Anatomopathological and Immunohistochemical Profile of Gliomas of Patients in the Region of Maringá-PR

doi: https://doi.org/10.32635/2176-9745.RBC.2021v67n3.1287

Perfil Anatomopatológico e Imuno-histoquímico de Gliomas de Pacientes da Região de Maringá-PR

Perfil Anatomopatológico e Inmunohistoquímico de Gliomas en Pacientes la Región de Maringá-PR

Adriana Domingues Valadares[1]; Alice Maria Souza-Kaneshima[2]; Edilson Nobuyushi Kaneshima[3]; Igor Lima Fernandes[4]; Igor Passareli Jordão[5]; Paola da Costa Souza[6]; Tarik Radi Campos Maftoum[7]

ABSTRACT

Introduction: Gliomas represent 80% of the central nervous system tumors. World Health Organization (WHO) has added, in 2016, molecular features to the classification of gliomas. The pathophysiology and risk factors of these tumors are not yet fully understood. **Objective**: Perform a retrospective analysis of immunohistochemical and anatomopathological reports of gliomas. **Method:** Cross-sectional, retrospective and descriptive study carried out from anatomopathological and immunohistochemical exams made between January 2014 and December 2018 in a pathological anatomy laboratory in the city of Maringá-PR. Of the 234 reports related to the term glioma, 204 were selected for this study. **Results:** Astrocytic, ependymal and oligodendroglial tumors were found, with astrocytomas accounting for the majority (86.8% of the cases found). Mean age at diagnosis was 51.8 years and the prevalence was higher in men. Furthermore, immunohistochemically detectable mutations were analyzed, such as *p53* (mutated in 66.7% of those tested), isocitrate dehydrogenase (IDH) (28.6% mutated), X-linked alpha-thalassemia mental retardation (ATRX) (21.0%) and diagnostic markers such as positive epithelial membrane antigen (EMA) in all analyzed ependymomas. **Conclusion:** The necessity of further researches on gliomas is undeniable , both epidemiologically considering the new classification and within the clinical and pathophysiological scope in order to improve the understanding of the pathology and the treatment for the patients.

Key words: Glioma; Glioblastoma; Astrocytoma; Immunohistochemistry; Molecular Epidemiology.

RESUMO

Introdução: Os gliomas representam 80% dos tumores do sistema nervoso central. A Organização Mundial da Saúde (OMS) adicionou, em 2016, critérios moleculares na classificação dos gliomas. A fisiopatologia e os fatores de risco desses tumores ainda não são totalmente conhecidos. **Objetivo:** Realizar uma análise retrospectiva dos laudos anatomopatológicos e imuno-histoquímicos de gliomas. **Método:** Estudo transversal, retrospectivo e descritivo, a partir de exames anatomopatológicos e imuno-histoquímicos realizados entre janeiro de 2014 e dezembro de 2018 em um laboratório de anatomia patológica na cidade de Maringá-PR. Dos 234 laudos relacionados com o termo glioma, 204 foram selecionados para este estudo. **Resultados:** Foram encontrados tumores astrocitários, ependimários e oligodendrogliais, sendo que os astrocitomas corresponderam à maioria (86,8% dos casos encontrados). A média de idade ao diagnóstico foi de 51,8 anos e houve maior prevalência desses tumores no sexo masculino. Também foram analisadas mutações detectáveis por imuno-histoquímica como *p53* (mutada em 66,7% dos testados), isocitrato desidrogenase (IDH) (28,6% mutados), *X-linked alpha-thalassemia mental retardation* (ATRX) (21,0%) e marcadores diagnósticos como o *epithelial membrane antigen* (EMA) positivo em todos os ependimomas analisados. **Conclusão:** É inegável a necessidade de novas pesquisas sobre os gliomas tanto no campo epidemiológico, tendo em vista a nova classificação, quanto no escopo fisiopatológico e clínico, com o objetivo de melhorar o entendimento sobre a patologia e o tratamento dos pacientes.

Palavras-chave: Glioma; Glioblastoma; Astrocitoma; Imuno-Histoquímica; Epidemiologia Molecular.

