability of the condition; the current limitations and future perspectives of the treatment options are discussed.

Key words: Extraneural metastasis, medulloblastoma, multimodal therapy of brain tumors, prognostic factors

Introduction

Medulloblastoma is the most frequent brain tumor in children accounting for more than 15% of the pediatric cases.[1] While most of the intracranial tumors spread through either direct extension of the formation or leptomeningeal seeding, medulloblastoma is notable for its ability to give metastases outside the nervous system.

Since the first description of extraneural metastasis of medulloblastoma in 1936 by Nelson more than 100 cases have been described in the literature. Several reports indicate that primary medulloblastoma is responsible for more than half of the cases of extraneural spread of intracranial tumors.[2-5]

Although only 1–2% of the medulloblastoma patients present with extraneural metastasis at the time of initial diagnosis the cumulative incidence during follow-up reaches values of up to 5–10%. The most common sites of metastasis are bone and bone marrow, followed by lymph nodes and, to a lesser extent, liver and lung, and peritoneum.[4,6]

Despite the rarity of the condition, it could be associated with the early occurrence, rapid progression, and poor prognosis.

Access this article online	
Quick Response Code:	Website: www.asianjns.org
	DOI: 10.4103/1793-5482.162723

Address for correspondence:
Dr. Slavomir Iliev Kondoff, Department of Neurosurgery, Tokuda Hospital Sofia, Vaptsarov Boulevard 51B, Sofia 1407, Bulgaria.
E-mail: slavi.kondoff@gmail.com

Case Report

In August 2012, a previously healthy 28-year-old female patient was hospitalized with a 1-month history of progressing symptoms of raised intracranial pressure and ataxia. The symptoms have been progressing for nearly a month until unassisted walking has become impossible. Neuroradiological examinations were performed upon admission, which revealed a cerebellar tumor positioned deeply and mainly to the left, leading to obstructive hydrocephalus [Figure 1]. Following diagnosis the tumor was resected totally. Postoperative computed tomography displayed resolved obstructive hydrocephalus, which suggested against the implantation of a ventriculoperitoneal shunt. Histopathological analysis revealed the tumor to be desmoplastic medulloblastoma. The patient underwent a postoperative course of total craniospinal axis radiotherapy.

Posttreatment, the patient was in good condition, without symptoms suggestive of persisting disease or recurrence. The 4th-month follow-up magnetic resonance imaging (MRI) of the head revealed no signs of recurrence.

However, 8 months after the operation the patient began to experience low-back pains with irradiation toward the frontomedial surface of the left lower extremity. MRI of the lumbosacral region did not reveal pathological abnormalities.

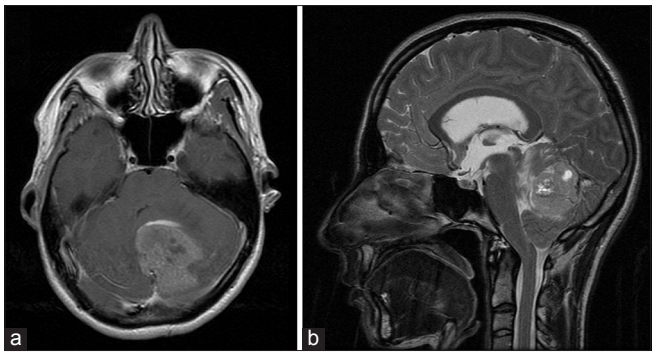

Figure 1: Initial diagnostic magnetic resonance imaging head scan of the patient with axial T1 contrast-enhanced sequence (a) and sagittal T2 sequence (b) views demonstrating a cerebellar lesion with perilesional edema and obstructive hydrocephalus

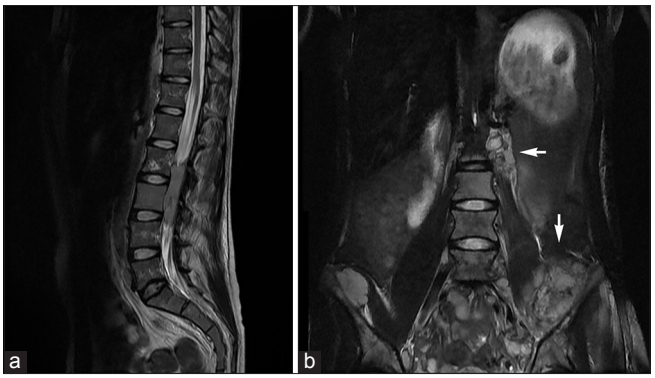

Figure 2: T2 sequence views of magnetic resonance imaging scan performed 10 months after operative treatment revealing lesions in the lumbar segment of the vertebral canal (a) and the retroperitoneal region ((b)white arrows)

