Advances in Bioscience and Clinical Medicine
ISSN: 2203-1413
www.abcmed.aiac.org.au

Case Report

Multi-nodular Desmoplastic Medulloblastoma in a Child: A Rare Radiological Physiognomy

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ARTICLE INFO

Article history
Received: September 01, 2018
Accepted: December 10, 2018
Published: January 31, 2019
Volume: 7 Issue: 1

Conflicts of interest: None
Funding: None

Key words:
Multi-nodular,
Medulloblastoma,
Desmoplastic,
Hydrocephalus,
Physiognomy

ABSTRACT

Introduction: Nodular desmoplastic variant of medulloblastoma although very common, can present with very challenging radiological feature that mimics others lesions in the inferior and lower vermis in children. We present a case of rare radiological appearance of desmoplastic medullobastoma. **Case Presentation:** A one year and nine months old male presented with unstable walking and projectile vomiting of two weeks' duration. He was apparently walking well prior this illness. The vomiting was usually in the morning and associated with headaches. Radiological imaging revealed very unusual masses in the cerebellum vermin region with obvious bilateral ventricular enlargement as well as the third ventricle, indicating hydrocephalus. Surgery was successful carried out and microscopic as well as immunohistochemistry confirmed desmoplastic medullobastoma. **Conclusion:** Desmoplastic medulloblastoma although not very rare can be very problematic in terms of radiological diagnosis. We are of the option that our imaging finding will throw more light on the radiological features of this tumor.

INTRODUCTION

Medulloblastoma is a malignant tumor associated with the central nervous system. It is extremely prevalent among children. It is one of the most frequent malignant posterior fossa neoplasms (PFN) in children [1, 2]. Most cases occurs between the ages of three to seven years [1, 3]. The desmoplastic variants of the tumor constitute about 15% in children cases and as high as 50% in adult cases [2]. Most of the tumor are located at the cerebellum with their origin from the midline and predominantly in the inferior and lower vermis [1]. The most common clinical manifestations are headache, clumsiness, vomiting, general malaise as well as refusal of food due to increased intracranial pressure (ICP) [4, 5]. Spreading of the tumor into cerebrospinal fluid (CSF) as well as metastases into spinal cord and leptomeningeal at the time of presentation have been observed in about 19.4% of children [1, 6]. The distinctive imaging characteristic of the tumor relies on its consistency. The cells are often well-packed, small and round with inadequate cytoplasm as well as less fluid component [1, 7]. Usually, the treatment schemes for this tumor is in three parts; that is maximal safe resection with or without CSF diversion, neuraxis radiotherapy, and chemotherapy [4]. We present an unusual radiological finding in a child diagnosed with desmoplastic medulloblastoma and review of literature.

CASE REPORT

We present a one year and nine-month-old male child with unstable walking and projectile vomiting for two weeks. He was apparently walking well prior to the presentation above. The vomiting was usually in the morning and associated with headaches. He had no fever, cough, visual disturbance or urinary incontinence. He could feed very well. All other systems were essentially normal. His immunization was complete according to his age. His past medical history was unremarkable. His parents denied exposure to radiation or chemicals. On examination, he was conscious but very lethargic and could move his limbs freely. The head circumference was slightly above the normal range for his age. The anterior fontanelle was closed. Systemic examination did not yield any abnormalities. On neurological examination, there was no neck stiffness or photophobia. Brudzinski and Kernig signs were negative. Muscle bulk on the lower limbs was normal and power was 5/5 on both limbs with normal

Published by Australian International Academic Centre PTY.LTD.

http://dx.doi.org/10.7575/aiac.abcmed.v.7n.1p.49

reflexes. Babinski reflex revealed upwards movement of the toes. Ophthalmic examination was unremarkable. All routine laboratory investigations were normal.

CT scan done showed a hyper-density mass in the cerebellum vermin region with obvious bilateral ventricular enlargement as well as the third ventricle, indicating hydrocephalus. MRI also showed some unique images. The images were iso-dense, numerous, nodular, and separated from each other with the largest one measuring 3.5 x 2.5 x 2 cm while the smallest one measured 1.5 x 1.0 x 0.5 cm and all were uniformly enhanced. The nodules have no clear boundaries or borders and were surrounded by massive peripheral edema (Figure 1a-d). A working diagnosis of medulloblastoma was made. After taking his parents through a series of education and counselling surgery was scheduled the next day.

