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Case report

Metastatic medulloblastoma in a young male with abdominal, mediastinal, and bone marrow infiltration: A case report

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Medulloblastoma is much less common in adults, accounting for less than 1% of all primary CNS tumors, with an incidence peak between the ages of 30 and 40 years. The tendency to grow within the cerebellum, especially in the vermis, may explain the shortness of clinical symptoms, typically fewer than 3 months. Extraneuraxial metastases are infrequent, and the bone seems to be the preferred site because the neurosurgery allows neoplastic cells access to the vascular system, followed by peripheral spreading. The ventriculoperitoneal shunt (VPS) device, inserted to avoid increasing intracranial pressure often associated with the primary neoplasm, can be a potential path of abdominal dissemination. We present a case of metastatic medulloblastoma in a young male.

Key words: Medulloblastoma, hydrocephalus, ventriculoperitoneal shunt, metastases.

INTRODUCTION

Medulloblastoma is an infratentorial primitive neuroectodermal tumor that accounts for approximately 1.5% of all intracranial tumors. The incidence of medulloblastoma varies between 20% and 35% of pediatric intracranial tumors; however, it is rare in the adult population and the metastatic cases are very rare. Several subtypes of medulloblastoma have been recognized including: (1) desmoplastic/nodular type, (2) medulloblastoma with extensive nodularity, (3) large-cell variant and (4) anaplastic medulloblastoma. The CNS nature of this primitive neuroectodermal tumor can be confirmed by immunohistochemical studies. In the current case report, the patient developed metastases after insertion of the VP shunt, was treated with chemotherapy, and is symptom free at present with regression of the mediastinal mass.

CASE SUMMARY

A 30 year male residing in a hilly district of the state of Jammu and Kashmir (India) was admitted in Sher-i-Kashmir Institute of Medical Sciences (SKIMS) with complaints of headache, vomiting, and vertiginous sensations of 25 days duration, without any accompanying history of fever, head trauma, or drug abuse. There was no history of altered sensorium or disorientation. On examination, patient had pulse 64 beats / min and blood pressure 160/96 mm hg. Neurological examination showed positive cerebellar signs with dysdiadokinesia and impaired heel-shin test. Hemogram demonstrated anemia (Hb 9.1 g/l) and low platelet count (Plt= 95000) although cerebrospinal fluid analyses were normal.

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Contrast enhanced tomography brain scan (CECT) showed evidence of a posterior fossa space occupying lesion. The lesion measuring 4x5 cm was solid-cystic involving the right cerebral hemisphere, and associated with obstructive hydrocephalus (Figure 1).

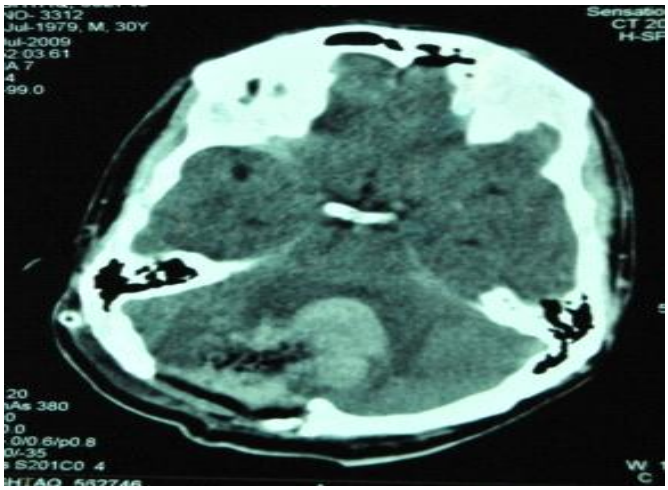

Figure 1. CECT Brain showing contrast enhancing lesion in the left cerebral hemisphere

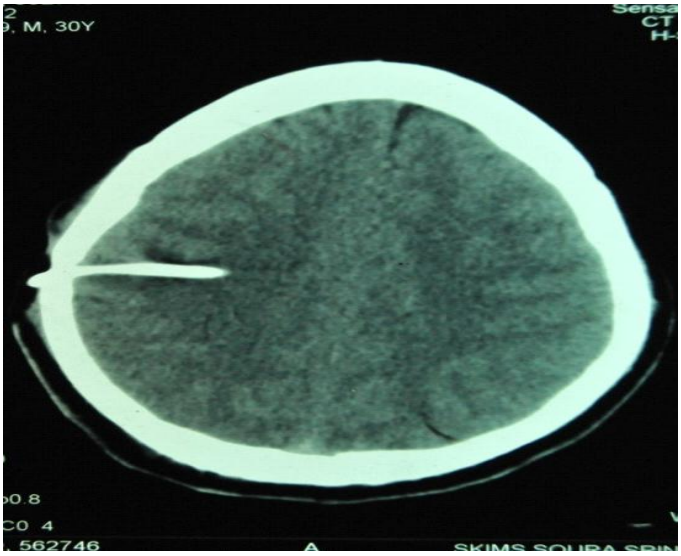

Figure 2. CECT Brain showing VPMP shunt coming out of the skull.

