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GLIOBLASTOMA MULTIFORME OF THE PINEAL REGION

Case report

Emerson Leandro Gasparetto[1], Danny Warszawiak[2], Guilherme Pradi Adam[1], Luiz Fernando Bleggi-Torres[3], Arnolfo de Carvalho Neto[4]

ABSTRACT - *Purpose*: pineal region tumors are uncommon, and comprise more frequently three categories: germ cell, parenchymal cell and glial tumors. Most pineal gliomas are low-grade astrocytomas. Glioblastoma multiforme, the most aggressive and common brain tumor, is extremely rare at this location with only few cases reported. *Case description*: a 29-year-old woman with a two month history of headache, nuchal pain, fever, nausea and seizures and physical examination showing nuchal rigidity, generalized hypotony, hypotrophy and hyper-reflexia, Babinski sign and left VI cranial par palsy. CT scan examination revealed a ill-defined hypodense lesion at the pineal region with heterogeneous contrast enhancement. MRI showed a lesion at the pineal region infiltrating the right thalamic region. The patient underwent a right craniotomy with partial resection of the mass. The histological examination of paraffin-embedded material defined the diagnosis of glioblastoma multiforme. Post-operative radiotherapy was indicated but the patient refused the treatment and died two months afterwards. *Conclusion*: in spite of its rarity at this location, glioblastoma multiforme should be considered in the differential diagnosis of aggressive lesions at the pineal region.

KEY WORDS: brain tumor, pineal gland, glioblastoma multiforme.

Glioblastoma multiforme de região pineal: relato de caso

RESUMO - *Objetivo*: Os tumores da região pineal são incomuns e podem ser divididos em três categorias de acordo com a sua origem: células germinativas, células do parênquima e células gliais. Em sua maioria, os gliomas de pineal são astrocitomas de baixo grau, sendo que o seu correspondente maligno, glioblastoma multiforme, é o mais comum e agressivo tumor encefálico e é extremamente raro nesta localização, com apenas alguns casos relatados na literatura. *Caso*: Mulher com 29 anos apresentando há 2 meses cefaléia, nucalgia, febre, náuseas e crises convulsivas. O exame físico mostrou rigidez de nuca, hipotonia, hipotrofia e hiperreflexia generalizadas, sinal de Babinski e paralisia do VI nervo craniano. A tomografia computadorizada revelou lesão hipodensa mal delimitada na topografia de pineal, com captação heterogênea de contraste. A ressonância magnética demonstrou lesão na região pineal com infiltração de tálamo à direita. A paciente foi submetida a craniotomia direita com ressecção parcial do tumor. O exame histológico definiu o diagnóstico de glioblastoma multiforme. No pós-operatório foi indicada radioterapia, mas a paciente recusou o tratamento e morreu dois meses depois. *Conclusão*: Apesar de raro nesta topografia, os glioblastomas multiformes devem ser considerados no diagnóstico diferencial de lesões agressivas localizadas na glândula pineal.

PALAVRAS-CHAVE: tumor encefálico, glândula pineal, glioblastoma multiforme.

Pineal region tumors are rare, comprising 0.4% to 1% of adult brain tumors[1,2]. Despite its small size, the pineal gland is the origin of a surprisingly diverse array of tumor types. The three major categories are germ cell tumors, parenchymal cell tumors, and the supporting tissues neoplams (glial tumors). Germinomas are the most common histological type, comprising 50-60% of all pineal tumors[3,4]. Gliomas account for 33% of pineal neoplams, but are mainly low grade astrocytomas[1,4]. Pineocytomas and pineoblastomas can also be found. Glioblastoma multiforme (GBM), the most malignant and frequent brain tumor, is rare at this location with only few cases reported[1, 5-12].

Discipline of Diagnostic Radiology (ELG, DW, GPA, CAN) and Department of Pathology (LFBT), University of Parana School of Medicine, Curitiba PR, Brazil. (UFPR): [1]Resident of Diagnostic Radiology, Hospital de Clinicas, UFPR; [2]Medical Student, UFPR; [3]Professor of the Department of Pathology, UFPR; [4]Professor of the Discipline of Diagnostic Radiology, UFPR.