The symptoms were manageable through conservative treatment and resolved completely. Yet, the stable clinical condition was only temporary and due to reemergence and progression of the symptoms the patient was rehospitalized in June 2013. Head MRI was performed that showed no signs of tumor recurrence. However, the MRI of the lumbosacral and retroperitoneal areas revealed an epidural tumor along L2 to L4 levels, protruding through the two respective left neuroforamens and sheathing the neural radices [Figure 2a]; hypo- and hyperintense lesions were found in the lumbar vertebrae, sacrum, and two iliac bones. Additional lesions were found in the region including multiple enlarged retroperitoneal and inguinal lymph nodes predominantly on the left side and nondistinct hypodense zones in the left iliac and medial gluteal muscle [Figure 2b]. The patient underwent intervention with the partial extirpation of the tumoral mass in the vertebral canal, the paravertebral, and the gluteal musculature. The histological examination of the formation revealed it as a metastasis from desmoplastic medulloblastoma. Despite certain alleviation of the pain syndrome early after the operation, the intervention was with only a temporary effect and adjuvant radiotherapy of the tumor locus was performed to achieve control of the pain. The patient developed progressive myelodysplastic syndrome, which hindered adequate chemotherapeutic treatment of the metastatic disease. The severity of the patient's condition, unfortunately, lead to fatal end on the 12th month after the initial diagnosis.

Discussion

The medulloblastoma metastases usually occur along the route of the cerebrospinal flow – ventricular system and spinal cord. The extraneural metastases of primary brain tumors are relatively rare and most frequently arise from medulloblastomas in children and, after adjustment to primary tumor incidence, adults.[7] The blood-brain barrier is generally an effective obstacle for the systemic dissemination of brain tumors but this principle is only partially true when applied to medulloblastomas.

Different mechanisms of extraneural spread of primary brain tumors and medulloblastomas in specific have been suggested through the years.[8] Pasquier *et al*. demonstrated in 1980 that 96% of the medulloblastoma patients with extraneural metastases have undergone craniotomy.[9] The surgical interventions mechanically disrupt the efficacy of the blood-brain barrier as a border against the migration of the tumor cells. Both hematogenic and lymphatic (involving cervical and retroauricular lymph nodes) pathways for the dissemination of primary brain tumors have been suggested.[10,11] However, these findings could be biased due to the generally better overall survival of patients undergoing surgical resection, which increases their overall survival and, therefore, the chances to develop metastatic disease.

Another frequently suggested mechanism for the extraneural spread of medulloblastomas is the iatrogenic dissemination with ventriculoperitoneal shunts which leads primarily to peritoneal metastases.[4] Shunt filters have been suggested as an effective measure against this complication.

Tumors such as medulloblastoma and germinoma are generally more friable and with higher adhesiveness when compared to other types of brain tumors. Overexpression of several proteins with an important role in adhesion to the extracellular matrix has been discovered in medulloblastoma cells, which could account for the propensity of this tumor to migration and invasion.[12,13] Extracranial medulloblastoma metastases show relatively higher grades of anaplasia when compared to general medulloblastoma samples; the same phenomenon has been associated with higher degree of recurrence.[14]

Mazloom *et al*. showed in a recent review that the majority of extraneural metastases from medulloblastoma occur relatively early after initial diagnosis.[6] While leptomeningeal and posterior fossa metastases are diagnosed in the first 5 years in 80–85% of the pediatric cases, nearly 80% of the extraneural metastases are discovered at an earlier period in the first 3 years after initial diagnosis. The authors found that factors

associated with worse prognosis are concurrent central nervous system involvement, pulmonal or liver metastasis, early development of the extraneural metastasis (in <18 months after initial diagnosis), and patient age of <16 years at the time of extraneural metastasis diagnosis. Although only one of the poor prognostic factors was valid for our patient, we witnessed a rapid progression of the disease leading to hematopoietic suppression and fatal outcome in only 2 months after diagnosis of extraneural spread.

In the presented case, the patient underwent postoperative craniospinal axis radiotherapy and, after diagnosis of the extraneural metastases, systemic chemotherapy was envisioned. The latter, however, was not performed due to the brisk progression of a severe myelodysplastic syndrome. In a historical perspective, the utilization of intensive postoperative craniospinal radiotherapy has led to an increase in the number of cases with extraneural spread.[15] The more recent approach of combined radiotherapy and systemic chemotherapy allows for a minimization of the incidence of extraneural metastases.[16] Recent reports have suggested that high-dose chemotherapy and autologous stem cell transplantation could be effective in cases of extraneural medulloblastoma recurrence.[17,18]

Although considered as a late development of the disease, the extraneural spread of medulloblastoma could be expected in as early as several months to a year after initial diagnosis. Furthermore, the early development of systemic metastases is correlated with a significant decrease in overall and progression-free survival. In the light of these disconcerting observations, while keeping in mind the fact that the expected lifetime incidence of medulloblastoma extraneural metastases is in the region of 5–10%, a closer and more thorough follow-up could be recommended for this group of patients. Further modifications of the current therapeutic regiments might prove to be essential for a more adequate control of this disease.

