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CEREBELLAR LIPONEUROCYTOMA

A newly recognized clinico-pathological entity

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ABSTRACT - The term "cerebellar liponeurocytoma", recently adopted by the World Health Organization Working Group (WHO), replaced many other different terms used up to now to give name to this rare tumor. To our knowledge, less than 20 cases have been related up to now under different names like as "lipomatous medulloblastoma, lipidized medulloblastoma, neurolipocytoma, medullocytoma and lipomatous glioneurocytoma". The new nomenclature eliminates the word "medulloblastoma", reinforces its benign caracter, and includes it in the category of glioneuronal tumors. We describe an adictional case of this distinct clinico-pathological entity removed from the right cerebellar hemisphere of a 53-year-old woman. With the present case report, we hope to contribute to the knowledge on the diagnostic and prognostic implications derived from the finding of mature adipose-like tissue within a medulloblastomatous tumour.

KEY WORDS: liponeurocytoma, medulloblastoma, adipose tissue, mixed tumour.

Liponeurocitoma cerebelar: uma nova entidade clínico-patológica

RESUMO - O termo "liponeurocitoma cerebelar" recentemente adotado pela Organização Mundial de Saúde (Classificação de Tumores Cerebrais - versão 2000), surgiu em substituição a vários outros utilizados até então, para denominar esta rara neoplasia. De nosso conhecimento há na literatura menos de 20 casos relatados sob termos diferentes tais como "meduloblastoma lipomatoso, meduloblastoma lipidizado, neurolipocitoma, medulocitoma e glioneurocitoma lipomatoso". A nova nomenclatura elimina a palavra "meduloblastoma", enfatiza seu caráter benigno e o coloca na categoria dos tumores glioneuronais. Descrevemos mais um caso desta rara entidade clínico-patológica, ressecada do hemisfério cerebelar direito em uma mulher de 53 anos. Com este caso esperamos contribuir para o melhor conhecimento sobre o diagnóstico, prognóstico e possibilidades terapêuticas advindas da presença de tecido adiposo em tumor meduloblastomatoso de adultos.

PALAVRAS-CHAVE: liponeurocitoma, meduloblastoma, tecido adiposo, tumor misto.

Medulloblastoma is the most common primitive neuroectodermal tumor of the central nervous system. It occurs usually in childhood in the first decade of life[1], being also found in adults[2-4]. According to World Health Organization (WHO) it is considered a grade IV neoplasm[5]. Its heterogeneity as well as its potential to differentiate has been largely related in the literature, happening in 40% of cases[6]. Cartilaginous, rhabdomyoblastic and neuro-glial variants have been reported[7-9]. The uncommon finding of adipose tissue in medulloblastomatous neoplasms has been related rarely and correlates with better prognosis[10-15]. This kind of tumor was recently included in the WHO working group for classification of central nervous system neoplasms under the name "Cerebellar Liponeurocytoma"[5]. The term adopted omits the word "medulloblastoma" clearly pointing to a better prognosis.

We describe here such a particular posterior fossa neoplasm in a 53-year-old woman, especially composed of mature adipose tissue closely admixed with undifferentiated small blue cell areas consistent with medulloblastoma.

CASE

A 53-year-old white previously healthy woman, developed a progressive occipital headache. Computed tomography (CT) scan disclosed a contrast enhancing heterogeneous mass in the right cerebellar hemisphere, displacing IV ventricle and causing hydrocephalus. She was, at first, submitted to a ventriculoperitoneal shunt followed by

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surgical exploration with subtotal resection of the lesion. Because of a residual tumor the patient received postoperative cranial radiotherapy (5600 rads).

The surgically removed tumor fragments were received at the laboratory fixed in 10% formallin. They were processed for paraffin sectioning and stained with hematoxylin-eosin (H&E), periodic acid-Schiff (PAS), Gomori, Fontana-Masson and reticulin.

