



ORIGINAL RESEARCH PAPER

Pathology

MEDULLOBLASTOMA WITH MYOGENIC DIFFERENTIATION; CASE REPORT AND REVIEW OF LITERATURE.

KEY WORDS:

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ABSTRACT	Medulloblastoma with myogenic differentiation (Medulloblastoma) its an entity first described in 1933, consisting in a medulloblastoma conformed by primitive neuroectodermal cells intermixed with cells featuring myogenic differentiation, where the two tumoral populations share the same genetic alterations and occurs almost exclusively in children. Historically, patients with medulloblastoma have been considered to have a poor prognosis. We present the case of a 3 year old patient with history of gait disturbances, emesis, headache, generalized weakness and loss of sphincter control. Cranial CT scan revealed a 5 cm. tumor located in the posterior fossa compressing the fourth ventricle with an heterogeneous appearance that enhances with contrast administration. Histological exam showed a tumor with biphasic configuration, consisting of poorly differentiated small cells with abundant mitosis and marked pleomorphism, with areas that had an evident myogenic differentiation. Immunohistochemistry revealed positivity for INI-1, desmin and synaptophysin.
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Introduction

A rare entity called Medulloblastoma with myogenic differentiation, was first described in 1933 by Marinesco and Goldstein [1], it consists in a medulloblastoma conformed by poorly differentiated small cells intermixed with cells featuring myogenic differentiation, where the two tumoral populations share the same genetic alterations and occurs almost exclusively in children [2,3]. Although, historically, patients with medulloblastoma have been considered to have a poor prognosis, survival has improved with the development of modern treatment regimens. [4].

Case Presentation

A 3 years old male patient with no prior medical history, presents with a three weeks history of frequent falls, gait disturbances, headache and emesis, that was initially treated as labyrinthitis without improvement, subsequently generalized weakness and loss of sphincter control was added. At physical and neurological examination the patient showed intracranial hypertension with a total of 10 points in modified pediatric Glasgow coma scale. Cranial CT scan revealed a tumor located in the posterior fossa with a maximum diameter of 5 cm. that compressed the fourth ventricle and had a heterogeneous appearance, with nodular areas that enhance with contrast administration, In addition necrotic areas were identified [Image 1]. Emergency ventriculostomy was performed with subsequent ventriculo-peritoneal bypass valve placement. The patient was posteriorly admitted to the surgical pediatric ward where he remained stable. Biopsy of this lesion was taken and sent to pathology.

Tissue fragments of the tumor were received, measuring approximately 7 cm. they presented a brownish-white coloration and had a friable appearance, they were processed with the habitual histological technique, and sections taken from paraffin-embedded blocks were stained with hematoxylin and eosin. The

histological image showed a lesion with a biphasic configuration that consists in hypercellular sheets and clusters of poorly differentiated small round cells with abundant mitosis and marked pleomorphism [Image 2a], these were intermingled with some other areas that had sparse large cells with abundant eosinophilic cytoplasm round nuclei and a voluminous nucleoli, characteristic of an evident myogenic differentiation [Image 2b,2c] . Immunohistochemistry was performed, synaptophysin showed positivity in the small round undifferentiated cells component, also desmin positivity was seen in the strap cells and also in few undifferentiated cells, positivity for INI-1 was observed. [Image 3a,3b]. Diagnosis of medulloblastoma was reported.

Discussion

Medulloblastoma is the most common central nervous system embryonal tumor and the most common malignant brain tumor of childhood,[5,6] it is defined by the world health organization as an embryonal neuroepithelial tumor arising in the cerebellum or dorsal brain stream, consisting of densely packed small round undifferentiated cells with mild to moderate nuclear pleomorphism and a high mitotic count. Currently the World Health Organization (WHO) recognizes four histologic variants of medulloblastoma: Classic, desmoplastic / nodular medulloblastoma, with extensive nodularity and large cell anaplastic medulloblastoma. The classic medulloblastoma subtype represents 80% of cases and the other subtypes are generally rare. [7] And four molecular subtypes: Mutant WNT, Mutant SHH, Group 3 and group 4.

There is a secondary histologic description called medulloblastoma with myogenic differentiation (medulloblastoma) this term was first used in 1933 by Marinesco and Goldstein and about 50 cases have been reported in literature since then, this entity is characterized by a variable number and distribution of spindle-shaped rhabdomyoblastic cells and large cells with abundant

eosinophilic cytoplasm. [3,8,9] Occasionally elongated straps cells, with the cross striations of skeletal muscle are evident, this can be demonstrated by electron microscopy by dark strands with parallel running myofibrils with abortive Z-lines [10] these cells are reactive to desmin, myoglobin and myosin by immunohistochemistry. [11,12]

A variety of genetic alterations have been described in medulloblastoma, with some of the most frequently encountered involving chromosome 17, including losses or deletions at 17p, either in isolation or together with a concomitant i(17q), the deletion or mutation of the INI1 gene, present in the majority of atypical teratoid/ rhabdoid tumors, has not been detected in medulloblastomas. [13,14]

Several theories have been proposed regarding the origin of the rhabdomyoblastic component in Medulloblastoma with myogenic differentiation. Ingraham and Bailey first postulated that this entity may simply be a variant of malignant teratoma or teratoid tumor [15]. Two subsequent groups proposed that the muscular component arises when multipotent endothelial or mesenchymal cells [10] near or within the tumor proper are induced to undergo rhabdomyoblastic differentiation. One final theory, which was proposed by Smith and Davidson, suggests that it is the primitive neuroectodermal tumor cells themselves that have the capability to undergo rhabdomyoblastic differentiation.