References

1. Crawford JR, MacDonald TJ, Packer RJ. Medulloblastoma in childhood: New biological advances. Lancet Neurol 2007;6:1073-85.
2. Campbell AN, Chan HS, Becker LE, Daneman A, Park TS, Hoffman HJ. Extracranial metastases in childhood primary intracranial tumors. A report of 21 cases and review of the literature. Cancer 1984;53:974-81.
3. Duffner PK, Cohen ME. Extraneural metastases in childhood brain tumors. Ann Neurol 1981;10:261-5.
4. Rickert CH. Extraneural metastases of paediatric brain tumours. Acta Neuropathol 2003;105:309-27.
5. Varan A, Sari N, Akalan N, Söylemezoglu F, Akyüz C, Kutluk T, *et al.* Extraneural metastasis in intracranial tumors in children: The experience of a single center. J Neurooncol 2006;79:187-90.
6. Mazloom A, Zangeneh AH, Paulino AC. Prognostic factors after extraneural metastasis of medulloblastoma. Int J Radiat Oncol Biol Phys 2010;78:72-8.
7. Hoffman HJ, Duffner PK. Extraneural metastases of central nervous system tumors. Cancer 1985;56:1778-82.
8. Schweitzer T, Vince GH, Herbold C, Roosen K, Tonn JC. Extraneural metastases of primary brain tumors. J Neurooncol 2001;53:107-14.
9. Pasquier B, Pasquier D, N'Golet A, Panh MH, Couderc P. Extraneural metastases of astrocytomas and glioblastomas: Clinicopathological study of two cases and review of literature. Cancer 1980;45:112-25.
10. Dolman CL. Lymph node metastasis as first manifestation of glioblastoma. Case report. J Neurosurg 1974;41:607-9.
11. Henriquez AS, Robertson DM, Marshall WJ. Primary neuroblastoma of the central nervous system with spontaneous extracranial metastases. Case report. J Neurosurg 1973;38:226-31.
12. Fiorilli P, Partridge D, Staniszewska I, Wang JY, Grabacka M, So K, *et al.* Integrins mediate adhesion of medulloblastoma cells to tenascin and activate pathways associated with survival and proliferation. Lab Invest 2008;88:1143-56.
13. Osawa H, Smith CA, Ra YS, Kongkham P, Rutka JT. The role of the membrane cytoskeleton cross-linker ezrin in medulloblastoma cells. Neuro Oncol 2009;11:381-93.
14. Eberhart CG, Cohen KJ, Tihan T, Goldthwaite PT, Burger PC. Medulloblastomas with systemic metastases: Evaluation of tumor histopathology and clinical behavior in 23 patients. J Pediatr Hematol Oncol 2003;25:198-203.
15. Tarbell NJ, Loeffler JS, Silver B, Lynch E, Lavally BL, Kupsky WJ, *et al.* The change in patterns of relapse in medulloblastoma. Cancer 1991;68:1600-4.
16. Paulino AC, Mazloom A, Teh BS, South M, Okcu MF, Su J, *et al.* Local control after craniospinal irradiation, intensity-modulated radiotherapy boost, and chemotherapy in childhood medulloblastoma. Cancer 2011;117:635-41.
17. Clement J, Varlotto J, Rybka W, Frauenhoffer E, Drabick JJ. Unusual case of recurrent extraneural metastatic medulloblastoma in a young adult: Durable complete remission with Ewing sarcoma chemotherapy regimen and consolidation with autologous bone marrow transplantation and local radiation. J Clin Oncol 2013;31:e316-9.
18. Foa C, Magné N, Bondiau PY, Otto J, Thyss A. High-dose chemotherapy with autologous stem cell support in an adult with bone marrow relapse of medulloblastoma. Bone Marrow Transplant 2000;26:1029.

How to cite this article: Kondoff SI, Milev MD, Laleva LN, Tzekov CC, Kostadinova CP, Kirova-Nedyalkova GI, *et al*. A case of early extraneural medulloblastoma metastases in a young adult. Asian J Neurosurg 2015;10:331-3.

Source of Support: Nil, **Conflict of Interest:** None declared.