Hipertensão intracraniana relacionada a um raro padrão de neoplasia: gliomatose cerebral

Intracranial hypertension related to a rare pattern of neoplasm: gliomatosis cerebri

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RESUMO

Gliomatose cerebral (GC) é um raro padrão de crescimento dos gliomas cerebrais, que infiltra difusamente os hemisférios cerebrais e estruturas adjacentes. As características radiológicas e histopatológicas são fundamentais para estabelecer *ante mortem* o diagnóstico. Em geral, a GC corresponde a uma neoplasia com diferenciação astrocítica e de grau histológico III / alto grau, a qual apresenta um curso clínico variável. No presente relato, os autores apresentam um caso de GC determinando hipertensão intracraniana, descrevem os principais achados histopatológicos e o diagnóstico diferencial desta neoplasia pouco frequente.

UNITERMOS: Gliomatose Cerebral, Glioma, Astrocitoma, Neoplasias Encefálicas.

ABSTRACT

Gliomatosis cerebri (GC) is a rare growth pattern of brain gliomas, which diffusely infiltrates the cerebral hemispheres and adjacent structures. Radiological and histopathological characteristics are key to establish ante-mortem diagnosis. In general, GC corresponds to a neoplasm with astrocytic differentiation and histological grade III/high degree, which presents a variable clinical course. In this report, the authors present a case of GC determining intracranial hypertension and describe the main histopathological findings and the differential diagnosis of this uncommon neoplasm.

KEYWORD: Gliomatosis Cerebri, Glioma, Astrocytoma, Brain Neoplasms.

INTRODUCTION

Gliomatosis cerebri (GC) is a rare, aggressive, diffuse glioma showing an extensive infiltration of a large region of the central nervous system (CNS), usually bilateral, with involvement of at least three cerebral lobes, including deep gray matter. The most common affected areas are the cerebral hemispheres (76%), the mesencephalon (52%), the pons (52%), the thalamus (43%), the basal ganglia (34%), and the cerebellum (29%). (1, 2, 3)

GC most commonly shows an astrocytic differentiation, with occasional cases exhibiting an oligodendroglioma and/or oligoastrocytoma pattern. The peak of incidence is found between 40 and 50 years and males presenting somewhat earlier than females. (1, 2, 4)

Herein, the authors present a case of GC in a male patient exhibiting intracranial hypertension, and discuss morphologic and clinical findings of this uncommon neoplasm.

CASE REPORT

A male patient, 36 years, was taken to hospital service referring headache, nausea and dizziness in the last thirty days. On physical examination, there were no focal neuro-

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logical deficits. The hypothesis of intracranial hypertension was then suggested. The computed tomography (CT) and magnetic resonance (MR) imaging showed a large infiltrating process compromising left frontal lobe, which extended to the corpus callosum, parietal lobe, and right frontal lobe, with discrete contrast uptake (figure 1). The CT/MRI scans of the chest and abdomen found no changes. The symptoms showed moderate remission after employment of corticosteroids. During hospital stay, papilledema of the optic nerve and an increased cerebrospinal fluid pressure on lumbar puncture were identified. Cytological examination of cerebrospinal fluid showed no atypical or malignant cells. The patient underwent to a stereotactic biopsy. Various fragments of the lesion (measuring 1.1x0.2 cm on average) from seven different areas were obtained (targets distanced from each other 0.5 mm). At microscopy, an infiltrating neoplasm constituted by monomorphic glial cells, with an astrocytic phenotype, bland cytologic atypias and low cellularity, was evaluated. The lesion exhibited a low mitotic index (figure 2), without recognizable areas of necrosis, significant atypia, and exuberant vascular proliferation. The process revealed positive immunoexpression for GFAP, and a weak immunoexpression for Ki67 in about 02% of cells. Occasional cells showed weak immunoexpression for p53 protein. The pathological findings associated with clinical and imaging data were then consistent with GC. The patient was referred for radiotherapy, without relevant signs of tumor regression after a clinical follow-up of sixty days.