No fresh tumor tissue was available to make oil red O stain to lipid droplets or ultrastructural examination. Immunohistochemical staining using DAKO monoclonal antibodies following avidin-biotin techniques included: glial fibrillary acidic protein (GFAP-1:200 dilution), vimentin (Vim-1:200 dilution), neuron-specific enolase (NSE-1:400 dilution), synaptophysin (Syn-1:300 dilution) and Ki 67 - 1:25 dilution).

Pathologic findings - Microscopically we observed a neoplasm consisting of two distinct cellular elements: a predominant poorly differentiated component of small cells, intermixed with another element indistinguishable from mature fat cells at optic microscopy examination (Fig 1). No distinct separation was observed between these two elements (Fig 2). The small cell component disclosed scanty cytoplasm and round or oval nuclei arranged in a fibrillary background (Fig 3). The lipomatous component was composed of grouped vacuolated cells indistinguishable from mature fat cells (Fig 4). Other tumor areas contained smaller vacuoles recalling an apparent transition between the two populations. In the lipomatous component there was no cellular immaturity or nuclear atypia. Only few mitosis were found in poorly differentiated areas. Recent hemorrhage as well as necrotic areas were also observed in both components. The non-tumoral cerebellar tissue circumjacent to tumor was devoid of fat cells, disclosing only hypoxic cellular alterations. The lipomatous cells showed a peripheral ring shape immunopositivity to GFAP (Fig 5), VIM and NSE. Medulloblastomatous areas were immunopositive to NSE and SYN. MIB 1 antibody immunolabelling index was positive in less than 5% of the cells.

DISCUSSION

Medulloblastoma, a malignant cerebellar tumor of childhood, is heterogeneous in regard to tissue pattern. Its potential of differentiation has been largely reported in the literature, including neuronal, glial and mesenchymal elements[6-8]. Authors have attempted to correlate some histological characteristics with prognosis and this has lead, sometimes, to different conclusions[4]. We report a case that represents a rare example of cerebellar tumor in adult, exhibiting an extraordinary morphology characterized by an uncommon mixture of mature adipose tissue with medulloblastomatous areas. The presence of adipose cells in neuroglial neoplasms has been exceptionally related in the literature not being restricted to cerebellum neither to medulloblastomas[16]. It has also been described in spinal cord neoplasms[17] and in supratentorial ependymomas[18]. The origin of these adipocytic elements is still disputed and it hasn't yet been completely elucidated. Some authors consider that the presence of such cells suggests that the neoplasm has evolved in dysgenetic areas where distinct cellular elements co-exist intimately[9].