RESUMEN

Introducción: Los gliomas representan 80% de los tumores del sistema nervioso central. La Organización Mundial de la Salud (OMS) agregó, en 2016, criterios moleculares sobre como clasificar los gliomas. La fisiopatología y los factores de riesgo de estos tumores aún no se comprenden completamente. **Objetivo**: Realizar un análisis retrospectivo de informes inmunohistoquímicos y anatomopatológicos de gliomas. **Método:** Estudio transversal, retrospectivo y descriptivo con base em pruebas anatomopatológicas e inmunohistoquímicas realizadas entre enero de 2014 y diciembre de 2018 en un laboratorio de anatomía patológica de la ciudad de Maringá-PR. De los 234 informes relacionados con el término glioma, se seleccionaron 204 para este estudio. **Resultados:** Se encontraron tumores astrocíticos, ependimarios y oligodendrogliales, siendo los astrocitomas la mayoría (86,8% de los casos encontrados). La edad media al diagnóstico fue de 51,8 años y hubo una mayor prevalencia de estos tumores en el sexo masculino. También se analizaron mutaciones detectables inmunohistoquímicamente, como *p53* (mutado en 66,7% de los analizados), isocitrato desidrogenase (IDH) (28,6% mutado), *X-linked alpha-thalassemia mental retardation* (ATRX) (21,0%) y marcadores de diagnóstico como *epithelial membrane antigen* (EMA) positivo en todos los ependimomas analizados. **Conclusión**: Es innegable la necesidad de profundizaren las investigaciones sobre los gliomas, tanto en el campo epidemiológico, ante la nueva clasificación, como en el ámbito fisiopatológico y clínico, con el objetivo de mejorar el conocimiento sobre la patología y el tratamiento de los pacientes.

Palabras clave: Glioma; Glioblastoma; Astrocitoma; Inmunohistoquímica; Epidemiología Molecular.

[1]Independent Investigator. Maringá (PR), Brazil.
[2,3,5,6,7]Universidade Estadual de Maringá (UEM). Maringá (PR), Brazil.
[4]Laboratório Bacchi. Botucatu (SP), Brazil.
[6]Laboratório Souza. Maringá (PR), Brazil.
[1]E-mail: advaladares@icloud.com. Orcid iD: https://orcid.org/0000-0002-7891-9290
[2]E-mail: amskaneshima@uem.br. Orcid iD: https://orcid.org/0000-0002-9460-4643
[3]E-mail: enkaneshima@uem.br. Orcid iD: https://orcid.org/0000-0002-2725-8007
[4]E-mail: igor_lfernandes@hotmail.com. Orcid iD: https://orcid.org/0000-0003-0377-0441
[5]E-mail: igorjordao98@gmail.com. Orcid iD: https://orcid.org/0000-0003-4217-5557
[6]E-mail: pcsouza2@uem.br. Orcid iD: https://orcid.org/0000-0002-9661-6736
[7]E-mail: tarikmaf@gmail.com. Orcid iD: https://orcid.org/0000-0002-3266-7921
Corresponding author: Igor Passareli Jordão. Rua Marechal Hermes da Fonseca, 50 – Centro. Loanda (PR), Brazil. CEP 87900-000. E-mail: igorjordao98@gmail.com

INTRODUCTION

Gliomas are part of a heterogeneous group of tumors of the central nervous system (CNS), arising from glial cells, that is, astrocytic, oligodendrocytes and ependymal cells[1]. It is estimated that annually, nearly 11 thousand cases of primary tumors of CNS occur in Brazil, causing more than nine thousand deaths[2]. Approximately 80% of the CNS malignant tumors are gliomas[3].

The incidence of gliomas varies broadly worldwide; the world mean is 3.4 cases per 100 thousand inhabitants annually with predominance of males. In USA, the estimate is 7.15 cases per 100 thousand inhabitants per year, while in Brazil, is 5.8 cases per year for each 100 thousand inhabitants. The occurrence in the Southern Region is considerably higher, with 10.17 cases in males per 100 thousand inhabitants per year and 8.52 cases in women per each 100 thousand inhabitants per year[2,4].

The 2016 WHO classification is based in phenotypes and molecular parameters to typify the tumors, adding the immunohistochemical and molecular biology to the classical anatomopathological exam[1].

Gliomas are subdivided in diffuse astrocytic, other astrocytic, ependymal gliomas and other gliomas. Diffuse astrocytic gliomas include most of the astrocytoma and oligodendroglioma. The glioblastoma multiforme (GBM), diffuse astrocytoma, anaplastic astrocytoma, diffuse midline glioma and all the oligodendroglioma are part of this group. The isocitrate dehydrogenase gene (IDH) plays a key role in the diagnostic of gliomas. The enzyme IDH catalyzes the reaction of the isocitrate for alpha-ketoglutarate, the mutation of isoforms 1 and 2 produces the oncometabolite 2-hydroxiglutarate, inhibiting the functions of enzyme-dependent alpha-ketoglutarate. More than 90% of these mutations occur in the residue IDH-1 132, which is the alteration identified by immunohistochemical technique, allowing to classify the gene in mutant or wild[5,6].