DISCUSSION

GC is currently defined as a pattern of extensive glioma infiltration. Early studies of GC consisted exclusively of autopsy examination, since the antemortem diagnosis of GC can be difficult. The term gliomatosis is reserved for tumors in which the infiltrative capability is seemingly out of proportion to the degree of anaplasia observed, and without tendency to form areas of concentrated celularity. The employment of MR imaging techniques (especially T2- weighted and FLAIR sequences) combined with adequate tissue sampling, allow diagnosis during life. GC is radiologically widespread, and the lesion usually occupies a greater part of a cerebral hemisphere. (1, 2, 3, 5, 6, 7, 8) On CT scans, GC may appear as a poorly defined, very subtle low density or isodensity lesion. On T2- weighted or FLAIR MR scan, the lesion is an extensive area of high signal intensity, and the extension of GC can be fully appreciated. The results of these techniques are comparable with autopsy studies. The radiologic features of some lesions include the involvement of one entire cerebral hemisphere, others show an infiltrating process bilaterally, and some processes center on the basal ganglia and thalamus. In contiguity, GC can involve supratentorial compartment, posterior fossa, and spinal cord. Mass effects may be subtle and cortical gray matter can be expanded in some cases. Contrast enhancement is not a common finding of GC, except in cases related to malignant progression. (1, 2, 3, 5, 6, 7, 8)

The neoplasm usually affects adults. The signs and symptoms vary considerably depending on the CNS areas compromised. Alterations in behavior and dementia are frequent clinical expressions. Lethargy, seizures, headache, pyramidal symptoms / gait disturbances, cranial nerve disfunction, increased intracranial pressure, spinocerebellar deficits, sensory deficits, paraesthesia, and visual disturbances are also apparent in some cases. (2, 3, 6, 8, 16)

GC can be divided into primary and secondary types. Primary GC (PGC) shows extensive involvement of CNS at the initial clinical investigation. Secondary GC is characterized by progressive infiltration of the CNS by a locally infiltrative diffuse glioma previously determined on clinical investigation. PGC can also be divided in type 1 (classical form in which no tumor mass is present at initial clinical evaluation), and type 2 (in which an extensive CNS involvement is associated with a tumor mass). (2) On gross examination, GC is a widely invasive, swollen, firm,

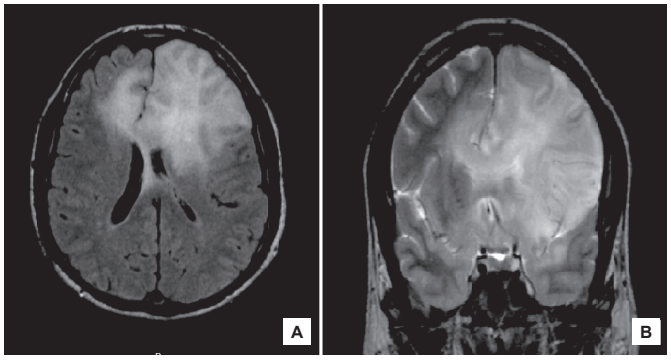


Figure 1 – Gliomatosis Cerebri: an infiltrating process that permeate large regions of the brain (A= axial FLAIR MR imaging, B= coronal T2-weighted MR imaging).

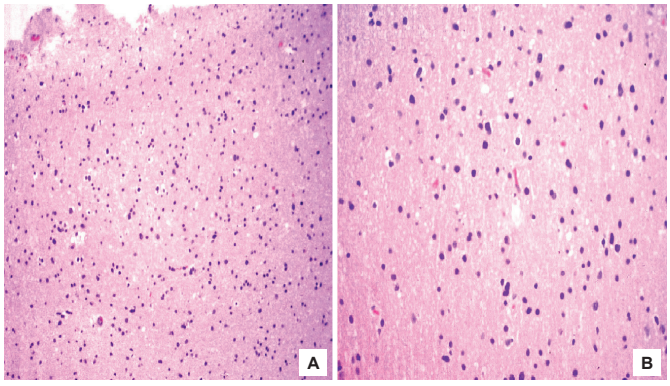


Figure 2 – Gliomatosis Cerebri: a neoplastic process showing low degree of cellularity and bland cytologic features, HE, (A= 100x, B = 200x).

Table 1 – Summary of some rare cases of GC.