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Dr. Emerson Leandro Gasparetto - Avenida Silva Jardim 296/502 - 80230-000 Curitiba PR - Brasil. FAX: 41 360 1800. E-mail: gasparetto@hotmail.com

We present a patient with GBM of the pineal region emphasizing the imaging findings and the review of the literature reported cases.

CASE

A 29-year-old woman presented with a two-month history of headache, nuchal pain, drowsiness, fever, nausea, dizziness and seizures. Physical examination revealed nuchal rigidity, horizontal nistagmus, generalized hypotony, hypotrophy and hyper-reflexia, decrease in muscle strength in all four limbs, Babinski's sign and left VI cranial nerve palsy. At this time, a hydrocephalus was diagnosed and the patient underwent a ventricle-peritoneal shunt. The CT-scan examination showed a rounded hypodense ill-defined lesion at the pineal region with extension to the right thalamus. After contrast administration the mass showed heterogeneous enhancement (Fig 1 and 2). The MRI revealed a lesion at the pineal region with malignant characteristics infiltrating discretely the right thalamic region.

On account of the size of the mass and its extension to thalamus, the patient underwent a right parieto-occipital craniotomy with a transtentorial approach (Ausman technique) in order to exsiccate the lesion. The surgery revealed a yellow swelling and bleeding mass, which was partially (60%) exsiccated.

Histopathological study of the resected tissue revealed a lesion composed of highly anaplastic glial cells, with mitotic activity, microvascular proliferation and areas of necrosis, defining the diagnosis of GBM (Fig 3 and 4).

The after surgery period elapsed normally in spite of a right hemiparesis, which was not present when the patient went home. At this time radiotherapy was recommended but the patient refused the treatment and died two months afterwards.

DISCUSSION

The pineal region is defined as the space delimitated superiorly by the splenium of the corpus callosum and choroid plexus of the third ventricle, anteriorly by the third ventricle, antero-inferiorly by the lamina quadrigemina, inferiorly by the anterior face of the cerebellum culmen and laterally by the thalami and medial faces of the cerebral hemispheres[13]. The tumors of the pineal region are uncommon, ranging from 0.5 to 2% of all intracranial neoplasms in several review papers [3,5,6,14]. The origin of the tumors of this region can be the pineal gland itself, the posterior portion of the third ventricle and the quadrigemina cistern. The symptoms are generally related to the compression of the adjacent structures and not related to the histopathology of the tumor. The most frequent symptoms are hydrocephalus (compression of the Sylvius aqueduct) and dysfunctions of the eyes movement. CT-scan and MRI make the diagnosis of the presence of the pineal region tumor. These tumors are usually variable in shape, often irregular, with thick walls (more than 2 mm), larger than 20 mm, frequently compressing neighbor structures and infiltrative[13]. The MRI is essential to analyze the tumor characteristics and its relation to neural and vascular structures. The association of the MRI (or CT image) and the clinical data may suggest a possible diagnosis. For instance, a young man with a homogeneous, round tumor probably has a germ cell tumor. The hypodense pineal mass with heterogeneous contrast enhancement and invasion of the adjacent