Other astrocytomas can be differentiated from other diffuse astrocytic tumors by the circumscribed growth pattern and for not presenting IDH mutation. The pleomorphic xanthoastrocytoma and the pilocytic astrocytoma belong to this group. The ependymal gliomas are tumors of ependymal origin, being ependymoma the main example. Other gliomas are rarer variants that do not fit in the other groups[1,7].

The physiopathology of gliomas remain obscure in several aspects. The most studied risk factors are mobile phones and ionizing radiation. Allergies are considered protective factors. Family carcinogen syndromes as for instance, neurofibromatosis types I and II, Li-Fraumeni syndrome among others cause gliomas, however, correspond to less than 5% of the cases[4]. Pesticides, mainly organophosphates have also been studied as possible risk factors for gliomas[8,9].

The objective of this article was to conduct a retrospective study of the prevalence of brain tumors of the type glioma in a laboratory of Pathological Anatomy in the city of Maringá-PR from January 2014 to December 2018.

METHOD

Cross-sectional, retrospective, and descriptive study from anatomopathological and immunohistochemical reports from January 2014 to December 2018 in a laboratory of Pathological Anatomy in the city of Maringá-PR. The Institutional Review Board of *Universidade Estadual deMaringá* (Report number 4.254.657) approved the study.

A proprietary form was elaborated to collect the data with general information about the patients (age; sex and diagnostic hypothesis) and the tumor (identification of the tumor type, staging and grading) in addition to molecular markers identified by immunohistochemistry, specially IDH, X-linked alpha-thalassemia mental retardation (ATRX) and p53. The key-words gliomas, astrocytomas and ependymomas were utilized to access the information in the system and in the reports selected, the patient identification was coded, the name or any identifying information was unable to be obtained. All the reports where age and sex were not informed or with incomplete data or that failed to present morphological findings of the gliomas were excluded. The anatomopathological and immunohistochemical results obtained from the data collected were tabulated and classified in different biological categories as recommended by The 2016 World Health Organization Classification of Tumors of the Central Nervous System[1].

RESULTS

237 anatomopathological reports with diagnosis or suspicion of glioma (204 reports were utilized in the study, 33 were rejected) were selected from January 2014 to December 2018, in addition to 106 reports of immunohistochemistry.

In the present casuistic, 178 cases were encountered (87.2%) diagnosed as astrocytomas, of which, 139 (78.1%) were glioblastomas (one of them was diagnosed as gliosarcoma and another case, as large cells glioblastoma, subtypes of IDH glioblastomas by WHO), 20 (11.2%), diffuse astrocytomas grade III, six (3.4%), anaplastic astrocytomas grade III, ten (5.6%), pilocytic astrocytomas

and three (1.7%), xanthoastrocytoma. Of the 14 (6.9%) ependymal tumors found, nine (64.3%) were ependymomas grade II, two (14.3%) sub-ependymoma, with positive RELA-fusion and one (7.1%), anaplastic ependymoma. Among the nine oligodendroglial neoplasms (4.4%), two were anaplastic oligodendrogliomas (22.2%) and seven (77.8%), oligodendrogliomas grade II. One case (0.5%) of oligoastrocytoma (mixed tumor) and two diffuse midline gliomas (1%) were also found.

Table 1 shows great occurrence of astrocitary lineage tumors (178) followed by ependymal and oligodendroglial neoplasms. Male patients represent more than two thirds of the cases, with 69.1% and female patients correspond to 30.9% of the total analyzed in this article. The mean age at diagnosis was 51.8 years (SD±18.7). In average, gliomas in males were identified at 49.9 years while in females, it was around 55.2 years old. Incidence increases with age until reaching the peak between 50 and 59 years, declining later as shown in Figure 1.

