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Rhabdoid Tumor: an Unusual Pediatric Brain Tumor

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Rhabdoid tumors of the brain are rare with an invariable dismal prognosis despite treatment. This is the case of a 3 year old boy who presented lethargy, somnolence, nausea, vomiting, and headaches one week prior to hospitalization. A posterior fossa tumor with hydrocephalus was noted on a head computed tomography (CT) scan. A ventriculoperitoneal shunt was placed with subsequent gross total tumor resection. Pathology findings were those of a rhabdoid tumor. The histopathology, immunohistochemistry and ultrastructure of this unusual pediatric cerebral neoplasia is discussed.

Key words: Atypical teratoid, Brain tumors, Rhabdoid tumor

Rhabdoid tumor is a highly aggressive malignancy clinically characterized by an early age of onset and very poor prognosis despite aggressive therapy. Mortality is associated to its highly invasive capacity and metastatic potential. The tumor was originally described in 1978 by Beckwith and Palmer (1) as a rhabdomyosarcomatoid variant of Wilm's tumor of the kidney and later in 1981, classified by Haas et al. as a separate entity because of its immunohistochemistry and ultrastructural properties (2). Since its recognition, extrarenal primaries have been identified almost in any site including the paravertebral region, chest wall, heart, liver, pelvis, uterus, vulva, prostate, skin, soft tissues, and brain (3). The main age of presentation is 2 years, with a 3:2 male preponderance. Adults have been rarely reported (4). Those described in the brain are most commonly located in the posterior fossa.

Case report

A 3 year old boy with history of febrile seizures since the age of one year and treated with phenobarbital with adequate control, presented somnolence, lethargy, nausea, vomiting and headache one week prior to hospitalization. At a local health center, an assessment of a viral infection was done, but symptoms were soon followed by hypoactivity and lethargy prompting hospitalization. A head CT scan revealed a hypodense mass in the posterior fossa and the diagnoses of a brain abscess or malignancy were considered. The patient rapidly deteriorated with respiratory failure, requiring orotracheal intubation and mechanical ventilation. He was then transferred to the University Pediatric Hospital for neurosurgery evaluation and management. At admission, the patient was hypoactive, lethargic, with signs of increased intracranial pressure, requiring a ventriculoperitoneal shunt. The rest of the physical exam was unremarkable. The child had a negative history of head trauma, accidents, or childhood illnesses other than febrile seizures. He had adequate milestones; the family history was essentially non contributory.

A magnetic resonance imaging (MRI) without contrast revealed a 5.1 x 4.8 x 4.3 cm solid mass in the right cerebellar hemisphere with mass effect and compression of the fourth ventricle and brainstem, with midline shift. An occipital craniotomy and C1 laminectomy were performed with gross total removal of a necrotic tumoral mass. Smear preparations from fresh tissue showed pleomorphic tumor cells with margination of the chromatin, and macronucleoli in a background of tumoral diathesis. Many of the cells presented bare nuclei while in others, eosinophilic cytoplasmic inclusions were noticeable (Figure 1). Additional tumor tissue was received fixed in formalin, and consisted of multiple irregular fragments of tan-white soft tissue measuring in aggregate 6.3 x 3.0 x 1.2cm. Microscopic sections showed a highly aggressive tumor with extensive areas of necrosis. Tumor cells were round or polygonal with abundant cytoplasm and occasional

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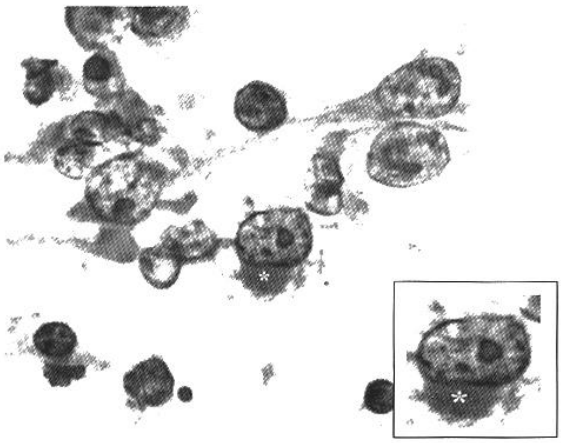

Figure 1. Smear. Tumor cells with eccentric nuclei, margination of chromatin, prominent nucleolus and insinuated cytoplasmic inclusions(*). H&E, oil immersion.

intracytoplasmic inclusions displacing eccentrically the nuclei. The nuclei were pleomorphic and presented a macronucleolus (Figure 2).

