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Case Report

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A Rare Case of Bone Marrow Infiltration of Disseminated Medulloblastoma in a Young Adult

Ruchee Khanna[1], Nithya Roopa Prem[2], Vishwapriya Mahadev Godkhindi[3], Geeta V[4]

Department of Pathology, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal, Karnataka, India

Corresponding Author: Nithya Roopa Prem, Department of Pathology, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal, Karnataka, India
E-mail: nithya.p@manipal.edu

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ABSTRACT

Medulloblastoma is the most common primary CNS malignant neoplasm in the paediatric age group, accounting for 12 to 20 % of all childhood malignancies, but medulloblastoma in an adult is rare. We report a case of a 31-year-old male who presented with an inability to walk and episodic vomiting. MRI of the brain revealed a midline lesion involving the vermis and cerebellar hemispheres. Excision and immunohistochemistry confirmed the diagnosis of medulloblastoma, desmoplastic/nodular. After 10 months, he had a recurrence of the tumour and a redo surgery was attempted, followed by 6 # cycles of chemotherapy. The patient was lost to follow-up; 3 years later, PET-CT showed multiple metastases to the lung and cervical lymph node along with bicytopenia. The bone marrow study revealed interstitial infiltration by small round blue cells. Immunohistochemistry showed these cells were positive for synaptophysin, supporting a diagnosis of medulloblastoma metastasis to the bone marrow.

Keywords: Adult medulloblastoma; Bone marrow; Metastasis

INTRODUCTION

Medulloblastoma is the most frequent central nervous system (CNS) tumour in children, potentially accounting for up to 20% of CNS tumours in the paediatric population[1,2]. However, this entity only makes up 0.4% to 1% of adult CNS neoplasms[3]. The most common organs involved for metastases includes skeleton, lymph nodes, lung and liver[4]. Bone marrow involvement is a rarity and hitherto the incidence is undefined. We report a rare case of recurrent metastatic medulloblastoma with bone marrow infiltration in a young adult and attempt a short review of literature.

Case presentation

A 31-year-old male, labourer by occupation presented to the neurology department with complaints of acute onset headache, giddiness, blurring of vision, episodic vomiting and imbalance. On examination, his vitals were stable. Glasgow Coma Scale was E4V5M6. Systemic examination was unremarkable. Routine laboratory blood evaluations including liver and renal function tests were within normal range. Serology for HIV/HBV/HCV was negative. Brain MRI showed an ill-defined T1 hypointense/ T2 hyperintense midline lobulated mass lesion measuring 3.6 x 4.6 x 3.2 cm with diffusion restriction and post-contrast enhancement involving vermis and adjacent bilateral cerebellar hemispheres (Figure 1). The image finding raised a suspicion of medulloblastoma or glioma. After that, the patient had a suboccipital craniotomy and extensive complete resection.

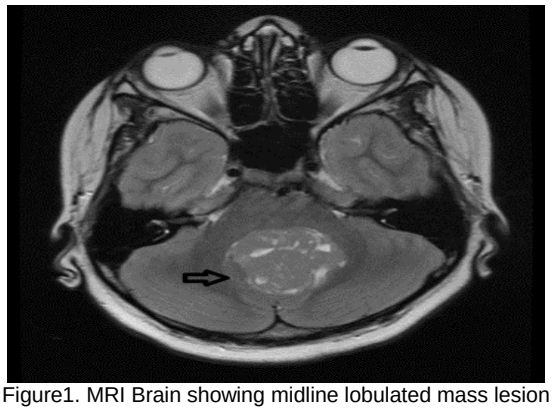

Figure1. MRI Brain showing midline lobulated mass lesion involving vermis and adjacent bilateral cerebellar hemispheres (arrow)

Intraoperative, the tumour was soft, with areas of focal haemorrhage and was easily extricated by suction. The postoperative period was uncomplicated. Histopathological examination revealed a cellular tumour consisted of small round blue cells with a high nuclear-to-cytoplasmic ratio, arranged in nodules (Figure 2). Reticulin stain highlighted the increase in intratumoral reticulin and delineated the reticulin-poor nodules. Foci of neuronal differentiation with spindling were seen. The tumour cells were immunopositive with synaptophysin and a final diagnosis of medulloblastoma, desmoplastic/nodular, CNS WHO grade 4 was rendered. CSF examination was unremarkable. Adjuvant chemotherapy (6# Cyclopospham ide+Vincristine+Cisplatin) and radiotherapy (36Gy in #20 with a local boost to the tumour bed) were administered to prevent the risk of metastasis.