Authors	Age / Gender	Clinical Findings	Treatment Modality	Outcome
Gleiznienė (12)	43 / M	Pain in the legs and headache	Radiotherapy	Unavailable
Jimenez Caballero (13)	38 / M	Partial seizures and behavior disorder	Surgery	Developed Glioblastoma several months later
Inoue (14)	33 / F	Visual disturbance	Surgery + chemotherapy + radiotherapy	Developed Glioblastoma, died 9 years
Komeno (15)	77 / F	Left hemiparesis and dysartharlgia	Surgery	Unavailable
Nishioka (4)	46 / F	Right hemiparesis and disorientation	Clinical status precluded treatment	Died 2 weeks
San Millan (6)	68 / F	Gait disturbance and episodic seizures	Clinical status precluded treatment	Died 2 months
Schoenen (7)	62 / M	Right hemiparesis, sensory aphasia and right hemianopsia	Clinical status precluded treatment	Died 8 months
Sun (16)	39 / F	Dizziness, headache, unsteady gait, vomiting, and consciousness disturbance	Surgery + radiotherapy	Signs of tumor regression after 19 months
Val Filho (17)	3 / M	Hydrocephalus, paraparesis and difficult in walking	Surgery, chemotherapy and radiotherapy	Clinically stable after 6 years, marked syringomyelia
Yamada (11)	29 / M	Mild headache	Surgery + radiotherapy + chemotherapy	Died 12 months
Present report	36 / M	Headache, nausea and dizziness	Radiotherapy	Follow-up of 60 days without relevant signs of tumor regression

ill-defined process affecting large regions of the brain. GC may not be evident even in large lobectomy specimens. The gray-white matter transition is effaced. At microscopy, GC shows a wide variety of histological and cytologic findings, including considerable variation in cellularity. Some cases show so minimally increase in cellularity that the diagnosis is very difficult to make in small biopsies. The accumulation of neoplastic cells around vessels, neurons, and subpial / subependymal regions are common. The degree of cytologic atypia varies from bland cells to those with anaplastic features. In most cases, the cytologic features are those associated with a low- to medium grade process. Nuclear conformation varies from round to elongate. Given the often low cellularity of GC, mitotic figures are sparse. The presence of cytologically atypical and mitotically areas are found in grade III lesions. The overall biological behavior of GC is usually of a grade III lesion. Microvascular proliferation and necrosis develop are seen only in some cases. The neoplastic cells exhibit variable immunostaining for GFAP and S100. The proliferation index correlates with grade. Ki-67 labelling index can range from 1% to 30%. In the presence of anaplastic lesions (WHO grade III), Ki-67 imunoexpression is usually higher than grade II tumors. (1, 2, 4, 5, 6, 8, 9, 11) The table shows some similar cases of GC found in the international literature and comparable to the present report.

The diagnosis of GC can be established only in conjunction with characteristic radiological findings. The differential diagnosis includes normal brain, reactive gliosis, and diffuse astrocytoma of grade II, III or IV. The distinction from normal brain is based on cellularity and nuclear atypia. In reactive gliosis, the astrocytes are uniformly spaced, with neither atypical proliferative activity nor abnormal clustering. The reactive astrocytes shows long, radiating cytoplasm processes. Increased cellularity, microcyst formation, and radiologic parameters are fundamental to establish the diagnosis of infiltrative diffuse glioma, since GC shows cytologic findings similar to a diffuse astrocytoma. The clinical course of GC varies considerably, with survival periods that range from months to many years. It´s expected a more aggressive behavior in cases of GC associated with high mitotic index and/or significant cytological atypia. (1, 4, 5, 6, 7, 9, 11, 13)

FINAL COMMENTS

Classical GC most commonly exhibits an astrocytic phenotype, and the process can represent a subtype of otherwise diffuse glioma showing exceptional infiltrative capacity, or it results from a synchronous neoplastic transformation of an extensive area within the CNS. (1, 2) Herein, the authors described a case of GC in a male patient showing symptoms related to an increase in the intracranial pressure. Although a short clinical follow-up of 60 days, and a discrete sign of tumor regression, it is expected a poor prognosis to this case.

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