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Epidemiological Profile and findings found intra operatively of Glioblastoma at the Neurosurgery Service of Santa Casa of Ribeirão Preto Hospital - SP - Brazil

Perfil epidemiológico y hallazgos intraoperatorios de los Glioblastomas en el Servicio de Neurocirurgia del Hospital Santa Casa de Ribeirão Preto - SP - Brasil

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Resumen

Introducción: El Glioblastoma (GB) o Astrocitoma grado IV (OMS), representan 15-20% de los tumores del SNC y aproximadamente 50% de los gliomas en adultos. **Objetivo:** Revelar el perfil epidemiológico del HSCMRP, correlacionar los hallazgos macroscópicos y microscópicos durante la cirugía de enero de 2011 a noviembre de 2015. **Método:** Estudio epimedeológico observacional, descriptivo, retrospectivo, 429 casos de tumores intracraneales a partir de los datos obtenidos de los archivos de La institución y los registros patológicos de los pacientes tratados quirúrgicamente. **Resultados:** Tumores encontrados 429 y 96 (22,37%) GB, edad media de 59 años, predominante séptima década 33%. Una relación entre mujeres y hombres fue de 1:1.12, respectivamente. Las quejas más frecuentes: dolor de cabeza (58%), confusión (41%), hemiparesia 37%. Comorbilidades frecuentes: hipertensión (64%), diabetes (22%) y fumadores (24%). La topografía más común fue la frente izquierdo. El tiempo medio de inicio de los síntomas a la cirugía fue de 39 días. Resección completa en 76% de los casos. La duración media de la recurrencia fue de 96 días, en 68% de los pacientes se observó una exuberancia de los vasos trombosados durante la cirugía Hallazgos patológicos: necrosis 98%, mitosis atípica 96%, proliferación microvascular 73% y polimorfismo nuclear 57%. **Discusión:** GB estado del arte. **Conclusión:** Nuestros resultados son similares con la literatura. Observación intraoperatoria de vasos trombosados y agresividad tumoral en pacientes con peor pronóstico y menor tiempo de recaída sugiere que es real, sin embargo. El pequeño número de casos, necesita más investigación, incluyendo otros hallazgos y resultados inmunohistoquímicos.

Palabras clave: Glioblastoma, Intra operatorio, perfil epidemiológico, Neurocirugía, cirugía Neurológica.

Abstract

Introduction: Glioblastoma (GB) or Astrocytoma grade IV (WHO), represent 15-20% of CNS tumors and approximately 50% of gliomas in adults. **Objective:**Reveal the epidemiological profile of HSCMRP, correlate macroscopic and microscopic findings during surgery treated from January 2011 to November 2015. **Method:** Observational epimdeiological study, descriptive, retrospective, of medical records of 429 cases of intracranial tumors from data obtained from the files of the institution and pathological records of patients treated surgically. **Results:** Total tumors found 429 and 96 (22.37%) GB with a mean

age of 59 years, predominant seventh decade of life 33%. A relationship between women and men was with little difference 1:1.12, respectively. The most common complaints were headache (58%), confusion (41%), hemiparesis 37%. Most prevalent comorbidities: hypertension (64%) and diabetes (22%) and smokers (24%). Most common topography were followed by left front lesions. The average time of onset of symptoms to surgery was 39 days. Complete resection in 76% of cases. The mean length of postoperative recurrence was 96 days, in 68% patients were noticed an exuberance of thrombosed vessels during surgery. Pathological findings: necrosis 98%, atypical mitosis 96%, microvascular proliferation 73% and nuclear polymorphism 57%. **Discussion:** GB state of art. **Conclusion:** Our results are very slightly with the literature. The association of intraoperative observation thrombosed vessels, and tumor aggressiveness in patients with worse prognosis and shorter time to relapse, suggests that it is real, however, the small number of cases, needs further investigation, including other findings and immunohistochemical results.

Key words: Glioblastoma, Intra operative, epidemiological profile, Neurosurgery, Neurological surgery.