The immunohistochemical analysis of the astrocytic tumors (Figure 2) shows mutation of IDH in 18 tumors (27.7%) and the wild gene in 47 (72.3%). It is observed an increasing presence of IDH-wildtype with age; the case of the oldest patient with IDH-mutant was at 56 years old. Among the astrocytomas grade II, 11 presented mutation

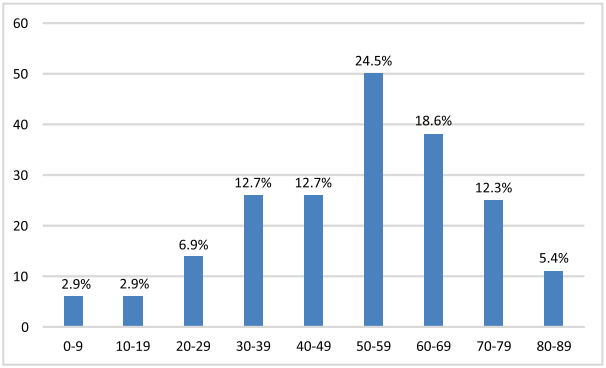

Figure 1. Tumors per age-range

and five were negative; of the anaplastic astrocytomas with immunohistochemistry, two had IDH mutated and two did not present mutation. For glioblastomas, six had IDH-mutant and 37, IDH-wildtype.

Of the 106 tumors where immunohistochemistry was performed, 84 (76.4%) had positive glial fibrillary acidic protein (GFAP). The mutation of histone H3.3K27M was present in the two diffuse midline gliomas and no negative results were found.

There was loss of ATRX in 13 (21.0%) of the 62 tumors, where the antigen was tested, all with IDH-mutant. For the remaining 49 (79.0%) without loss of

Table 1. Classification of gliomas and incidence related to sex and age

Origin	Diagnosis	Men (%)	Women (%)	Total	Mean Age	Age-range
Astrocyte	Glioblastoma	96 (69.1%)	43 (30.9%)	139	58.7 (SD±14.2)	12-88
Astrocyte	Diffuse astrocytoma (grade II)	14 (70.0%)	6 (30.0%)	20	39.9 (SD±13.9)	21-80
Astrocyte	Anaplastic astrocytoma (grade III)	5 (83.3%)	1 (6.7%)	6	53.5 (SD±20.1)	28-70
Astrocyte	Pilocytic astrocytoma	8 (80.0%)	2 (20.0%)	10	14.9 (SD±11.3)	2-30
Astrocyte	Xanthoastrocytoma	2 (66.8%)	1(33.3%)	3	36 (SD±19.7)	18-57
Ependymal	Ependymoma (grade II)	4	5	9	43 (SD±17.9)	23-69
Ependymal	Subependymoma	2	0	2	56.5 (SD±0.7)	56-57
Ependymal	RELA-fusion positive ependymoma	2	0	2	13.5 (SD±10.6)	6-21
Ependymal	Anaplastic ependymoma	1	0	1	18	18
Oligodendroglial	Oligodendroglioma	6 (66.7%)	3 (33.3%)	9	46.78 (SD±12.6)	34-74
Mixed	Oligoastrocytoma	0 (0)	1 (100%)	1	45	45
Astrocyte	Diffuse midline glioma	1 (50%)	1 (50%)	2	18 (SD±14.1)	8-28
	Total	**141 (69.1%)**	**63 (30.9%)**	**204**	**51.8 (SD±18.7)**	**2-88**

ATRX, there was predilection for IDH-wildtype, adding 40 of this type (83.7% of which did not have loss). Mutations of p53 were examined in 27 tumors, with positivity in 18 (66.7%); most (9; 81.8%) of the IDH-mutant also had alteration of p53; in the IDH-wildtype, nine (56.3%) had the mutation and seven (43.8%) were normal for p53. All ependymomas, where the epithelial membrane antigen – EMA was tested, were positive.

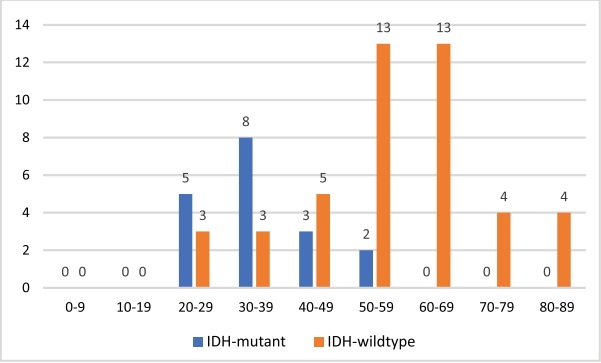

Figure 2. Distribution of IDH-wildtype and mutant per age-range in diffuse astrocytomas

DISCUSSION

The 2016 WHO classification changed the criteria of category of CNS tumors, giving to immunohistochemistry analysis the central role and adding molecular parameters for more conclusive diagnoses[1]. Few are the studies that bring new markers, it is very important to review the epidemiology of the gliomas under this new classification.

It is also important to highlight that not always the molecular biology-based techniques are available, hindering the diagnosis considered ideal by WHO. In Brazil, it is difficult to utilize these techniques since in this study it was not possible to perform the immunohistochemistry analysis of all the patients and of the other molecular tests suggested in the 2016 WHO classification[1].

