Primary cerebral alveolar rhabdomyosarcoma in adult

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Abstract

Primary cerebral rhabdomyosarcomas are very rare and malignant tumors that occur predominantly in the posterior fossa of pediatric patients. We report a rare case of primary cerebral rhabdomyosarcoma located in the supratentorial compartment of a 51 year-old woman together with a review of the pertinent literature especially regarding the histological diagnosis and pitfalls.

Introduction

Primary cerebral rhabdomyosarcomas (PCR), defined as pure mesenchymal tumors composed by both embryonal and mature striated muscle cells, are very rare malignant neoplasms that bear a poor prognosis.[1-3] In the pediatric population they are preferentially located in the infratentorial compartment. Only sporadic cases are described in adults. Treatment for these lesions is not yet standardized, but maximal safe resection followed by radiation therapy is widely suggested, whereas the role of chemotherapy is still discussed.[1,4-6] We report the case of a 51 year-old woman, affected by supratentorial primary cerebral rhabdomyosarcoma, treated with gross-total surgical resection and adjuvant radiation treatment initially and followed by radioimmunotherapy thereafter, along with a review of the literature on adult primary cerebral rhabdomyosarcomas.

Case Report

A 51 year-old woman was admitted to our hospital complaining of a persistent headache developed over a few days. Her neurologic examination revealed only a moderate right hemiparesis with sensory disturbances. A brain CT scan displayed a 5-cm-diameter solid-cystic lesion in the left parietal lobe. Magnetic resonance imaging (MRI) confirmed the presence of a right-sided parietal intra-axial mass with a cystic component, a heterogeneous iso-hypointense signal on T1-weighted images and a heterogeneous hyperintense signal on T2-weighted images of the solid portion (Figure 1a), enhancing after Gadolinium administration (Figure 1b). The tumor was gross-totally removed (with a post-operative confirmation of the MRI that did not show any sign of contrast enhancement) through a left parietal craniotomy with the aid of neuronavigation and neurophysiological intraoperative monitoring of the motor function. The tumor was gray, soft and apparently well demarcated from the surrounding brain. The cystic portion contained a transparent yellowish fluid. Its global intraoperative aspect was that of a metastatic lesion.

Microscopic examination showed a malignant lesion composed by small cells with elongated nuclei arranged in irregular fascicles, mixed with multinucleated giant cells with an intense mitotic activity and focal necrosis (Figure 2a). The lesion appeared highly vascularized. Immunohistochemical analysis revealed a focal positivity to GFAP and synaptophysin, together with a 60% positivity to vimentin and 90% to desmin (in this latter case sometimes with a perinuclear dot-like pattern). Staining for cytokeratin, epithelial membrane antigen (EMA), CD99 and CD45 were negative. After an initial diagnosis of small-cell glioblastoma, the pathologist considered the hypothesis of a secondary localization of pulmonary microcytoma. A staging chest and abdomen-CT scan were negative and so were blood levels for neuron-specific enolase (NSE). A new and more detailed pathological examination was therefore performed. Neoplastic cells resulted positive for myogenin (Figure 2b) and muscle-specific actin. A final diagnosis of cerebral rhabdomyosarcoma of the alveolar type (since the microscopic architectural appearance of *lining-up* along pseudospaces that are reminiscent of lung alveoli) was made. Staging confirmed the primary source of the disease and the definitive diagnosis was primary cerebral rhabdomyosarcoma. Our patient received adjuvant external radiation therapy (with the same standard technique used for high-grade gliomas) for a total dose of 60 Gy (2 Gy fractions) and refused chemotherapy. After 11 months a local recurrent tumor with the same neuroradiological features of the neoplasm previously removed was displayed after MRI. Given the good performance status of the patient, a new surgical procedure was undertaken, but the lesion recurred in less than four months. A third craniotomy was performed and a Rickham's reservoir was left in the tumor cavity for radioimmunotherapy. She died after 20 months from diagnosis.

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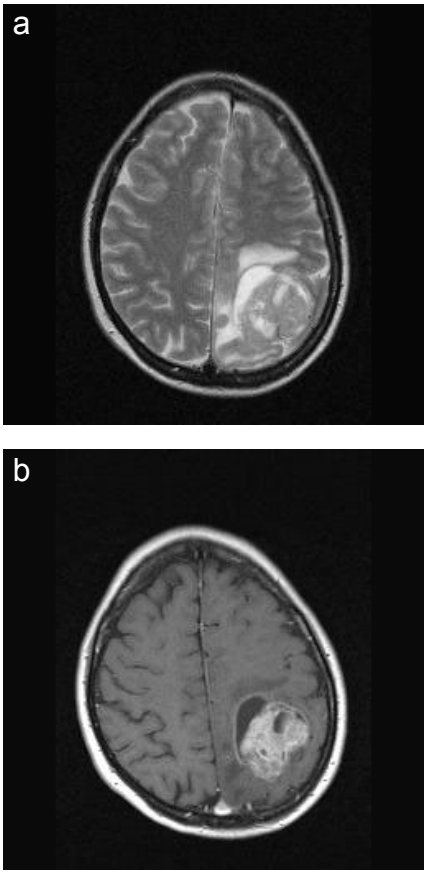

Figure 1. (a) Magnetic resonance imaging scan of the head showing the radiological appearance of left-sided parietal primary rhabdomyosarcoma on T2-weighted and (b) T1-weighted images after Gadolinium administration

Discussion

Primary cerebral rhabdomyosarcoma (PCR) is extremely rare and occurs almost exclusively in the pediatric age group.[1,3-5,7,8] To the best of our knowledge, only 9 cases (including our patient) of adult PCR were described in the English-speaking literature,[1,4-6,9-12] and for some authors it represents a distinct entity. In adult cases patient ages ranged from 24 to 68 years (mean 47.1 years) without a gender predilection (4 males and 5 females). While in the pediatric population PCR is mainly situated in the infratentorial compartment, in adults there is a tendency to supratentorial localization (7 out of 9 cases) (Table 1).