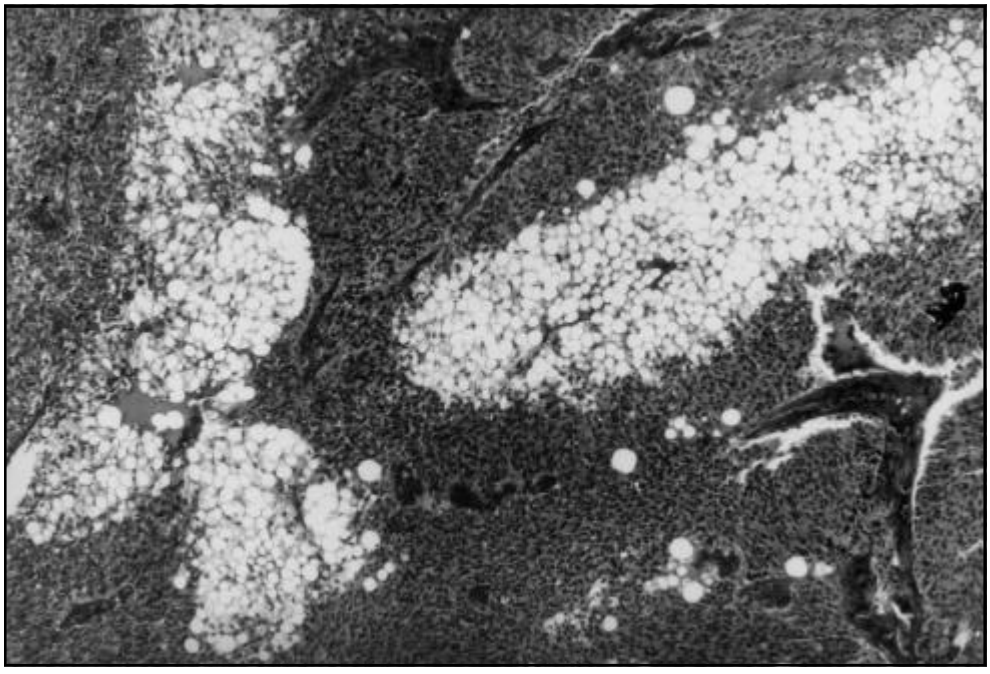

Fig 1. Histological architecture of the neoplasm focusing islands of lipomatous tissue intermingled with a small blue cell component (HE; x 100).

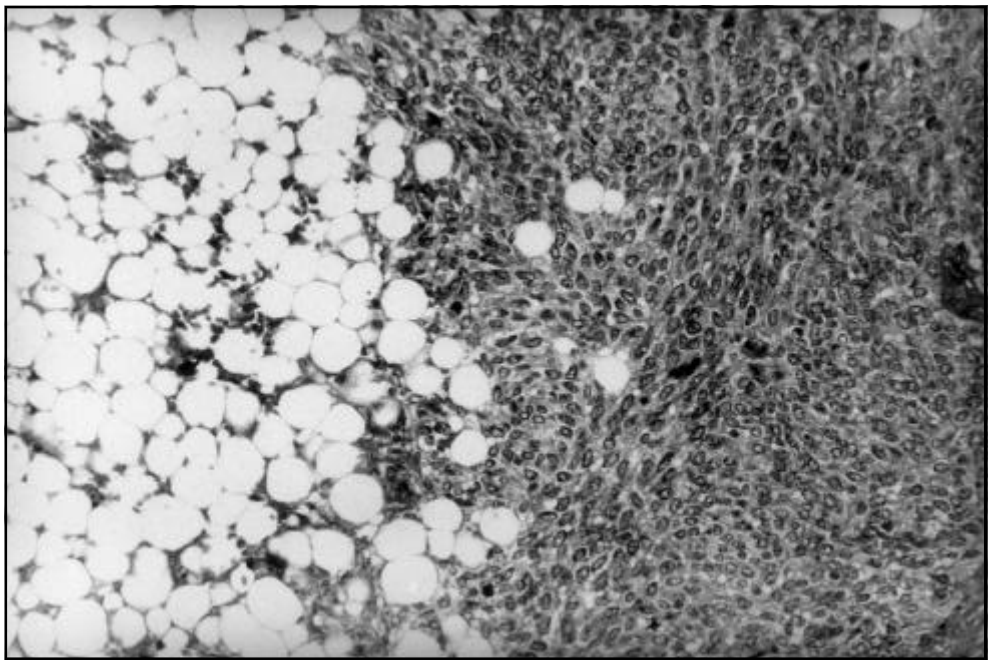

Fig 2. Higher power of the neoplasm demonstrating both cellular components merging one into another (HE; x 200).

