American Journal of Medical Case Reports, 2021, Vol. 9, No. 1, 71-74
Available online at http://pubs.sciepub.com/ajmcr/9/1/18
Published by Science and Education Publishing
DOI:10.12691/ajmcr-9-1-18

Adult Large Cell/Anaplastic Medulloblastoma with Myogenic Differentiation: Case Report with Molecular Analysis

Simin Laiq[1,*], Jaragh M[2], Ginsberg H[3], David G Munoz[2]

[1]Histopathology Department, Directorate General of Khoula Hospital, Muscat, Oman
[2]Division of Pathology, St. Michael's Hospital, Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario, Canada
[3]Division of Neurosurgery, St. Michael's Hospital, Department of Surgery, Toronto, Ontario, Canada
*Corresponding author: siminlaiq@hotmail.com

Received October 05, 2020; Revised November 06, 2020; Accepted November 12, 2020

Abstract Medulloblastoma with myogenic differentiation (MMD), previously termed medullomyoblastoma, is a distinctive subtype of medulloblastoma. It is an uncommon neoplasm in children and very rare in adults, with oldest reported case being 49-years of age. We present a case of large cell/anaplastic medulloblastoma with myogenic differentiation arising in the right cerebellar hemisphere of a 54-year-old man treated by surgical resection and radiotherapy. Despite *C-MYC* amplification in the tumor, he survived tumor-free for nearly 2 years (726 days), which greatly exceeded the expected total survival. His death was attributed to complications of treatment rather than recurrence.

Keywords: *Large cell/anaplastic medulloblastoma with myogenic differentiation, medullomyoblastoma, cerebellum, adult, C-MYC amplification*

Cite This Article: Simin Laiq, Jaragh M, Ginsberg H, and David G Munoz, "Adult Large Cell/Anaplastic Medulloblastoma with Myogenic Differentiation: Case Report with Molecular Analysis." *American Journal of Medical Case Reports*, vol. 9, no. 1 (2021): 71-74. doi: 10.12691/ajmcr-9-1-18.

1. Introduction

Medulloblastoma with myogenic differentiation (MMD), previously termed medullomyoblastoma (MMB), includes any variant of medulloblastoma with focal rhabdomyoblastic element. It was initially considered a variant of medulloblastoma in the World Health Organization's classification system until 2007, after which it was changed to a subtype on the basis that its epidemiology, biologic behavior, metastasis, recurrence patterns and genetic changes were similar to other medulloblastomas [1]. Most MMD occurs in children at a mean age of 7.4 years with a male predilection [2]. Only a few adult cases have been reported and no case above the age of 50-years has ever been reported [3]. We report a very rare case of medulloblastoma with myogenic differentiation in a 54 year-old adult patient.

2. Case Report

A 54 -year-old male with no significant past medical history, presented on March 29, 2006, with a 7-week history of posterior neck pain and occipital headache. This was associated with progressive nausea and vomiting. Later he developed unsteadiness and had falls always toward his right side. He was not on any medication at the time of presentation. He was a non-smoker, and non-alcohol abuser. Physical examination was unremarkable except for unsteadiness with ataxic gait and tendency of falling to the right. No associated nystagmus or dysmetria was noted. Magnetic resonance image (MRI) (Figure 1) showed a well circumscribed intra-axial mass within the right cerebellum. It was predominantly intermediate to low signal density on T1 (Figure 1A) and heterogeneous with small foci of low signal on FLAIR (Figure 1B) and demonstrated patchy heterogeneous enhancement on post contrast images (Figure 1C), associated with mass effect on the brain stem and the fourth ventricle with early signs of hydrocephalus. CT scan of the chest, abdomen, and pelvis did not show any other tumors. The patient underwent a posterior fossa craniotomy, which resulted in resection of more than 90% of the tumor mass. Post-operative imaging (Figure 1D), done one day after surgery showed no residual tumor. On follow-up, six weeks after the surgery, he showed significant improvement in his neurological status after having completed fifteen courses of radiation treatment consisting of 3600cGy in 20 fractions to the whole brain and spine and 1800cGy in 10 fractions to the posterior fossa. He was then regularly followed up every three months with brain MRI scans to ensure lack of tumor recurrence. Two years after his tumor

surgery, he presented acutely to the emergency department with decreased level of consciousness. The imaging studies showed no tumor recurrence but the ventricles were dilated and the diagnosis of acute hydrocephalous was entertained, but surgical intervention with insertion of external ventricular drain revealed lack of elevated ventricular pressure. A presumptive diagnosis of progressive radiation induced damage was made and the patient passed away, after extubation, on March 24, 2008, seven days after admission and 726 days after initial surgery. No autopsy was performed.