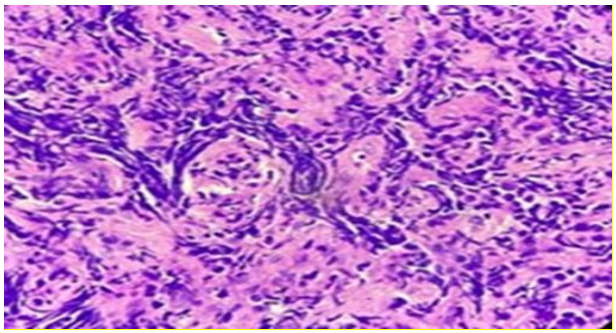

Figure 2 H & E, 400X: Section shows densely packed undifferentiated small round blue cells with streaming of tumour cells. No anaplastic or large cell morphology noted.

At 10-months post-operative period, the patient presented with recurrent cerebellar signs. MRI Brain revealed a recurrence of tumour. A redo midline posterior fossa craniotomy was attempted, and the histopathology confirmed the recurrence. The patient was lost to follow-up post-surgery.

At 36-months post-surgery, the patient presented with recurrent cerebellar signs and PET-CT discerned multiple metastasis to cervical lymph node and lungs. Excision biopsy of the cervical lymph node revealed metastatic deposits from medulloblastoma. Routine haematological investigations revealed bicytopenia (anaemia with thrombocytopenia) for which bone marrow studies were advised.

A dry tap was obtained from bone marrow aspiration and bone marrow biopsy revealed infiltration by small round blue cells which were immunopositive for synaptophysin, along with marked suppression of the haematopoietic elements (Figures 3, 4, 5).

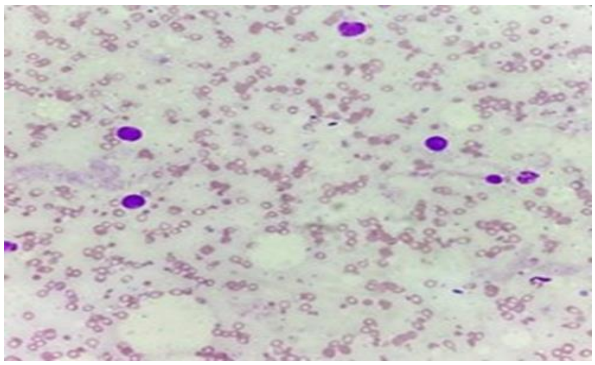

Figure 3. Wright- Giemsa, 400x: Bone marrow aspirate showing small to medium sized cells with high N:C ratio

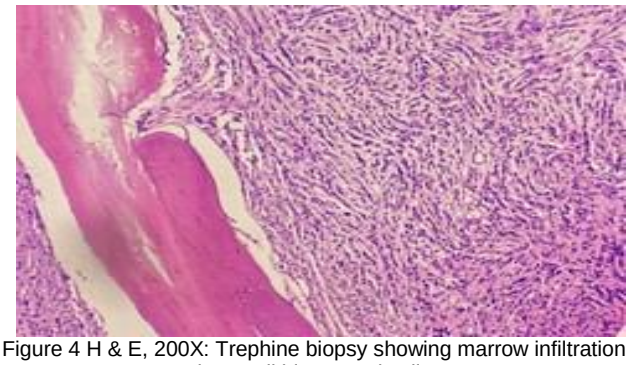

Figure 4 H & E, 200X: Trephine biopsy showing marrow infiltration by small blue round cells

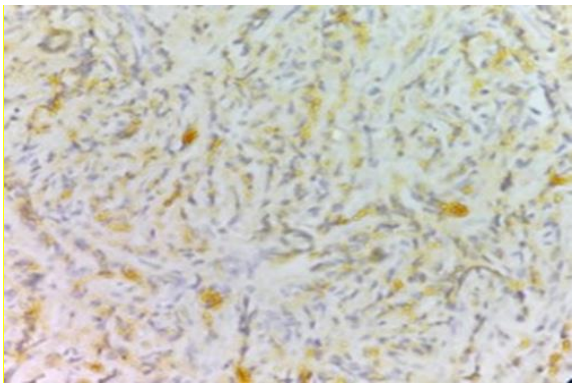

Figure 5. Synaptophysin, DAB, 400x: The tumour cells are immunopositive for synaptophysin.

The patient was recommended for palliative chemotherapy and supportive care.