Introduction

GB is the most frequent primary brain tumor and the most malignant neoplasm with predominant astrocytic differentiation; histopathological features include nuclear atypia, cellular pleomorphism, mitotic activity, vascular thrombosis, microvascular proliferation and necrosis. It typically affects adults and is preferentially located in the cerebral hemispheres. Most GB manifest rapidly, without recognizable precursor lesions primary glioblastoma. Secondary GB develop slowly from diffuse astrocytoma WHO grade II or anaplastic astrocytoma (WHO grade III). Due to their invasive nature, GB cannot be completely resected and despite progress in radio/chemotherapy, less than half of patients survive more than a year, with older age as the significant adverse prognostic factor. GB and its variants correspond to WHO grade IV.
Incidence GB is the most frequent brain tumor, accounting for approximately 12-15% of all intracranial neoplasms and 60-75% of astrocytic tumors[3,4]. Age and sex distribution GB may manifest at any age, but preferentially affects adults, with a peak incidence at between 45 and 75 years of age[3]. Localization GB occurs most often in the subcortical white matter of the cerebral hemispheres. In a series of 987 GBV from the University Hospital Zurich, the most frequently affected sites were the temporal (31%), parietal (24%), frontal (23%) and occipital lobes (16%)[5,17,19].

Methods

Epidemiological study observational, descriptive, retrospective, of medical records of 429 cases of intracranial tumors from January 2011 to November 2015 period, obtained from the files of the institution and pathological records of patients treated surgically. The variables were: age, sex, comorbidities, preoperative clinical, time of onset of symptoms to surgery, topography, preoperative clinical, macro and microscopic aspects intraoperatively, degree of resection and time to relapse. A literature review were made using PubMed, Medline, Science Direct, Embase, Clinical Trials, Ebsco, and Scielo. Found 120 articles, selected 39, incluing articles worldwide about GBM. Not all variables were found in all patients in the medical records, so the statistics were made on the amount of patients in the variable appeared. It was a retrospective study there were losses of medical records, segment losses in service.

Results

Total tumors found 429 from January 2011 to November 2015 period. The total of GBM were 96 (22.37%). The statistics were analyzed considered a total population = 96. Variable age was identify in 78 patients. The mean age was 59,19 years (6-89 years). The majority is between the sixth decade of life: 25,64% (51-60 years) and the seventh decade of life 33,13% (61-70 years). The race variable was identify in 79 patients, predominated white people (86%), followed by, and brown (8,97%), black (3,8%). A relationship between women and men was with a little difference 1:1.12. Men was 53%, and women 47%.The clinics variable were identify in 80 patients. The most common complaints were headache (58%), confusion (41%), hemiparesis (37%) dizziness (8%), depression (8%) and seizures (8%), less than 6% were others. The comorbidities variable were identify in 54 patients. Most prevalent comorbidities: hypertension (64%) and diabetes (22%), smokers (24%). Most common topography were left front 17,18%, followed by right temporal (14,06), left temporal, 10,9% each one. The average time of onset of symptoms to surgery were identify in 75 patient. Spent 39,26 days for inicial symptoms. The resection variable were identify in 68 patients, doing in 76,47% of cases. The recurrence variable were identify in 36 patients. The mean length of postoperative recurrence was 96 days. In 22 cases of this group (22.9%) who had relapsed in less than 60 days,15 patients (68%) were noticed an exuberance of thrombosed vessels during surgery, with matching patients with short time to relapse. The pathological findings variable were identify in 52 patients. Pathological findings: necrosis 98%, atypical mitosis 96%, microvascular proliferation 73% and nuclear polymorphism 57%.

Discussion

Tumor infiltration often extends into the adjacent cortex and through the corpus callosum into the contralateral hemisphere ('butterfly glioma'). GB of the basal ganglia and thalamus is not uncommon, especially in children. IntraventricularGB is exceptional[5]. Brain stem GB Is infrequent and often affects children[6]. Cerebellum and spinal cord are rare sites for this neoplasm. The natural history disease of the disease is usually short (less than 3 months in more than 50% of cases). Symptoms

and signs of raised intracranial pressure (for example headache, nausea/vomiting with papilledema) are common. Up to one third of patients will experience an epileptic seizure episode. Non-specific neurological symptoms such as headache and personality changes can also occur[5,17].

The central necrosis may occupy as much as 80% of the total tumor mass[6-17]. GB are typically stippled with red and brown foci of recent and remote hemorrhages. Macroscopic cysts, when present, contain a turbid fluid and represent liquefied necrotic tumor tissue, quite in contrast to the well-delineated retention cysts in diffuse astrocytomas WHO grade II[5,7,8].