3. Histological Examination

Gross examination showed fragments of tan gray hemorrhagic soft tissue. The tissue was divided; one part was fixed in 10% neutral buffered formalin, and second part was fixed in glutaraldehyde. Paraffin sections were stained with hematoxylin and eosin (H & E), and Hematoxylin-Phloxine-Saffron (HPS) stains. The sections showed a tumor infiltrating the cerebellum with marked nuclear pleomorphism and atypia. It was composed of intermingling populations of cells. The predominant cell type was primitive non-cohesive, with pleomorphic round to oval vesicular nuclei, prominent nucleoli, and inconspicuous cytoplasm (Figure 2A, Figure 2B), from which delicate processes could be seen issuing (Figure 2B). Focal areas showed large cells, cell-cell wrapping and nuclear molding. The other cell population consisted of groups of pleomorphic cells with single or multiple nuclei arranged at the periphery of eosinophilic cytoplasm with globular or vague strap morphology, lying in a myxoid background (Figure 2B, Figure 2C). Frequent mitosis including abnormal forms, apoptotic bodies and large areas of necrosis were noted. Immunohistochemical procedures were performed using the Benchmark Immunostainer. Most of the tumor cells showed intense cytoplasmic expression of vimentin (Ventana; prediluted, clone-V9). The eosinophilic cells with globular or vague strap morphology were immunopositive for desmin (DAKO; 1:50) (Figure 2D), smooth muscle myosin (Biogenex; 1:50), and sarcomeric actin (DAKO; 1:20). Most tumor cells did not express GFAP (DAKO; 1:1000), but GFAP positive processes of reactive astrocytes were seen lying in between tumor cells. Few tumor cells express weak granular cytoplasmic GFAP. There was no expression for synaptophysin (Intermedico; 1:50), or myoglobin (DAKO; 1:1000).