A right ventriculoperitoneal (VP) shunt (Figure 2) was placed. After a fortnight, he was readmitted with persistent headache. He underwent right suboccipital craniotomy with decompression of the tumour. Intraoperatively, a multilobulated, avascular, fleshy encapsulated tumour, arising from the right cerebellar hemisphere, was noted. Histopathologically, resected neoplasm was reported as a desmoblastic medulloblastoma, with immunohistochemistry (IHC) showing tumor cells expressing synaptophysin and B-catenin. The bone marrow biopsy demonstrated infiltration by medulloblastoma. He received 20 fractions of local irradiation External Beam Radiation Therapy (EBRT) but was not accompanied by any chemotherapy. Magnetic resonance imaging (MRI) brain showed no residual lesion (Figure 3). Patient was lost to follow up for about a year, although was asked to follow regularly in outpatient department.

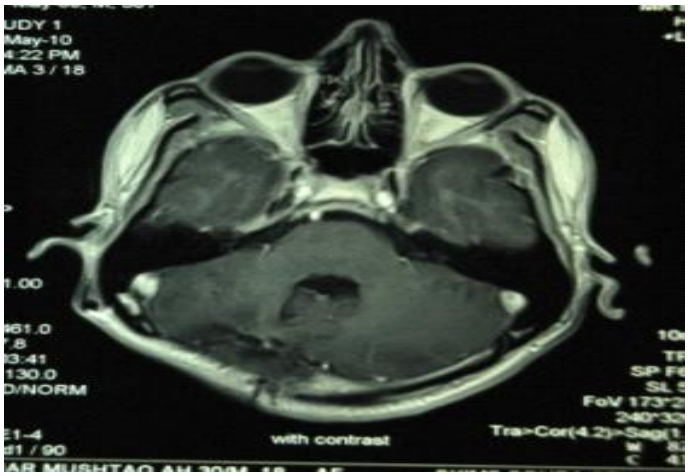

Figure 3. T1W MRI Brain of the patient after 1 year of surgery showing no evidence of disease in the left cerebral hemispheric region.

Patient was readmitted after 1 year with complaints of fever, backache and pain in extremities from last 3 months. On examination, he had pallor, spleen was palpated 3 cm below left costal margin and liver was also palpable. Complete blood count revealed bicytopenia (Hemoglobulin=8.5g/dl, Platelet=1.04 lac, Total Cell count=7550, Mean corpuscular volume 74.3, Mean corpuscular hematocrit (mch) 24.6, Mch concentration 28.7). Biochemistry panel showed Alkaline Phosphatase=938 u/l, Albumin 2.7g/dl, and the remaining variables were normal. Blood cultures were repeatedly sterile, widal was negative, and hepatitis and Human Immunodeficiency Virus serologies were negative. The bone marrow biopsy showed evidence of infiltration by small round cells with IHC displaying same immunostaing pattern as that of the original medulloblastoma (synaptophysin and B-catenin). Repeated CECT of the brain showed hyper intense lesion in the right cerebellar area, possibly gliosis. Ultrasonography abdomen showed hepatoslenomegaly with retroperitoneal lymphadenopathy. CECT chest showed anterior mediastinal mass, hepatospelenomagly and retroperitoneal lymphadenopathy. Bone scan showed increased focal uptake in long bones. Patient was treated with six cycles of Cisplatin, Vincristin, cyclophosphamide and prednisolone based chemotherapy. Now after receiving the systemic chemotherapy there is no clinical evidence of the disease. CT scan showed regression of mediastinal mass. Patient is following our department with no clinical deterioration and his performance is also satisfactory.

DISCUSSION

Medulloblastoma is an infratentorial primitive neuroectodermal tumor that accounts for approximately 1.5% of all intracranial tumors. The incidence of medulloblastoma varies between 20% and 35% of pediatric intracranial tumors, but it is rare in the adult population (Zhang zhou 1999). Kadin and Rubenstein suggested that medulloblastomas arise from germinal cells (or their remnants) anywhere along their migratory path. The primary symptoms are headache, vomiting, and an unsteady gait (Zhang zhou, 1999). Bilateral papilledema and signs of cerebellar vermis dysfunction are revealed at neurologic examination. The clinical use of contrast-enhanced CT and MRI for evaluation of medulloblastoma is common.