Extension within and along perivascular spaces is another typical mode of infiltration, but invasion of the vessel lumen seems to occur infrequently[9,10]. Hematogeneous spread to extraneural tissues is very rare in patients without previous surgical intervention[11,12]. Peritoneal metastasis ventriculoperitoneal shunt pathway has been observed[13]. Penetration of the dura, venous sinus and bone is exceptional[14,15,16].

GB are poorly delineated, the cut surface showing a variable colour with peripheral grey tumor and central areas of yellowish necrosis from myelin breakdown[6,17].

Atypical mitoses are frequently present. Mitotic activity, however, can vary widely between tumor and also shows regional heterogeneity within a tumor. The growth fraction, as determined by the antibodies Ki-67/MIB-1, shows great regional variation. Mean values of 15-20% have been reported[18,19,20,21,22].

The angiogeneses of GB are among the most vascularized tumors in humans. Glioblastoma vascularization occurs through several mechanisms including[23] vessel co-option, e.g. adoption of pre-existing vessels by migrating tumor cells[24], classical angiogenesis, e.g. sprouting of capillaries from preexisting vessels by endothelial cell proliferation and migration and[25] vasculogenesis, e.g. homing of bone marrow-derived cells that support vessel growth from the peripheral blood into the perivascular space[23,24].

Hypoxia is considered a major driving force of GB angiogenesis[25] and leads to intracellular stabilization of the hypoxia master-regulator hypoxiainducible factor 1-α (HIF-1α). HIF-1α accumulation leads to transcriptional activation of more than 100 hypoxiaregulated genes that control angiogenesis (VEGF, angiopoietin), cellular metabolism (carbonic anhydrase, lactate dehydrogenase), survival apoptosis (BNIP) and migration (c-met, CXCR4). Vascular endothelial growth factor (VEGF) appears to be the most important mediator of glioma-associated vascular dysfunctions. VEGF induces tumor angiogenesis, increases vascular permeability (edema) and regulates homing of bone marrow derived cells[25].

Tumor necrosis is a fundamental feature of GB, and its presence is one of the strongest predictors of aggressive clinical[26,27,28]. These regions appear grossly as a yellow or white granular coagulum[29,30,31,32]. These pseudopalisading necrosis are equally frequent in primary and secondary glioblastoma[33]. The relationship of pseudopalisading necrosis to the larger regions of confluent necrosis has not been clearly defined, yet some have suggested that there is a temporal evolution. Compared to adjacent tumour cells, pseudopalisading cells have higher rates of apoptosis and lower rates of proliferation[34]. They also are hypoxic and strongly express HIF-1α and its transcriptional target VEGF[35]. Hypoxic up regulation of VEGF and other pro-angiogenic factors is considered to be responsible for the microvascular proliferation noted in glioblastoma[36,37].

Genetics alteration in 95% of cases astrocytes or precursor originate Primary glioblastoma (grade IV), less 3 months (68%), less 6 months (84%). LOH 10q (70%), EGFR amplification (36%), p16 deletion (31%), TP53 Mutation (28%), PTEN Mutation (25%). In 5% of astrocytes or precursor originate secondary GB. Low grade astrocytoma(grade II) comes with TP53 mutation (59%), after about 5.1 years originate anaplasic astrocytoma (grade III) with TP53 mutation (53%), after about 1.9 years originate secondary glioblastoma (grade IV) with LOH 10q (63%), EGFR amplification (8%), p16 delection (19%), TP53 mutation (65%), PTEN Mutation (4%). Malignant transformation of neuroepithelial cells is a multistep process driven by the sequential acquisition of genetic alterations. One would therefore expect that of all astrocytic neoplasms, GB should contain the greatest number of genetic changes, and this is indeed the case. On the basis of the different combinations of TP53 mutations, loss of heterozygosity (LOH) on chromosomes 10 and 17p and EGFR amplification, the presence of subsets of GB with distinct genetic alterations[38,39].

The object of this paper is to make a review about GBin literature, and reveal the epidemiological profile of Santa Casa of Ribeirão Preto Hospital, correlate macroscopic and microscopic findings during surgery with tumor aggressiveness of GBMs, treated from January 2011 to November 2015.

Conclusion

Our results vary slightly with the literature. The association of intraoperative observation thrombosed vessels, tumor aggressiveness in patients with worse prognosis and shorter time to relapse, suggests that it is real, however, the small number of cases, needs further investigation, including other findings and Immunohistochemistry results.

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