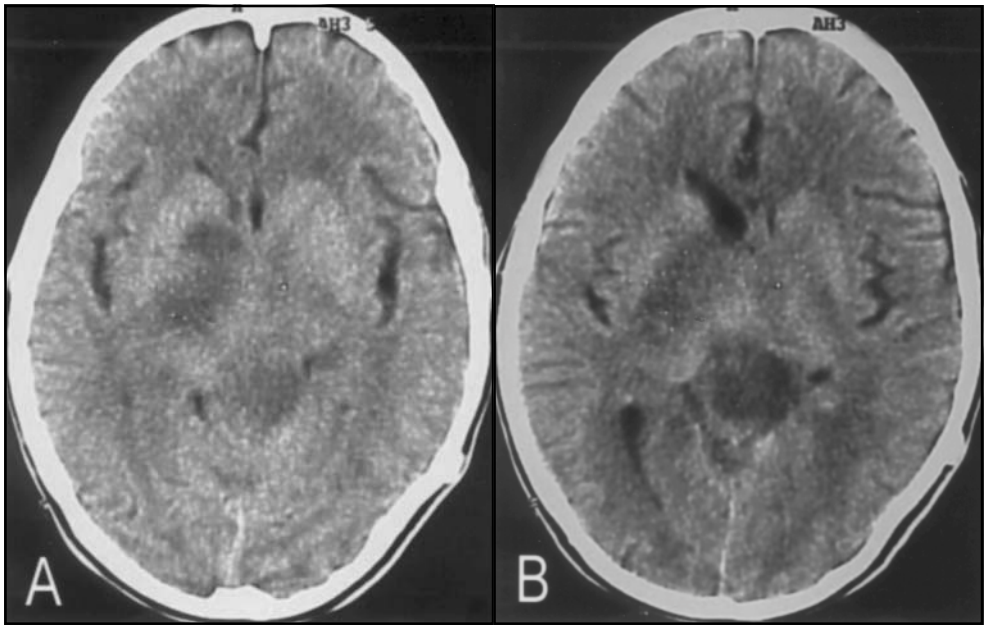

Fig 1 (A) and (B). Axial CT scan showing a hypodense ill-defined mass at the pineal region.

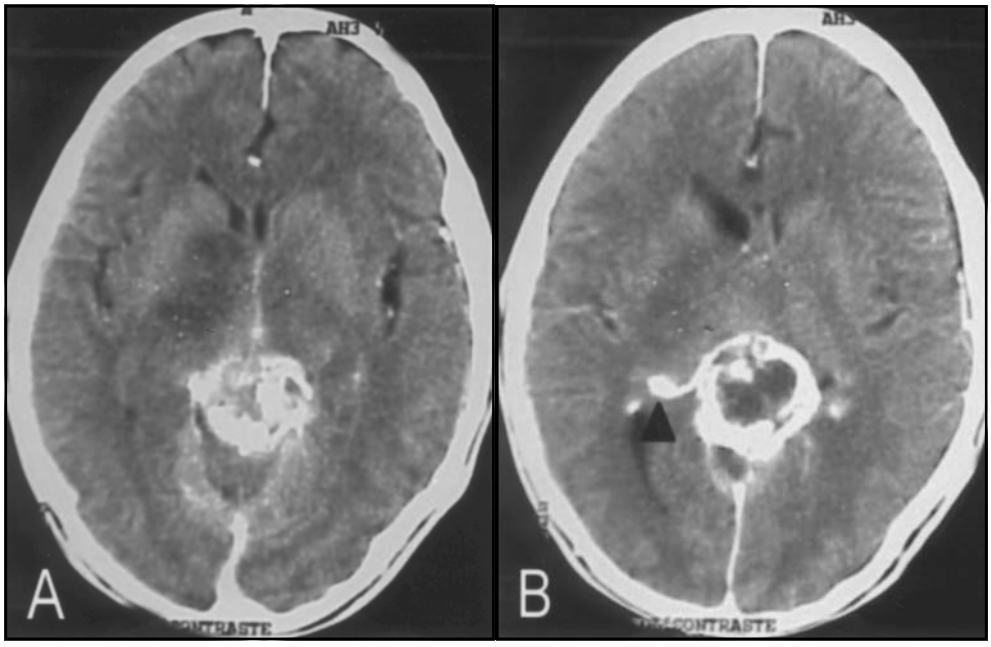

Fig 2 (A) and (B). Axial CT scan after contrast injection revealing heterogeneous enhancement of the mass and demonstrating the invasion of the right thalamus (arrow).