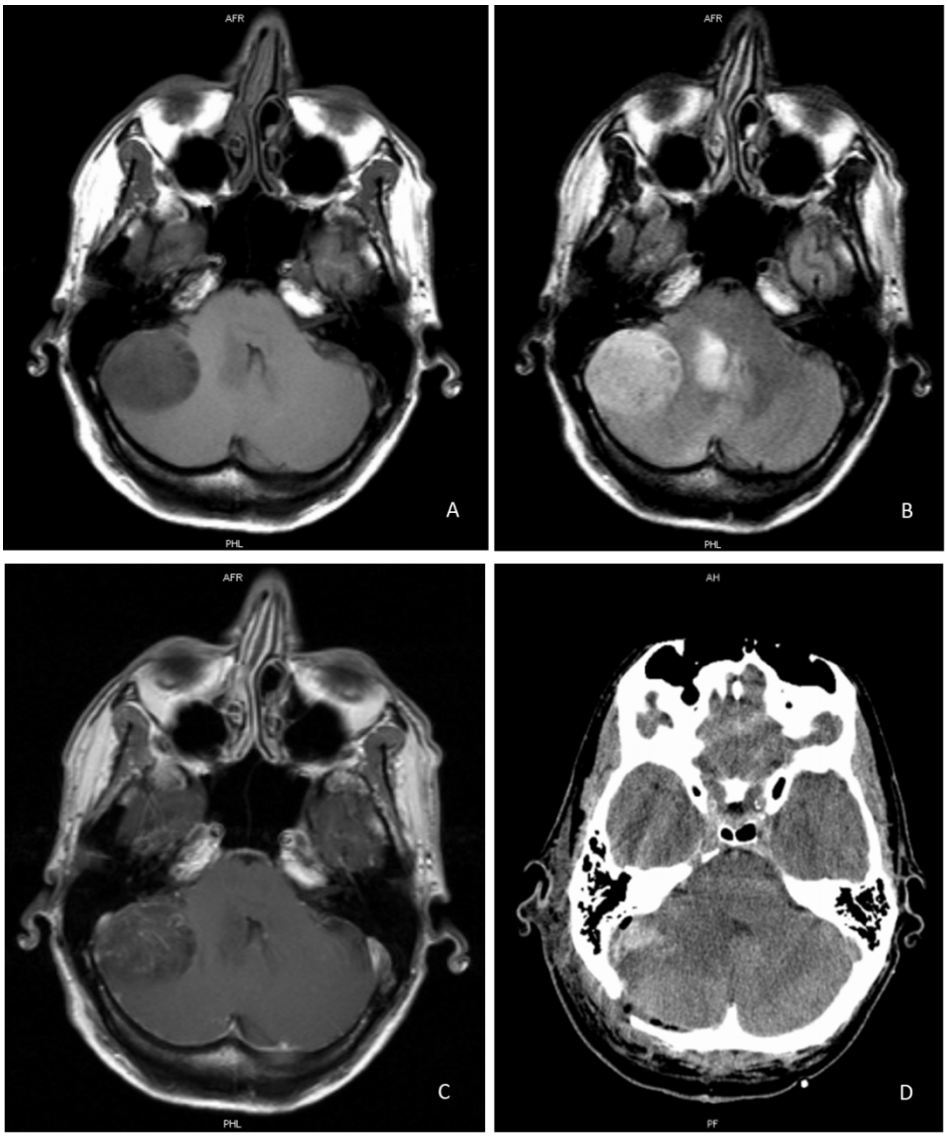

Figure 1. Imaging: **A**. Preoperative MRI T1 image. **B**. Preoperative FLAIR image. **C**. Preoperative post-contrast T1 image. **D**. Postoperative CT image