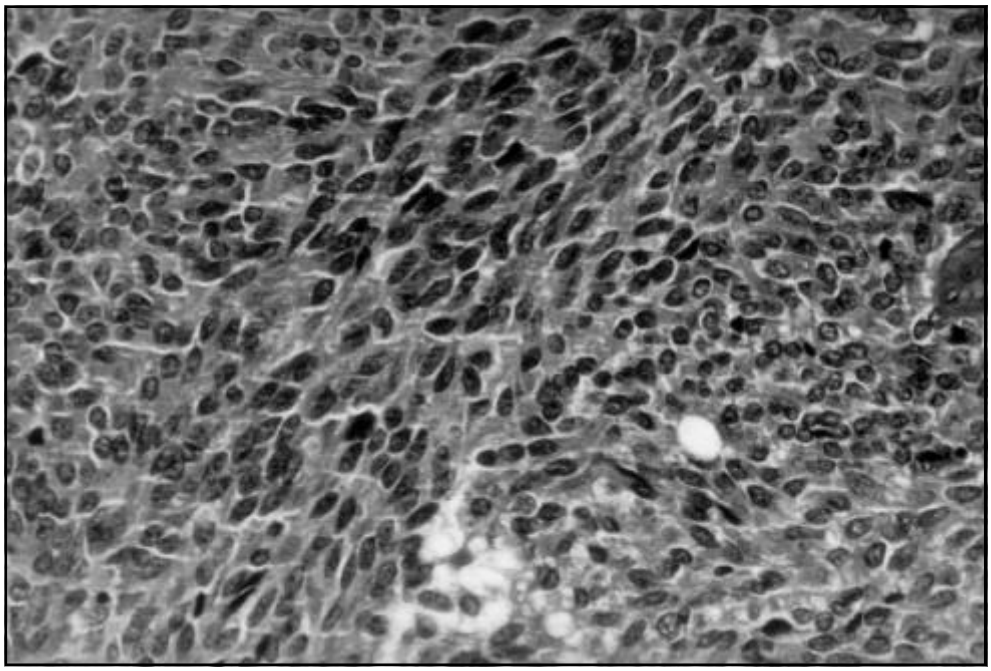

Fig 3. Cytological aspects of medulloblastomatous component with scanty cytoplasm and oval or round nuclei (HE; x 400).

Some others have found ultrastructural evidences that there is a progressive accumulation of lipid vacuoles in the cell's cytoplasm, probably due to some degenerative or metabolic change. So, those cells would become similar to adipocytes at optic microscopy. Analyzed under immunohistochemistry their neuroglial origin manifest themselves[18]. This explains the immunoreactivity in the remaining cytoplasm ring related by some authors[14,15,18]. What mechanism is in action in these tumors is still under consideration.

Apart from histopathological considerations, it should be pointed out that this variant, characterized by adult onset, shows a much more benign evolution. All these observations strongly suggest it is a clinicopathological entity distinct from its conventional correspondent.

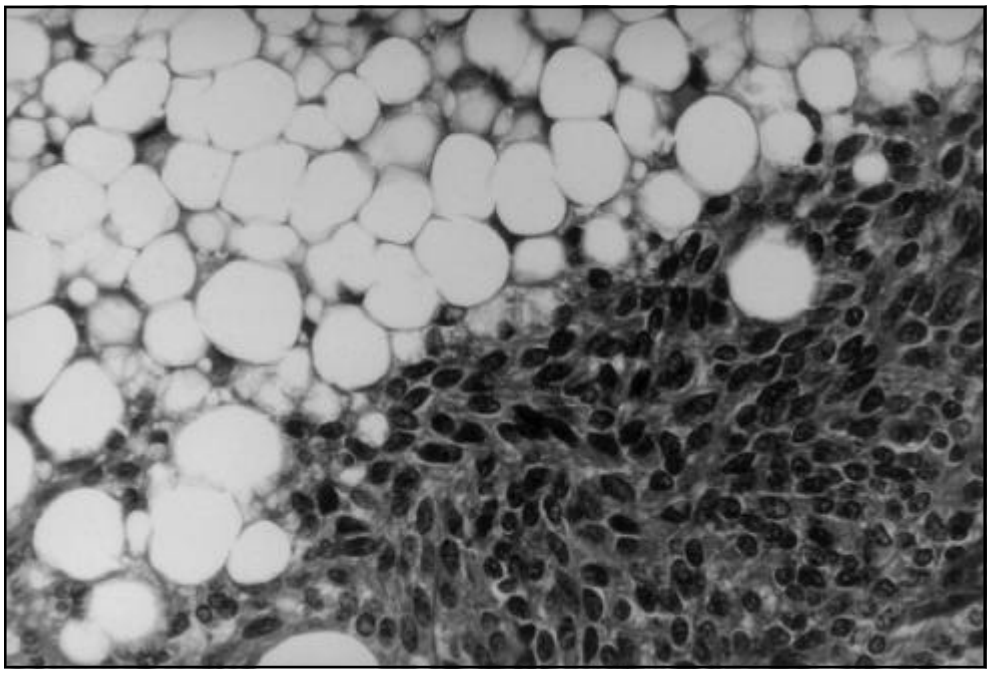

Fig 4 . High power of the lipomatous component shows large and small vacuolated fat cells (HE; x 400).