Before making the diagnosis of Medulloblastoma with myogenic differentiation is highly important to make the differential diagnosis with other tumours that originate in the posterior fossa and are histopathologically similar as other high grade gliomas, embryonal tumours and atypical teratoid/rhabdoid tumours.



Image 1.- The images show a tumor located in the posterior fossa, the tumor is heterogeneous with nodular, hemorrhagic areas which protrudes and compresses the fourth ventricle

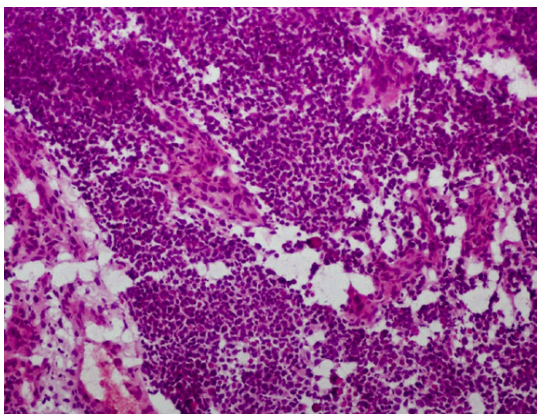


Image2a.- HE stain showing hyperchromatic undifferentiated small round cells component.

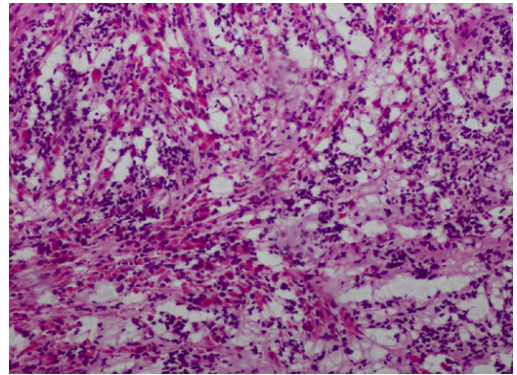


Image 2b.- areas with spindle cells with myogenic features were intermingled.

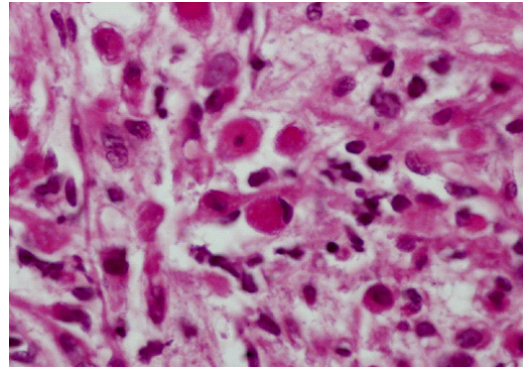


Image 2c sparse large cells with eosinophilic cytoplasm and round nuclei containing voluminous nucleoli.

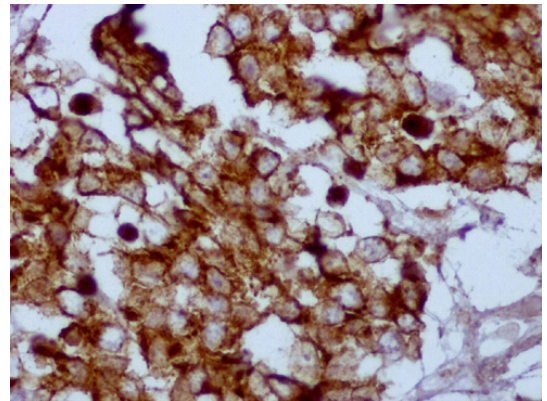


Image 3a synaptophysin positivity in the small cell component Image

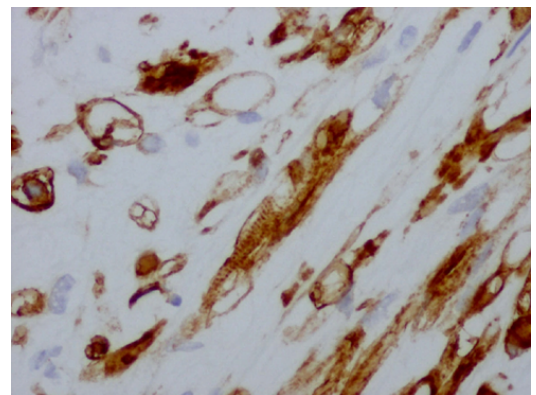


Image 3b positivity for desmin is shown, demonstrating striations.

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