The patient was put into supine position. Skin marking was done followed by draping with povidone iodine. We inserted an external ventricular drain (EVD) first to decompress the posterior fossa. After inserting the EVD, the child was put on lateral prone position. We used the sub-occipital midline approach to access the tumor. After marking the skin incision, hemostasis was secured and craniotomy done with initial burr hole followed by high speed drill. The bone flat was removed and hemostasis secured. We extended the craniotomy to the foramen magnum and C1 to gain more access to all the nodules of the tumor. The EVD was opened to decompress CSF after opening the dura and the cerebellum got relaxed. We still encounter slight intracranial pressure. The lesion was seen at the cerebella vermis extending to bilateral cerebellar hemispheres and the forth ventricle. The tumor was made up of separate nodules and each nodule was hyper-vascularized with tough texture. The boarder of each nodule was difficult to judge especial those around normal brain tissues and could easily to missed. We attained total resection of the lesions (Figure 2, a&b). After securing total hemostasis, the bone flap was put back and secured with plates and screws. The subcutaneous tissues, muscles and skin were closed in layers. After the operation, he was nursed at the pediatric intensive care unit for 24 hours then transferred to the ward. The EVD was removed on post-operative day five.

Microscopic pathological examination showed small cell cancer while immunohistochemistry revealed the following tumor feature; CD56 (+), Syn (some cells +), GFAP (-), CD99 (-), LCA (-), Desmin (-), β-catenin (cytoplasm +), YAP 1 (some nuclei +), GAB-1 (-), Ki-67 (MIB-1) positive rate of about 20%. (Figure 3, a&b) The substantive diagnosis of desmoplastic medulloblastoma was made base on the above morphological characteristics. The patient recovered very fast with no complication. He was discharged home on post-operative day ten and schedule radiotherapy and chemotherapy sessions arranged. The radiation therapy and chemotherapy were given appropriately. Scheduled outpatient visits arranged every three months. A two years' follow-up is still unremarkable with no tumor recurrence.

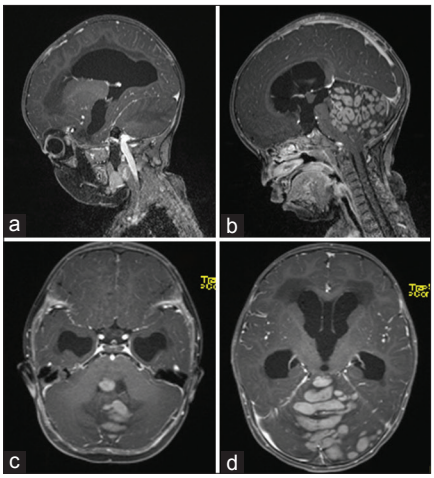

Figure 1. Is collection of MRIs of a one year and nine months old male infant with nodular desmoplastic variant of medulloblastoma. (a) and (b) are sagittal MRI. (a) Shows delated lateral ventricles while (b) Shows numerous nodules in the posterior fossa which are separated from each other. (c) and (d) are axial MRI images also showing numerous nodules in the posterior fossa which are separated from each other

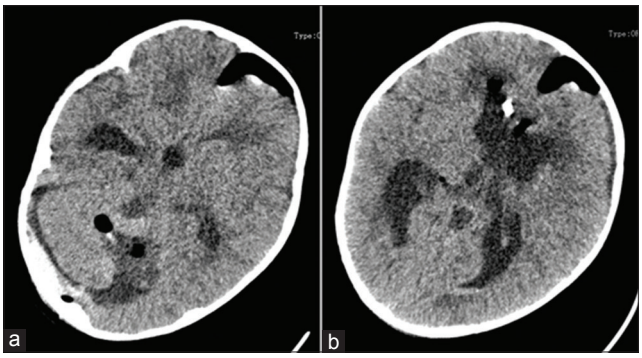

Figure 2. (a) and (b) are axial post-operative CT-scan images showing gross total resection of the tumor

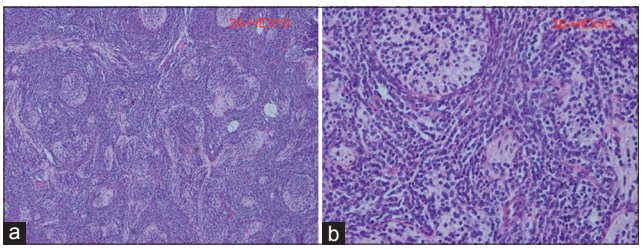

Figure 3. (a) and (b) are HEX10 and HEX40 staining of specimens after operation. This staining confirms small cell cancer