For many years, the specific expressions of proteins of intermediate filament by tissues have been instrumental in the diagnosis of tumors. The GFAP is an example of intermediate filament, is present in astrocytes (mature and in development), ependymal cells and radial glia of the brain in development; in addition, is the most frequent marker utilized in diagnostic neuropathology[10]. The positive reaction to GFAP was demonstrated in astrocytomas, ependymomas and astrocytic cells of mixed gliomas, large cells astrocytoma, sub-ependymal, pleomorphic xanthoastrocytoma, astroblastoma and gliosarcoma. In the present study, of the 106 tumors where immunohistochemistry was performed, 84 (76.4%) were positive for GFAP.

Diffuse gliomas

The patients with glioblastomas belong to a group with high incidence and mortality among the gliomas and CNS tumors. In the study sample, there is a slightly higher incidence in males than described in the literature and at earlier age[7]. GBM has a 5-year 6.8% survival[11]; its erratic form which needs great margin of dissection and high relapse rates explains the elevated mortality. The glioblastomas represent more than two thirds of the gliomas encountered in this casuistic. Similar results were found in other studies, making it indispensable a better understanding of a tumor whose mortality is so high[12-15].

It was not possible to identify the factor that led to a predilection of GBM for males (69.1%) in this study, while other national authors present this predilection between 55% and 66%[12,14,15].

The identification of the mutation or not of the isocitrate dehydrogenase is fundamental for the prognosis and in the response to temozolomide, main chemotherapeutic in the treatment of these tumors[16]. Glioblastomas which have this mutation also called secondary glioblastomas, evolve less aggressively (astrocytomas grades II and III) and have better prognosis/response to the chemotherapic – specially temozolomide. Primary GBM, which appears as astrocytomas grade IV are more common and have worse survival[3,17].

The IDH-mutant glioblastomas have prognosis of 31 months of life and represent 10% of GBM, while IDH-wildtype glioblastomas have prognosis of 15 months and represent 90% of the tumors. The IDH-mutant and wildtype glioblastomas occur according to the literature, at 44 and 62 years in average, respectively[17]. In the present study, IDH-mutant glioblastomas constitute 13.6% with mean age of 37.3 years against 86.4% of IDH-wildtype and mean age of 59.6. In Figure 2, it is seen a clear tendency of increase of IDH-wildtype in the astrocytomas as a whole according to the age.

In the astrocytomas grades II and III the percentage of mutation expected for IDH is from 70% to 80%, differing from grade IV which presents nearly a contrary relation[17]. These tumors evolve to more advanced forms in many cases and are called secondary glioblastomas. Among the 18 astrocytomas grade II and III with IDH investigated, two thirds present alteration. The mortality is variable and recent studies have related this number with specific mutations not yet utilized clinically. Excepting the pediatric age-range, said tumors are found in practically every age, with peak between 30 and 40 years old, declining progressively as age advances[18]. Typically, there is tumor progression along the years, even after the correct treatment[7]. The mutation of K27M of the histone H3 defines a new entity created by the classification of

2016, the diffuse midline glioma H3 K27M-mutant. In addition to the mutation, it stands out the location in sites close to the midline in the thalamus, brainstem, and bone marrow. Children and young adults are the groups generally affected by the midline gliomas[7,19], as the results show – one 8-year-old and another 28-years old patient.

The gene ATRX is a transcriptional regulator, its inherited mutations cause the disease they were name after, X-linked alpha-thalassemia mental retardation. However, the mutations acquired participate of the carcinogenesis, not only of the gliomas, as of the pancreatic neuroendocrine and pheochromocytoma. There is a close correlation of inactivating alterations of ATRX with IDH mutations[5]; all the cases of inactivation of ATRX were concomitant with IDH mutation in the present sample, corroborating this fact. However, nine tumors with IDH mutated had not inactivation of ATRX, that is, 14.5% of the total neoplasms with ATRX tested.

One of the genes more involved and investigated in human carcinogenesis is p53. Its mutation is strongly related to IDH mutation and is useful in the differentiation between oligodendrogliomas and astrocytomas. The mutation of the genes was concomitant in 81.8% of the cases when both were analyzed, therefore, they are astrocytomas. In IDH-wildtype, p53 has shown to be altered in 56.3% of the total.