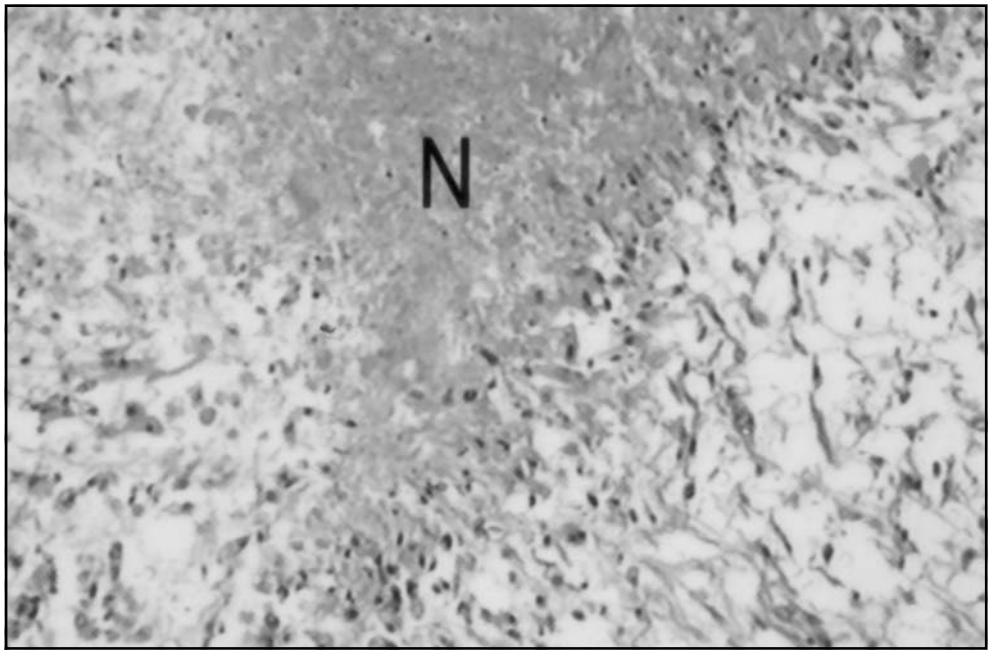

Fig 3. Histological section showing a tumor composed of anaplastic glial cells with mitosis and extensive area of necrosis (N) (HEx40).

thalamus presented in our case denotes a malignant lesion and has to be differentiated from any other malignant lesion of the pineal region. The main aspects for this differentiation are discussed below. However, the final diagnosis should only be given with the histopathologic examination. The majority of the pineal region tumors appears to be of germ cell origin and include germinomas, teratomas, and less commonly, embryonal carcinoma and choriocarcinoma. In fact, the pineal region is the most common site of intracranial germinomas and teratomas. These tumors usually develop in the first two decades of life and predominate in males[1,4,11]. The germinomas would appear hyperdense on CT-scan, with a strong contrast enhencement. MRI would show a lesion isodense to the gray matter. The teratomas do not have

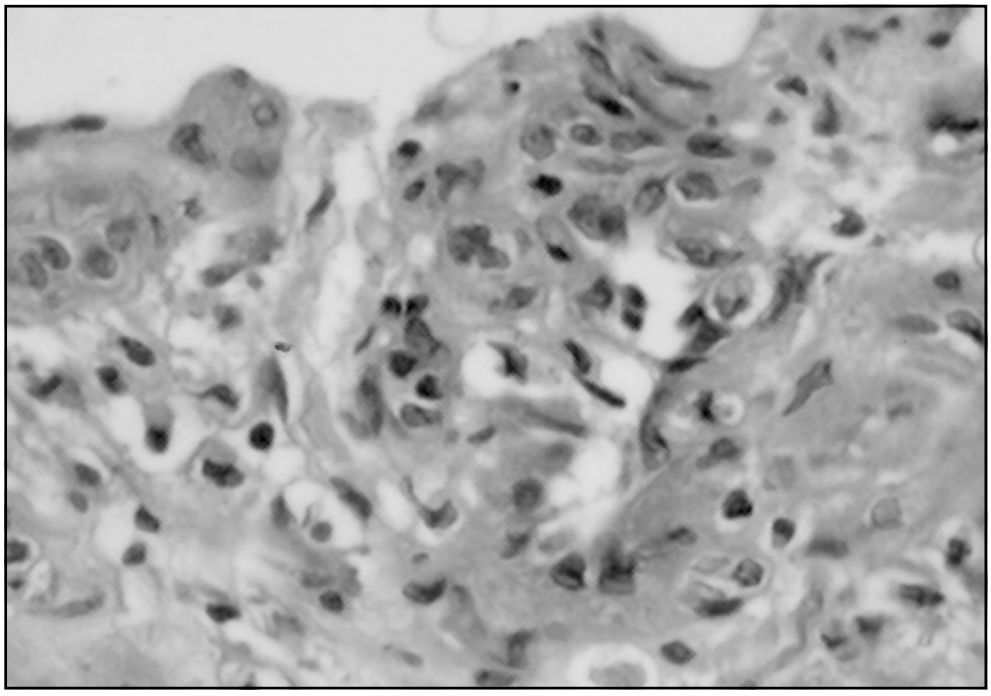

Fig 4. Histological section showing in detail a vessel with proliferation, common in glioblastoma multiforme (HEx100).