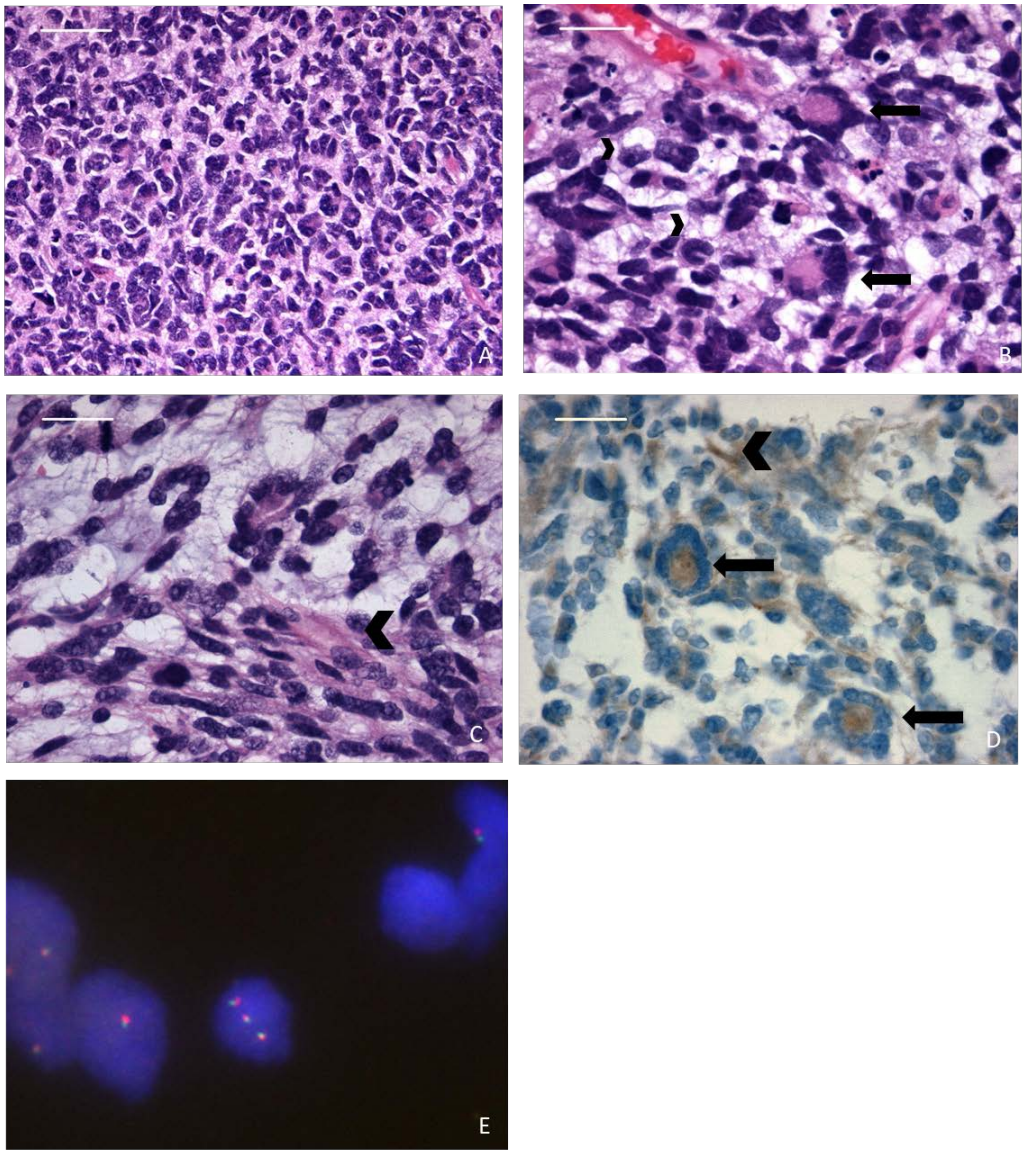

Figure 2. Histopathology: **A.** Small cells with pleomorphic nuclei, and inconspicuous cytoplasm (H & E staining, magnification 10X, bar 100um). **B**. Small processes seen arising from tumor cells (arrow-heads) and scattered eosinophilic multinucleated giant cells (black arrow) in myxoid background (H & E staining, magnification 40X, bar 25um). **C.** Cells with vague strap morphology (H & E staining, magnification 40X). **D.** Immunohistochemistry of tumor demonstrating desmin positivity in the eosinophilic multinucleated giant cells and cells with vague strap morphology (magnification 40X, bar 25um). **E**. Fluorescence in situ hybridization with Vysis *C-MYC* break-apart probe showing *C-MYC* amplification with centromere 5' *MYC* (flurophore spectrum orange) fused with telomere 3' *MYC* (flurophore spectrum green)

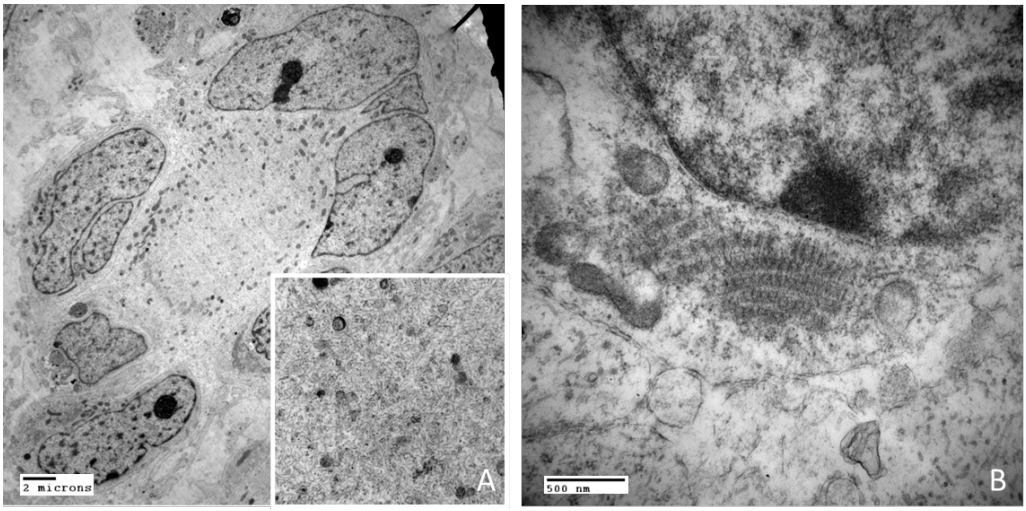

Figure 3 A. Poorly differentiated muscle cell with myofilaments in the cytoplasm. (x4000, inset x30000). **B**. Tumor cell with rhythmic arrangement of filaments in the cytoplasm, reminiscent of striated muscle morphology. (x40000)

Cytogenetic analysis of tumor with fluorescence in situ hybridization (FISH) was performed on 4 um paraffin-embedded section using Vysis *C-MYC* break-apart probe and it revealed gain in *C-MYC* in 32% of nuclei analyzed (Figure 2E), with karyotype: nuc ish (5'MYC,3'MYC)x3-4(5'MYC con 3'MYCx3-4)[64/200].

Ultra-structurally, the anaplastic medulloblastoma cell population consisted of closely packed primitive cell with large irregular nuclei containing clumped chromatin and occasional prominent nucleoli. The 'myogenic' cell population consisted of frequently seen poorly differentiated muscle cells with multiple nuclei arranged in the periphery and central collection of myofilaments in the cytoplasm (Figure 3A). These cells were similar in morphology to the cells highlighted by muscle immunostains. A single tumor cell with rhythmic arrangement of filaments in the cytoplasm, reminiscent of striated muscle morphology was also noted (Figure 3B).