Oligodendrogliomas and oligoastrocytomas represent less than 10% of the diffuse gliomas encountered in epidemiological studies. Recent studies revealed that molecular and epigenetic characteristics allow the reclassification of oligoastrocytoma or diffuse gliomas morphologically ambiguous in oligodendroglioma or astrocytoma. Some authors suggest, based in these conclusions, the exclusion of oligoastrocytoma as entity. Actually, the diagnosis of mixed gliomas presents the highest levels of discrepancy even among expert neuropathologists. In 1997, the discovery that low grade oligoastrocytoma typically have 1p/19q codeletion or TP53 mutation made the authors skeptical about the existence of truly mixed gliomas[20].

The oligodendrogliomas present less infiltrative pattern and have better prognosis than astrocytomas[21]. Males are more predominant[20], as the results show. Of the nine diagnoses of oligodendroglioma, only two are anaplastic. WHO recommends that both the IDH mutation and 1p/19q codeletion should be confirmed for the diagnosis of oligodendroglioma[1,21]. The oligoastrocytomas are tumors of oligodendroglial and astrocyte mixed origin. Only one oligoastrocytoma was diagnosed in a 45-years old female patient. In the last years, the diagnosis of oligoastrocytoma is not recommended as most of the tumors, earlier classified as such, can be astrocytoma or oligodendroglioma, utilizing molecular patterns[1,22].

Ependymal tumors

Ependymomas are gliomas that recapitulate normal ependymal cells. EMA shows "dot-like" and "ring-like" staining patterns, highlighting "microlumens" or intracytoplasmic rosettes, a pathognomonic ultrastructural feature of this neoplasm. It is considered a marker of normal and neoplastic epithelium and of perineural cells. Is also expressed in a variety of mesenchymal neoplasms, mesotheliomas and even lymphomas and in CNS is characteristically seen in meningiomas, chordomas, metastatic carcinomas and ependymomas[23].

RELA-fusion is the most important molecular test of ependymomas recommended currently with limited clinical implication. L1 cell adhesion molecule (L1CAM) still needs more studies, its expression in supratentorial ependymomas is associated with RELA-fusion, which indicates worse prognosis[1,24]. Only two tumors with RELA-fusion were tested, both positive. For L1CAM, two tumors were positive and one, negative. A higher percentage of male patients (64.3%) was observed also in this study. Despite occurring in any age, most of the ependymomas are detected in the pediatric population[24], which did not occur in this study, possibly because of the small sample of this subtype.

Other astrocytic tumors

Pilocytic astrocytoma is a typical tumor of the young population, brain tumor is more common in the age range from 0 to 19 years, representing 5% of the gliomas with predominance of males. The prognosis is good after surgical resection. It epidemiologically differs per age and morphologically from other astrocytoma (circumscribed pattern in contrast with irregular pattern of diffuse astrocytoma). In addition, the pilocytic astrocytoma has also its own molecular alterations as the KIAA1549-BRAF fusion which is present in 70% of these tumors[1,25]. In this study, ten cases of pilocytic astrocytoma (4.9% of the sample) with diagnosis in average at 14.9 years and 80% male patients were found.

Pleomorphic xanthoastrocytoma is a tumor that affects younger populations too and has good prognosis after surgical resection with more than 90% of 5-years survival. However, is rarer than ependymomas and is described in less than 1% of the gliomas in epidemiological studies. BRAF mutation has been the most investigated for this tumor subtype. The mean age at diagnosis is 29 years[26]. Only three patients were diagnosed with pleomorphic xanthoastrocytoma with 18, 33 and 57 years.

Risk factors for CNS tumors

Some risk factors are presented in this topic but need better evaluation in order to establish a possible relation

with other causes and allow the understanding of the high number of cases of CNS neoplasms in the State of Paraná, represented, at least partially, by this casuistic.

Between 5% and 10% of the patients affected by gliomas have relatives with the disease, which may indicate a genetic heritage and/or shared environmental risk factors[27].

The Li-Fraumeni syndrome, a mutation inherited from gene p53, is important for the genesis of several tumors, including the glial[7,27,28]. The South and Southeast Brazilian regions concentrate the cases of this syndrome, the state of Paraná has a prevalence of 0.3%, being more common in European descendants, which can be one of the causes for this population to develop more gliomas[29].

Pesticides are considered possible risk factors for the development of CNS tumors and Paraná, where this study was elaborated, is the second greatest user of pesticides in the country[30]. Since 2009, Brazil became the major user of pesticides worldwide[31], mainly glyphosate, representing 45% of the total volume[30]. Many articles have been relating the agriculture and exposure to these products, mainly organophosphates (as glyphosate) to a major risk of gliomas in young adults, in addition to leukemia, prostate and breast cancer[8,9,32]. However, it must be reminded that thorough genetic and sociodemographic studies are necessary to establish these correlations.