DISCUSSION

Medulloblastomas are extremely prevalent malignant brain tumor in children with an incident rate of more than 25% of all childhood intracranial neoplasms. More than one-half of these neoplasms are seen within the first 10 years of life with the highest occurrence at the ages of 3 to 7 years [1, 2]. These lesions are usually located within the posterior fossa normally around the vermis of the cerebellum [1]. These neoplasms are presumed to originate from neuroepithelial cells layers surrounding the roof of the fourth ventricle [8]. Desmoplastic variant of the neoplasms is a particular subtype that often has eccentric origin and may initiate a desmoplastic reaction within the overlying meninges [1, 9]. They

constitute about 15% of cases in children and as high as 50% cases in adult [2, 10].

This neoplasm is depicted with nodular reticulin-free islands encased in reticulin staining collagen fibers that are more peculiar in older children as well as adolescents [1, 9]. Additional well-defined characteristic features of the neoplasm in children is it's nodular and "grape-like" nature. These furthers usually make these lesions mimic dysplastic cerebellar gangliocytoma, or Lhermitte-Duclos disease, particularly on noncontrast radiological imaging [1, 11]. These unique characteristic features may envisage a histological diagnosis of the neoplasm with intense nodularity. This subtype principally occurs in children less than 3 years of age. Also this subset has a positive prognosis [1, 12]. Contrast enhancement usually distinguishes medulloblastoma from Lhermitte-Duclos disease, although the latter may occasional enhance with contrast too [1].

The most common clinical manifestation of this neoplasm is signs of ICP associated with obstructive hydrocephalus because the neoplasm outgrows and compresses the fourth ventricle [2]. Increased ICP leads to increased head circumferences in children with open anterior and posterior fontanelles. Also, increase ICP may result in early morning headache marked with vomiting, irritability, and lethargy [2]. Axial instability is one of the cardinal symptoms which always almost presents as an unsteady gait. This manifestation is as a result the neoplasm originating from the cerebellar, usually midline in children. A sizable number of children have also presented with dysequilibrium and altered eye movements when the flocculonodular lobe is involved [2]. Amusingly, there is direct opposite link between the extent of symptoms and stage of the neoplasm [2, 13].

The archetypal radiological characteristics of this neoplasm is based on its consistency. The cells are often well-packed, small and round with insufficient cytoplasm and demised fluid [1, 7]. Another characteristic feature is a hyper-attenuating midline mass close to the vermin. It often encased in vasogenic edema. The cardinal further is seen in 95% of cases on non-contrast CT [1, 14]. Although the level of hyper-attenuation is inconsistent, the mass enhances homogeneously when contrast administered [1, 15]. Furthermore, at presentation, hydrocephalus is often seen in about 95% of the cases [1].

However, on MRI the tumor is classically seen as iso- to hypo-intense in comparison with white matter on T1-weighted (T1-W) images. Moreover, the T2 signal is mutable and frequently heterogeneous, vacillating from hyper-intense to hypo-intense in comparison with grey matter [1, 15]. Also, on diffusion-weighted images (DWI), the amplified signal is linked to a reduced apparent diffusion coefficient (ADC). This is classic and may aid in distinguishing medulloblastoma from other numerous posterior fossa tumors like juvenile pilocytic astrocytoma (JPA) and ependymoma [1, 16]. Although variable in grade and magnitude, enhancement with contrast material is typically present. Moreover, MR spectroscopy characteristically reveals elevated choline and reduced N-acetyl aspartate and creatine. Taurine can also be determined with short-echo MR spectroscopy [1, 17]. Non-the less, diffusion tensor imaging (DTI) and functional MRI are very advantageous in the evaluation of corticospinal tract involvement before the commencement of treatment [1, 18].

The ultimate part of management is surgical resection of the neoplasm. A randomized control trials in children with localized lesions revealed improvement survival rate after surgery [2]. A ventricular shunt or third ventriculostomy is always almost necessary prior to resection of the neoplasm to decompress the posterior fossa due to increased ICP secondary to obstruction at the level of the foramen of Luschka, foramen of Magendie, or aqueduct of Sylvius [2]. Extension of the neoplasm into the fourth ventricle and sometimes the brainstem makes surgical resection much difficult. Also there is an increased risk of morbidity when total resection is endeavored [2]. Posterior fossa mutism syndrome is one of the most frequent neurological complications. This syndrome has been observed in about 8–38% of patients with midline cerebellar neoplasms [2, 19]. Mutism occurs around 48–72 hours after operation and can linger on for weeks to months, with related signs and symptoms like dysmetria, hypotonia, dysphagia, hemiparesis, as well as increased mood lability [2].