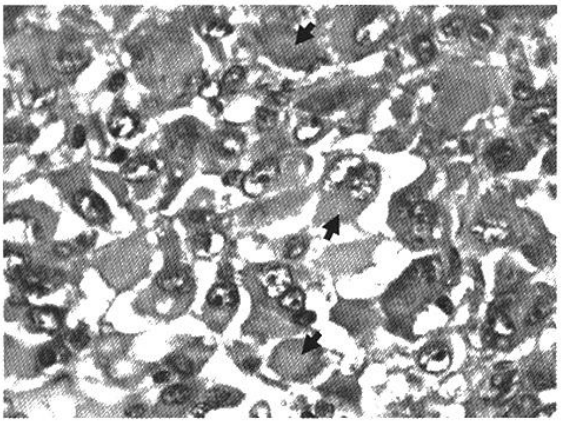

Figure 2. Tumor cells present abundant cytoplasm, occasional cytoplasmic inclusions, (arrow), pleomorphic vesicular nuclei, and macronucleolus. H&E stain, 200X

Immunohistochemistry showed tumor cells with positive immunoreactivity for vimentin and keratin. Myoglobin, desmin, glial fibrillary acidic protein (GFAP), placental alkaline phosphate (PLAP), and alpha-feto protein were negative. Neuron specific enolase (NSE) was weakly positive. Electron microscopy revealed primitive intercellular junctions, scarce organelles and perinuclear aggregates of intermediate filaments (Figure 3). Muscular or neural differentiation was not observed. The immunohistochemistry and electron microscopy studies supported the histological diagnosis of a rhabdoid tumor.

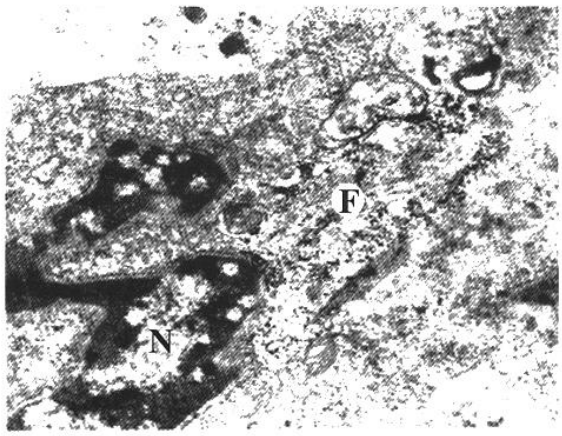

Figure 3. Electron microscopy. Note aggregates of unbound intermediate filaments (F); N: nucleus.

An MRI of the brain using T1W spell out parameters at the 9th postoperative day was interpreted as reactive tissue changes and an MRI of the cervical spine was negative for metastatic disease. The patient had an uneventful postoperative course with residual gait disturbance. He later went to the United States for follow up and further management.

Discussion

Rhabdoid tumor is a rare and highly aggressive malignancy. It was first described in the kidney by Beckwith and Palmer (1) who originally thought this tumor was a rhabdomyosarcomatoid variant of Wilm's tumor, but later it was classified by Haas et al. as a separate entity because of its immunohistochemistry and ultrastructural properties (2). The term rhabdoid derives from its similar histologic appearance in light microscopy to rhabdomyosarcoma, however the immunohistochemistry and ultrastructure do not support a muscle cell origin. The tumor occurs most commonly in pediatric patients, usually less than 2 years old. Adults have been rarely reported (4). Since its recognition, this tumor has been described in almost any site and is histologically indistinguishable from the ones described in the kidney.