CONCLUSION

Most of the data found in this study corroborates the literature as the higher prevalence of gliomas in males with advanced age. In addition, the astrocytomas and among them, the glioblastomas were the most incident; the IDH-wildtype predominates over the mutant.

It is undeniable the necessity of new epidemiological, because of the new classification further to clinical and physiopathological studies about gliomas with the objective of improving the understanding about the pathology and treatment of the patients.

CONTRIBUTIONS

Alice Maria Souza Kaneshima, Edilson Nobuyushi Kaneshima, Igor Passareli Jordão, Paola da Souza Costa and Tarik Radi Campos Maftoum contributed for the study design and conception, acquisition, analysis, interpretation of the data, wording, or critical review with intellectual contribution. Adriana Domingues Valadares and Igor Lima Fernandes contributed for the study conception or design, acquisition, analysis, and interpretation of the data. All the authors approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

FUNDING SOURCES

None.

REFERENCES

1. Louis DN, Perry A, Reifenberger G, et al. The 2016 World Health Organization classification of tumors of the central nervous system: a summary. Acta Neuropathol. 2016;131(6):803-20. doi: http://doi.org/10.1007/s00401-016-1545-1
2. Instituto Nacional de Câncer José Alencar Gomes da Silva. Estimativa 2020: incidência de câncer no Brasil [Internet]. Rio de Janeiro: INCA; 2019 [acesso 2020 maio 1]. Disponível em: https://www.inca.gov.br/sites/ufu.sti.inca.local/files/media/document/estimativa-2020-incidencia-de-cancer-no-brasil.pdf
3. Omuro A, DeAngelis LM. Glioblastoma and other malignant gliomas: a clinical review. JAMA. 2013;310(17):1842-50. doi: http://doi.org/10.1001/jama.2013.280319
4. Ostrom QT, Gittleman H, Stetson L, et al. Epidemiology of Gliomas. In: Raizer J, Parsa A, editors. Current understanding and treatment of gliomas. Switzerland: Springer International Publishing; 2015. p. 1-14. doi: http://doi.org/10.1007/978-3-319-12048-5_1
5. Brat DJ, Cagle PT, Dillon DA, et al. Template for reporting results of biomarker testing of specimens from patients with tumors of the central nervous system. Arch Pathol Lab Med. 2015;139(9):1087-93. doi: http://doi.org/10.5858/arpa.2014-0588-CP
6. Vega JEV, Brat DJ. Incorporating advances in molecular pathology into brain tumor diagnostics. Adv Anat Pathol. 2018;25(3):143-71. doi: http://doi.org/10.1097/PAP.0000000000000186
7. Wood MD, Halfpenny AM, Moore SR. Applications of molecular neuro-oncology - a review of diffuse glioma integrated diagnosis and emerging molecular entities. Diagn Pathol. 2019;14(1):29. doi: http://doi.org/10.1186/s13000-019-0802-8
8. Li HX, Meng HY, Peng XX, et al. A meta-analysis of association between pesticides exposure and glioma risk in adults. J Craniofac Surg. 2015;26(7):e672-3. doi: http://doi.org/10.1097/SCS.0000000000001707
9. Yiin JH, Ruder AM, Stewart PA, et al. The upper Midwest health study: a case-control study of pesticide applicators and risk of glioma. Environ Health. 2012;11:39. doi: http://doi.org/10.1186/1476-069X-11-39
10. Goyal R, Mathur SK, Gupta S, et al. Immunohistochemical expression of glial fibrillary acidic protein and CAM5.2 in

glial tumors and their role in differentiating glial tumors from metastatic tumors of central nervous system. J Neurosci Rural Pract. 2015;6(4):499-503. doi: http://doi.org/10.4103/0976-3147.168426