4. Discussion

The term medullomyoblastoma (MMB) was first introduced by Marinesco and Goldstein in 1933 to describe a tumor consisting of medulloblastic and myogenic elements [4]. Most MMD occurs in children at a mean age of 7.4 years with a male predilection [2]. Only a few adult cases have been reported and no case above the age of 50-years has ever been reported [3]. The current case expands the age range for this tumor, as our patient was 54-years old at the time of diagnosis.

MMD are identified by their densely packed primitive neuroectodermal cells, along with tumor cells showing cross-striations, or demonstrating ultra-structural myofilaments [5]. In cases where the cross striations or the myofilaments are not evident, demonstration of smooth and striated muscle differentiation now can be achieved by immunohistochemical methods, such as Desmin, Myoglobin, and Muscle Specific Actin which allow the identification of myogenic differentiation in MMD, even when incipient [1]. Considerable variation is seen in the degree to which myoblasts or more mature myocytes are represented [6]. In our case, the myogenic differentiation is evidenced by mostly myoblast forms.

One of the most common molecular abnormalities associated with medulloblastomas, is amplification of *C-MYC* or *N-MYC [1]*. The *C-MYC* or *N-MYC* gene is amplified in less than 10% of medulloblastomas, most significantly associated with large cell/anaplastic histology [7], and the protein is overexpressed in 42% to 90% of cases. *C-MYC* amplification has been correlated with resistance to therapy [7]. Our case showed *C-MYC* amplification in keeping with the large cell/anaplastic histology of the tumor.

Clinical presentation is usually very short, approximately 12 weeks or less [8]. The recommended treatment of this tumor includes radical surgery, craniospinal irradiation and adjuvant chemotherapy [8]. The prognosis and survival rate of MMD is worse than MD, even with aggressive treatment [9]. Recently, the longest post-diagnostic survival of 11 years was reported in a 21 year old MMD patient, treated with aggressive combination therapy including gross total resection of tumor, craniospinal radiotherapy, chemotherapy and autologous stem cell transplantation [10].

Our patient survived unusually long i.e., approximately 2 year (726 days) without any radiological evidence of recurrence, following only surgical resection, radiotherapy and close follow-up, despite having large cell/anaplastic histology and *C-MYC* amplification.

5. Conclusion

We report a case of large cell/anaplastic medulloblastoma with myogenic differentiation, in an unusual age group, thereby expanding the age range of these tumors. Additionally, despite the large cell/anaplastic histology and *c-myc* mutation associated with aggressive clinical behavior and receiving only surgery and radiotherapy, and no chemotherapy, our patient had an unexpectedly long tumor-free survival.

References

[1] Louis DN et al. (2007). The 2007 WHO classification of tumours of the central nervous system. Acta Neuropathol 114(2): 97-109.

[2] Schiffer D, Giordana MT, Pezzotta S, Pezzulo T, Vigliani MC. (1992). Medullomyoblastoma: report of two cases. Child's Nerv Syst 8: 268-272.

[3] Ke, C.-S & Deng, Z.-D & Lei, T. & Zeng, L.-C & Wu, S.-M & Wan, J.. (2008). Medullomyoblastoma: Report of an adult case and review of literatures. Chinese Journal of Contemporary Neurology and Neurosurgery. 8. 567-571.

[4] Marinesco G, Goldstein M. (1933). Sur une forme anatomique, non encore decrite, de medulloblastome: Medullomyoblastome. Ann. Anat. Pathol 10: 513-525.

[5] Smith T, Davidson R. (1984). Medullomyoblastoma: A histologic, immunohistochemical, and ultrastructural study. Cancer 54: 323-332

[6] Smith TW, Davidson RI. Medullomyoblastoma. A histologic, immunohistochemical, and ultrastructural study. Cancer 1984; 54: 323-32.

[7] Helton KJ et al (2004). Medullomyoblastoma: a radiographic and clinicopathologic analysis of six cases and review of the literature. Cancer 101(6): 1445-1454.

[8] Bartlett F, Kortmanny R, Saran F. (2013) Medulloblastoma. Clinical oncology 25: 36-45.

[9] Yoshino S, Etoh Y, Konishi Y, Iwaki T, Okada H, Nishida T, Imai T, Isobe K, Itoh S, Tamiya T (2011) A case of medullomyoblastoma. Pediatrics International. 53(3): 399-402.

[10] Rattenberry W, McDonough C H, Burger P C, Cohen K J (2011) Medulloblastoma with myogenic differentiation: long-term survival in a patient treated with aggressive combination therapy and autologous stem cell transplantation. J Neurooncol 105: 659-662.