DISCUSSION

Medulloblastoma is the most common tumour of the cerebellum, accounting up to 20% of all childhood brain tumours and rare in less than 1 % in adults [5, 6]. Medulloblastoma has a yearly occurrence rate of approximately 1.8 cases per 1 million people[6,7]. The median age at diagnosis of medulloblastoma is 9 years, with peak in incidence at 3 and 7 years of age[8].

Medulloblastoma commonly presents with headache (especially morning headache), lethargy, and cerebellar signs such as nausea, vomiting, and ataxia caused by increased intracranial pressure and cerebellar dysfunction[4]. The diagnosis of medulloblastoma is established on a constellation of clinical symptoms and imaging findings, such as Computed Tomography Scan and MRI scan [9].

The dissemination of medulloblastoma through the cerebrospinal fluid is well recognized[5]. In contrast, extra neural metastasis is rare – between 4.8% and 7.1% [5,10]. Nelson et al. documented the first case of extra-neuraxial spread of medulloblastoma to the skeleton [11]. On average, it takes 18 months from the initial diagnosis for medulloblastoma to metastasize extramurally. In our patient, the time interval of metastases was 3 years.

The most prevalent site for these distant metastases is the skeleton (77%), followed by lymph nodes (33%), bone marrow (20%), lung (17%) and liver (15%) [12].

Instances of isolated bone marrow infiltration and cervical lymph node metastases are rarely mentioned in the literature. Kochbati et al. and Sheikh et al reported a case of medulloblastoma that had metastasized to supraclavicular lymph node, in the absence of other foci of metastasis[12,13].

Our is an unusual case of a young adult male diagnosed with medulloblastoma desmoplastic/nodular, later presenting with local recurrence along with lymph node metastasis and marrow involvement which led to a diagnostic quagmire.

Extraneural metastases in medulloblastoma are still not well understood. Two potential pathways have been suggested by Pelissou et al., the first being haematogenous spread, where tumour cells penetrate the peritumour veins after the surgery of tumour removal, and the second is by the pathway between the lymphatic system and cerebrospinal fluid (CSF).

In our case, we assume the source of tumour metastasis to lymph node was by the latter mechanism proposed by Pelissou et al., specifically the diffusion through the pathway between lymphatics and CSF fluid[10].

Between the clinical outcomes and the histological subtypes of medulloblastoma, associations have been observed. Large cell or anaplastic type has worst prognosis and is associated with extraneural metastases[6,14]. However, our patient did not have any large or anaplastic cells on histomorphology.

Bone marrow involvement often occurs in together with skeletal metastases and peripheral blood abnormalities like anaemia and thrombocytopenia[4]. The bone marrow metastasis disrupts the normal haemopoiesis leading to myelophthisic anemia and other cytopenias[15]. Reticulin and collagen fibrosis are commonly seen along with osteosclerotic reaction and linked with skeletal involvement from medulloblastoma. All these elements contribute to making the bone marrow aspirate a dry tap as in our case[4].

Fibrosis, necrosis or osteoblastic hypertrophy along with bone infiltration by small round blue cell tumour with unknown primary in a marrow justifies a search for medulloblastoma as a possible diagnosis especially in rare instances, when this tumour presents extraneurally along with radiological investigations[16]. The other differentials to be ruled

out are Ewings sarcoma, rhabdomyosarcoma, neuroblastoma, hepatoblastoma.

Management of medulloblastoma consists of a chemotherapy regimen that includes combination of lomustine, vincristine, etoposide, cyclophosphamide and cisplatin along with craniospinal radiation therapy, which has been derived from the effectiveness in pediatric population[17]. In adults, high dosages tend to have bone marrow suppression. To prevent bone marrow toxicity, led to the use of vismodegib[18,19]. Advanced high precision photon techniques like proton beam radiation therapy can reduce the dose to organs at risk outside the target volume and improves the speed and quality of the treatment. The role of combining radio chemotherapy with immune therapy, tumour specific vaccinations, immune-checkpoint inhibitors such as peripheral death ligand (PD1/PDL1), remains to be defined in the future [17].

The prognosis for patients with extra-neuraxial metastases of medulloblastoma remains poor, with a mean survival of 6–9 months[12]. The expected lifetime incidence of medulloblastoma extraneural metastases is 5–10%. Therefore, a close monitoring and more follow-up care would be recommended for these patients[12]

CONCLUSION

We report a rare case of a 31-year-old man diagnosed metastatic medulloblastoma, desmoplastic / nodular, presenting with lymph node metastases and bone marrow infiltration. Thus, we enlighten the clinicians, radiologists and pathologists about the occurrence of this rare tumour in a young adult with its unusual presentation.

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