This tumor has no distinguishing imaging features from other primary or secondary malignant brain neoplasms.[1] The typical MRI appearance is that of a iso-hypointense lesion on T1-weighted images and hyperintense on T2-weighted images, most commonly with poorly defined margins and an intense but heterogeneous enhancement after Gadolinium administration. Sometimes this neoplasm may have a cystic component (as in our case) and/or an hemorrhagic presentation. Differential diagnosis should include high-grade glioma, lymphoma, metastases and PNET. Histological confirmation is essential for the definitive diagnosis.[1,4-6,9]

Table 1. Clinical summary of previously reported cases of primary cerebral rhabdomyosarcoma in adult population (English literature).

Author (reference)	Age (year)	Sex	Site	Therapy	Follow-up (months)
Lopes de Faria *et al.*[8]	52	F	Cerebellar	none	0
Leedham[6]	45	F	Parietal	S	10
Min *et al.*[9]	48	M	Frontal	S-R	8
Yagishita *et al.*[12]	50	F	Emispheric	S	9
Hayashi *et al.*	68	M	Basal ganglia	S-R	5
Dozic *et al.*	24	M	Lateral ventricle	S	Not reported
Celli *et al.*[1]	46	M	Frontal	GT	30
Grebe *et al.*[3]	40	F	Frontal	GT-R	17
Present case	51	F	Parietal	GT-R-RI	20

S, subtotal removal; GT, gross-total removal; C, chemotherapy; R, radiotherapy; RI, radioimmunotherapy

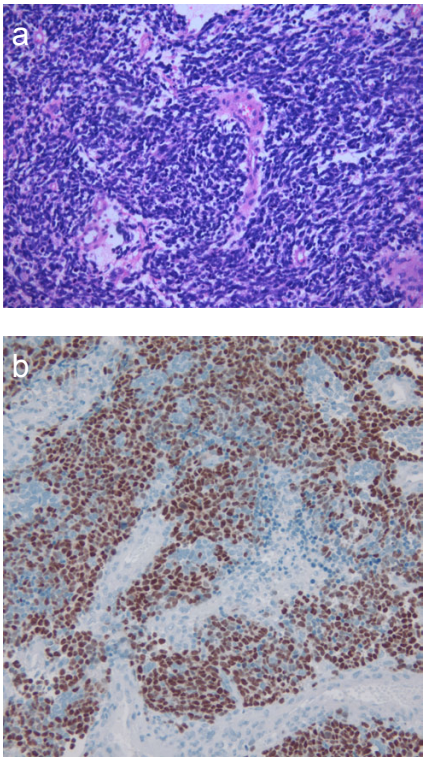

Figure 2. (a) Microscopic specimen of primary cerebral rhabdomyosarcoma: hematoxylin-eosin and (b) immunohistochemical analysis for myogenin.

Rhabdomyosarcomas constitute a unique group of soft tissue neoplasms that share a propensity to undergo myogenesis, a well-defined biologic process that primarily occurs during embryonal and fetal development. The most diffuse pathological classification identifies four subtypes: embryonal, alveolar, botyroid and pleomorphic.[3] A primary involvement of the brain has to be differentiated from an intracranial extension from skull or paramenigeal sites (orbit, nasopharynx, paranasal sinuses, middle ear, external auditory canal), but also from a metastatic seeding from a systemic rhabdomyosarcoma and from mixed primary cerebral tumors of the central nervous system in which rhabdomyoblastic areas are found in combination with sarcomatous, neuroectodermal, mesenchimal or teratomatous features.[1] PCR consists primarily of small cells that show little or no specific differentiation at the hematoxylin-eosin level. Thus, immunohistochemistry and/or electron microscopy are necessary for diagnosis, particularly immunostains for desmin and myogenin.[3,7,8] Histologically, PCR must be differentiated from other brain tumors that occasionally show skeletal muscle elements, such as medullomyoblastomas, gliosarcomas, germ cell tumors and even rare meningiomas. Histogenesis of this rare mesodermal tumour is still matter of debate. Some Authors concluded that it arises from pluripotential cells misplaced during embryonic life. An origin from primitive neural crest cells that have undergone mesoectodermal differentiation is also considered a possibility. These undifferentiated mesenchymal cells are normally described in pericapillary locations, particularly in the pia mater.[1,3-7)]

The aim of treatment should be gross-total surgical resection, followed by radiotherapy and/or chemotherapy, both in pediatric and adult PCRs. As for our case, we achieved a macroscopically complete surgical removal of the lesion, as confirmed by post-operative MRI. In the vast majority of cases radiation therapy is the adjuvant treatment of choice, with a total dose and fractionation similar to what is used for malignant gliomas. In fact, for our patient a total dose of 60 Gy in 30 fractions was administered. There is no consensus regarding the role, or type, of chemotherapy. Relatively good results were reported after the administration of VAC (vincristine, actinomycin D and cyclophosphamide) or ICE (ifosfamide, carboplatin and etoposide). Despite modern surgical techniques and adjuvant oncological treatments, PCR is associated with an extremely poor prognosis, as reported in the Literature, where survival is almost always less than 12 months with only few patients alive after 24 months.[1,4-6,9-12]

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