Radiotherapy is one of the treatment options that has proven efficient in the management of this neoplasm. In conservative radiotherapy procedures, an average-risk and high-risk groups need 36 Gy of photon radiation to the craniospinal axis, with a boost to the posterior fossa making up a total dose of 54·0–55·8 Gy [2]. The goal of irradiation of the craniospinal axis is to obliterate possible remints of the neoplasm that was not visible in the CSF or with MRI. Radiotherapy has a 5-year survival rates of about 60% [2, 20]. However, radiotherapy has detrimental adverse-effects like neurocognitive decline and endocrinopathies. These has resulted in decreasing the dose of radiation therapy in children with average-risk of the neoplasm [2, 21].

Chemotherapy is currently the standard treatment modality for children with this neoplasm. Chemotherapy has proven to be effective in all childhood risk groups and a range of these drugs have been used [2, 22]. The main aim of this treatment option is to augment, interrupt or even circumvent radiotherapy. Nevertheless, chemotherapy is much more effective in children with non-metastatic lesions. It is also adjunct in cases with gross total resection [2, 23]. The most commonly used chemotherapeutic agents are cisplatin, vincristine, lomustine, cyclophosphamide, Lomustine, as well as etoposide. They are either used alone or in combination [2]. Progressive-free survival rates of about 24- 40% have been achieved in cases with high-risk tumor who had surgery and radiotherapy [2, 24]. Progressive-free survival is now approximately 50% with the addition of chemotherapy although this is still not the best. Relapses of the neoplasm is often seen in cases treated with a combination of radiotherapy and chemotherapy. It has been observed that more than half of relapses cases have metastatic lesions [2, 25]. Approximately 75% of relapses cases are seen within 2 years [2].

On the basis of light microscopy and immunohistochemical feature, WHO has currently divided these neoplasms into subsets; which include classic medulloblastoma, the large-cell

anaplastic, desmoplastic, medullomyoblastoma, as well as melanotic variant. Conversely, for clinical and treatment purposes the lesion are usually classified into classic, desmoplastic, anaplastic or large-cell, as well as nodular variants [2]. The desmoplastic type is consist of highly proliferative, tightly packed, reticulin-rich as well as mitotically functional zones that border reticulin-free nodules [2, 26]. Nevertheless, within the nodules, there are a paucity of mitosis and cells that are immunoreactive to synaptophysin, neuron-specific enolase, as well as numerous neurofilaments [2, 27].

CONCLUSION

Desmoplastic medulloblastoma although not very rare can be very problematic in terms of radiological diagnosis. Most radiologist are not able to different this lesion from other lesions located in the posterior fossa. In most cases the substantive diagnosis of this desmoplastic variant of medulloblastoma was made during microscopy and immunohistochemical observation of specimens obtained after surgical resection. We are therefore of the option that our imaging finding will throw more light on the radiological features of this tumor variant.

Ethics Approval and Consent to Participate

The ethical committee of West China Hospital fully approved our case study. The patient and his relatives were informed about our intention to involve him in a case study and he/they agreed to partake in the study. He/they signed the consent form before the operation was carried out according to all surgical protocols and consent was also obtained for the case details and accompanying images to be published.

AUTHOR CONTRIBUTIONS

All authors contributed toward data analysis, drafting and critically revising the paper and agree to be accountable for all aspects of the work.

DISCLOSURE

The authors report no conflicts of interest in this work.

ACKNOWLEDGMENT

None

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ABBREVIATIONS

ACD = Apparent diffusion coefficent
GAB-1 = GRB2-associated-binding protein 1
CSF = Cerebrospinal fluid
DWI = Diffusion-weighted images.
DTI = Diffusion tensor imaging
EVD = External ventricular drain
GFAP = Glial fibrillary acidic protein
ICP = Increased intracranial pressure
JPA = Juvenile pilocytic astrocytoma
LCA = Leber's congenital amaurosis
YAP1 = Yes Associated Protein 1