Table 1. Clinical and imaging findings of 10 cases diagnosed as glioblastoma multiforme of the pineal region.

Case	Sex	Age (years)	Clinical presentation	CT scan findings	Treatment	Survival (months)
Cho et al.[5]	male	63	↑I CP and changing behavior	Hyperdense pineal mass with ring contrast enhancemente and hydrocephalus	Surgery and RTX	6
de Girolami et al.[6]	female	12	-	-	RTX and CTX	18
Frank et al.[7]	male	36	↑ICP, Parinaud's syndrome, hearing loss and tremors	Third ventricle mass and hydrocephalus	RTX	4
Kalynaraman [8]	female	52	↑ICP and oculomotor nerve disturbance	-	RTX	4
Norbut et al.[9]	female	68	Ataxic gait, dementia, blurred vision and upward gaze palsy	Calcified midline mass and hydrocephalus	Surgery and RTX	4
Pople et al.[10]	male	50	-	Hydrocephalus	-	6
Vaquero et al.[11]	female	6	-	-	-	-
Bradfield et al.[14]	-	-	↑ICP and vertical gaze palsy	-	Surgery and RTX	-
Bradfield et al.[14]	-	-	↑ICP	-	RTX	-
Bradfield et al.[14]	-	-	↑ICP	-	RTX	-
Gasparetto et al.	female	29	↑ICP, fever, seizures	Hypodense pineal mass with heterogeneous contrast enhancement	Surgery	2

↑ICP, symptoms of increased intracranial pressure; RTX, radiotherapy; CTX, chemotherapy.

a specific image characteristic usually appearing as mixed density/intensity lesions.

The neoplasms originating from the pineal parenchymal cells occur with considerably less frequency. This tumors include pineocytoma, which is composed of relatively mature pineal cells, and the pineoblastoma, a more immature, poorly differentiated neoplasm. These tumors tend to occur in a slightly older age group and occur evenly in males and females[6,7,11]. The pineocytomas are radiologically indistinguishable from the benign pineal cysts. The pineoblastomas appear as big non-encapsulated masses with a strong or heterogeneous contrast enhancement and frequently invade the adjacent parenchyma.

Additional tumors arising from the glial components of the pineal gland include ganglioneuroma, ganglioglioma, chemodectoma, meningeoma, and gliomas, more frequently low-grade astrocytomas. The gliomas origin either from the glial tissue of the pineal gland (astrocytes are a normal component of the pineal gland) or from the glial cells of the vicinity of this gland, such as the posterior portion of the third ventricle or the lamina quadrigemina. The low-grade astrocitomas would appear on CT-scan as iso or hypodense lesions with heterogeneous moderate contrast enhancement. MRI would show an iso or hypointense lesion on T1-wheighted image and hyperintese on T2-wheigthed images. Edema, hemorrhage and contrast enhancement are common features. Nonneoplastic processes that may also simulate a pineal tumor at this location include epidermoid, dermoid and glial cysts[3,4,7,14].

Although GBM (WHO's astrocytoma grade IV) is the most frequent brain tumor, it is exceedingly rare at the pineal region with only few-reported cases[1, 5-12]. Because these tumors are usually included within series of pineal region tumors it is difficult to study the clinical and imaging features of these cases (Table 1). However, in 7 cases the age and sex of the patients were recorded[1, 7-12]. The age ranged between 6 and 68 years (mean age: 50 years). The predominant symptoms were related to hydrocephalus and ophthalmologic symptoms (specially Parinaud's syndrome)[2,6,8,9,15]. The CT scan examination often showed hydrocephalus[8, 9,11,12]. The lesion on CT has different patterns such as a calcified mass in the midline[8], a mass lesion in the posterior third ventricle[9], or a rounded hyperdense mass at the pineal region with ring enhancement after contrast administration[12]. One of the reported cases had a diffuse leptomeningeal involvement, with spinal subarachnoid metastases[9]. In all cases which survival time has been reported the prognosis had been poor.

The presented case, along with the others previously reported, suggest that the GBM, in spite of its rarity at this location, should be considered in the differential diagnosis of aggressive lesions at the pineal region.

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