CNS malignancies were once believed to not metastasize extracranially. In Bailey (1930) demonstrated that medulloblastoma tends to seed along the cerebrospinal fluid pathway. In Nelson (1936) reported the first well-documented case of metastasis outside the central nervous system in a patient with cerebellar medulloblastoma (nelson 1936). In Weiss (1955) proposed rigid criteria for the diagnosis of extracranial metastasis from primary CNS malignancies. Skeletal metastases from brain tumours are rare, but when they occur, they almost always follow surgery for the primary tumour or after various shunting procedures for symptomatic relief of raised intracranial pressure (Bellezza G 1997). Medulloblastomas are highly malignant tumours of primitive neuroectodermal (PNET) origin, representing more than 20% of all childhood brain tumours and have the highest incidence of bone marrow metastasis among central nervous system malignancies (Girolami Ude 1999).

These included a single histologically characteristic CNS tumour, a clinical history indicating a primary CNS lesion, a complete postmortem examination to exclude peripheral primaries and similar histological findings between the CNS and peripheral lesions. In our patient, all these criteria were fulfilled antemortem. Though medulloblastoma is considered to be a highly malignant tumour, metastasis from medulloblastoma outside the craniospinal axis is rare, with an overall incidence of around 7.1% (Rochkind 1991). Bone is the most frequent site for extracranial metastasis (77%), whereas liver is the most frequent (13%) abdominal viscus involved as reported by Rochkind et al. Eberhart et al (2003) reported the predominant sites of systemic metastasis without shunting to be the bones or the bone marrow (91% of the cases). Metastases to soft tissues, lymph nodes, or lungs were found in 13% of the cases.

(Weiss L, 1955) . Several subtypes of medulloblastoma have been recognized including: (Bailley,1930) desmoplastic/nodular type, (2) medulloblastoma with extensive nodularity, (3) large-cell variant, and (4) anaplastic medulloblastoma. The CNS origins of this primitive neuroectodermal tumor can be confirmed by immunohistochemical studies. Synaptophysin, neuron-specific enolase, MAP-2, and class-III beta tubulin will be at least focally immunoreactive in most medulloblastomas Reticulin-free nodules of the desmoplastic variant are typically reactive for markers of neuronal lineage. Vimentin is typically reactive although quite nonspecific. Variable expression for neurofilament proteins has been documented, and immunoreactivity is dependent on the neurofilament subtype and the antibody used.. The tumour has the potential to express neurosecretory granules and Homer-Wright rosettes, as occur in neuroblastoma (McLendon 2002) . No case of medulloblastoma has been described in literature where skeletal metastasis was documented before any kind of intervention for the primary tumour. The iatrogenic haematogenous mechanism of metastatic spread was proposed to explain the development of metastasis following surgery. However Chretien reported a case of glioblastoma multiforme where metastasis developed in the absence of craniotomy where autopsy revealed invasion of dural venous sinuses by tumour mass, which could have facilitated haematogenous metastases (Chretien F, 1995).

The primary factors responsible for the rarity of extracranial metastasis are considered to be short postoperative lifespan of these patients, which does not allow metastasis to develop or manifest; absence of lymphatics in the central nervous system; early occlusion of venous channels due to compression by the tumour; and immune response to the tumour cells. On the other hand, it has been shown experimentally that primary brain tumour cells can keep on growing outside the central nervous system (Brisson C, 2002). The presence of skeletal metastases can change the treatment modality adopted for medulloblastoma; hence it is essential that a sensitive diagnostic modality be applied for the detection of skeletal metastases and Magnetic resonance imagiing appears to be superior (Gosfield E, 1993). Valéria Marques et al presented the clinical profile of five cases of medulloblastoma with systemic spreading of tumor cells. The children had bone marrow metastasis only, while the adults had several organs compromised. Interestingly, only one out five patients did not present hydrocephalus, consequently had no demand of ventriculoperitoneal (VP) shunt, and presented the longer interval between surgery and detection of extraneural metastasis (38 months). The adult patients that have developed abdominal metastasis had previously undergone a VP shunt procedure. However, the children did not have abdominal metastasis despite the VP shunt (Valéria Marques, 2011).

CONCLUSION

As no case of medulloblastoma with skeletal metastasis

has been described in literature where any kind of intervention for the primary tumour was not done. The iatrogenic haematogenous mechanism of metastatic spread was proposed to explain the development of metastasis following surgery, so when and how to treat these patients need to be discussed and planned as per the experience and data.

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