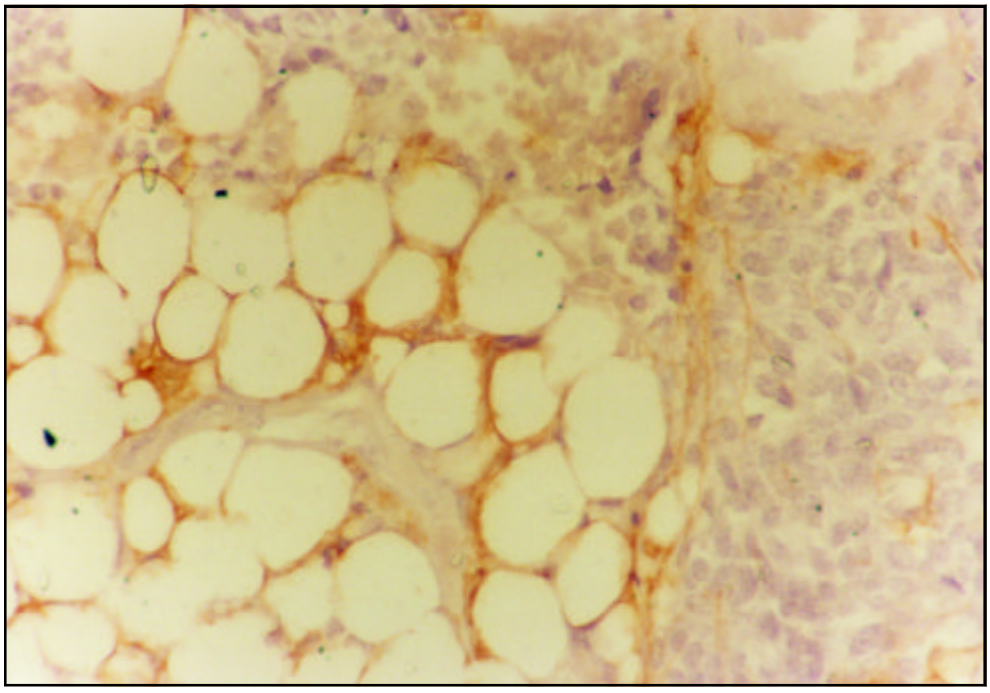

Fig 5. Immunostaining to GFAP showing positivity in a cytoplasmic ring of vacuolated cells (HE; x 400).

For the last years, many different terms have been proposed to designate these tumors, such as lipomatous medulloblastoma[15], lipidized medulloblastoma[14], neurolipocytoma[10] and medullocytoma[13]. Most of these terms clearly point to a more benign lesion than classical medulloblastoma. In accordance to a recent publication of the WHO working group on "Classification of Tumors of the Nervous System", they were included in the category of mixed glio neuronal tumors. The term "Cerebellar Liponeurocytoma" has been proposed and should be used from now on[5]. Bearing in mind that this kind of lesion is not restricted to cerebellum[16], maybe the word "cerebellar" should have been omitted.

Analyzing the postoperative approach in published cases up to now, we observed that there is no

consensus about the use of complementary radiotherapy[19]. In the majority of cases that had evidence of residual tumor, patients were submitted to radiotherapy[19,20]. Despite the presumed good prognosis, in one single case tumor behaved in a more aggressive way[21]. In our case, despite the presence of large necrotic areas, factor known to be associated with a poor prognosis, the patient is doing well almost four years after surgery and postoperative radiotherapy. We really believe the ideal post operative conduct is still to be determined.

The present report represents another step to determine whether the presence of lipomatous cells in medulloblastomatous tumors does, in fact, have a prognostic value, distinguishing them from conventional medulloblastomas.

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