The first unequivocal case of a primary central nervous system malignant rhabdoid tumor (MRT) was described in 1985 by Briner et al. in a child who died 2 weeks after the diagnosis was made and was found at autopsy to have a cerebellar mass with subarachnoid seeding (5). Thereafter, few primary central nervous system cases have been reported. The ones described in the brain, as opposed to those in the kidney, have shown immunophenotypic and histologic heterogenicity upraising the term "atypical

teratoid/rhabdoid tumors" (AT/RT)(6, 7, 8). These tumors in addition to the rhabdoid component may disclose areas of other embryonal tumors, mostly primitive neuroectodermal tumors (PNET). They also present positive immunoreactivity for epithelial membrane antigen (EMA), vimentin, glial fibrillary acidic protein (GFAP), actin, neurofilament protein and ocassionally chromogranin. Very few cases are pure rhabdoid tumors. Definitive diagnosis is only possible through tissue histological examination; radiologic images are nonspecific and indistinguishable from the ones described in the PNET (9, 10) although characterized by necrosis and cysts and sometimes hemorrhages. These latter features should flag one's mind of the possibility of a rhabdoid tumor. The easiness of making the diagnosis depends on the amount of the rhabdoid component present in the tumor. Extensive necrosis, and hemorrhages are suspicious for the diagnosis, but even more significant is the aggressive looking vesicular nuclei and macronucleolus. The absence of this cytologic feature should caution when making this diagnosis, since other tumors may present eosinophilic inclusions and have rhabdoid features withoud fulfilling the diagnostic criteria of a rhabdoid tumor. Eosinophilic intracytoplasmic inclusions are helpful but not always present. The distinction of this tumor is clinically important.

As of today, the histogenesis of rhabdoid tumors is not clear and many theories have suggested mesenchymal, histiocytic, and meningothelial origin (11). Others have suggested a primitive pluripotential cell origin due to the variable immunophenotyping and its association to renal rhabdoid tumors (12, 13) or a similar cell origin as the association of renal rhabdoid tumor with cerebral embryonal tumors such as: primitive neuroectodermal tumors (PNET), pinealoblastoma, medulloblastoma and astrocytomas has been well documented (14). However, the classic histologic features of this aggressive tumor with round or polygonal cells, pleomorphic vesicular nuclei and macronucleolus, in addition to its immunophenotype and ultrastructure makes this tumor a unique entity. Cytogenetics holds promise as to clarify its histogenesis and more specific evidence of abnormalities in the cell lines. (15,16).

Our case fulfilled the criteria of the most consistent findings for the diagnosis of a rhabdoid tumor including: 1) typical light microscope morphology with pleomorphic round/polygonal tumor cells, abundant eosinophilic cytoplasm with occasional round, eosinophilic intracytoplasmic inclusions, and vesicular nuclei with a macronucleolus, 2) cytoplasmic aggregates of filaments not bounded by membranes on electron microscopy and 3) positive immunoreactivity for vimentin and cytokeratin, but negative to desmin, and myoglobin.

No clear therapeutic strategy exists for rhabdoid tumor of the central nervous system. Therapy has included surgery, radiotherapy and chemotherapy in combination and high dose chemotherapy with autologous bone marrow rescue. Treatment results have been poor, with a tendency for early local relapses and meningeal dissemination. Unfortunately, despite this aggressive therapy, the mean survival time after diagnosis continues to be less than one year. Because of the rarity of this tumor there is great need to start collaborative studies in order to learn more about this tumor's biology and clinical behavior. This knowledge is essential for the development and establisment of effective therapeutic strategies.

Resumen

El tumor rabdoide de cerebro es un tumor de incidencia baja y con un pronóstico fatal a pesar del tratamiento. Informamos el caso de un niño de 3 años de edad que presentó letargia, somnolencia, náusea, vómitos y cefaleas una semana previa a su hospitalización. La tomografía computarizada de cabeza demostró una masa en la fosa posterior derecha e hidrocefalia, requiriendo un desvío ventriculoperitoneal seguido por una resección total del tumor. Se discute la histopatología, inmunohistoquímica y ultraestructura de este tumor cerebral.

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