11. Ostrom QT, Cioffi G, Gittleman H, et al. CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2012-2016. Neuro Oncol. 2019;21(Suppl 5):v1-v100. doi: http://doi.org/10.1093/neuonc/noz150
12. Correa C, Soares MS, Cabrera HTN, et al. Gliomas: casuística cirúrgica em um hospital-escola quaternário. Arq Bras Neurocir. 2011;30(1):34-7. doi: http://doi.org/10.1055/s-0038-1625629
13. Stark AM, Nabavi A, Mehdorn HM, et al. Glioblastoma multiforme-report of 267 cases treated at a single institution. Surg Neurol. 2005;63(2):162-9. doi: http://doi.org/10.1016/j.surneu.2004.01.028
14. Carvalho LA, Lino AIA, Sabiá AF, et al. Avaliação epidemiológica dos gliomas operados, unidade de neurocirurgia, no hospital de base do Distrito Federal. Com Ciênc Saúde. 2018;29(1):7-14. doi: https://doi.org/10.51723/ccs.v29i01.60
15. Lucena RCG, Mello RJV, Lessa Júnior JR, et al. Correlação clínico-topográfica em glioblastomas multiformes nas síndromes motoras: significados fisiopatológicos. Arq Neuro-Psiquiatr. 2006;64(2b):441-5. doi: https://doi.org/10.1590/s0004-282x2006000300017
16. Alexander BM, Cloughesy TF. Adult glioblastoma. J Clin Oncol. 2017;35(21):2402-9. doi: https://doi.org/10.1200/JCO.2017.73.0119
17. Strepkos D, Markouli M, Klonou A, et al. Insights in the immunobiology of glioblastoma. J Mol Med. 2020;98:1-10. doi: https://doi.org/10.1007/s00109-019-01835-4
18. Kumthekar P, Raizer J, Singh S. Low-grade glioma. In: Raizer J, Parsa A, editors. Current understanding and treatment of gliomas. Switzerland: Springer International Publishing; 2015. p. 75-87. doi: http://doi.org/10.1007/978-3-319-12048-5_1
19. Enomoto T, Aoki M, Hamasaki M, et al. Midline glioma in adults: clinicopathological, genetic, and epigenetic analysis. Neurol Med Chir (Tokyo). 2020;60(3):136-46. doi: http://doi.org/10.2176/nmc.oa.2019-0168
20. Wesseling P, van den Bent M, Perry A. Oligodendroglioma: pathology, molecular mechanisms and markers. Acta Neuropathol. 2015;129(6):809-27. doi: http://doi.org/10.1007/s00401-015-1424-1
21. van den Bent MJ, Smits M, Kros JM, et al. Diffuse infiltrating oligodendroglioma and astrocytoma. J Clin Oncol. 2017;35(21):2394-401. doi: http://doi.org/10.1200/JCO.2017.72.6737
22. Schwartzbaum JA, Fisher JL, Aldape KD, et al. Epidemiology and molecular pathology of glioma. Nat Rev Neurol. 2006;2(9):494-503. doi: http://doi.org/10.1038/ncpneuro0289
23. Nambirajan A, Sharma MC, Rajeshwari M, et al. A comparative immunohistochemical study of epithelial membrane antigen and NHERF1/EBP50 in the diagnosis of ependymomas. Appl Immunohistochem Mol Morphol. 2018;26(1):71-8. doi: http://doi.org/10.1097/PAI.0000000000000384
24. Gerstner ER, Pajtler KW. Ependymoma. Semin Neurol. 2018;38(1):104-11. doi: http://doi.org/10.1055/s-0038-1636503
25. Collins VP, Jones DTW, Giannini C. Pilocytic astrocytoma: pathology, molecular mechanisms and markers. Acta Neuropathol. 2015;129(6):775-88. doi: http://doi.org/10.1007/s00401-015-1410-7
26. Shaikh N, Brahmbhatt N, Kruser TJ, et al. Pleomorphic xanthoastrocytoma: a brief review. CNS Oncol. 2019;8(3):CNS39. doi: https://doi.org/10.2217/cns-2019-0009
27. Kim B, Tabori U, Hawkins C. An update on the CNS manifestations of brain tumor polyposis syndromes. Acta Neuropathol. 2020;139(4):703-15. doi: https://doi.org/10.1007/s00401-020-02124-y
28. Archer TC, Sengupta S, Pomeroy SL. Brain cancer genomics and epigenomics. Handb Clin Neurol. 2018;148:785-97. doi: https://doi.org/10.1016/B978-0-444-64076-5.00050-8
29. Achatz MI, Hainaut P, Ashton-Prolla P. Highly prevalent TP53 mutation predisposing to many cancers in the brazilian population: a case for newborn screening? Lancet Oncol. 2009;10(9):920-5. doi: https://doi.org/10.1016/S1470-2045(09)70089-0
30. Pignati WA, Lima FANS, Lara SS, et al. Distribuição espacial do uso de agrotóxicos no Brasil: uma ferramenta para a vigilância em saúde. Cien Saúde Colet. 2017;22(10):3281-93. doi: https://doi.org/10.1590/1413-812320172210.17742017
31. Cassal VB, Azevedo LF, Ferreira RP, et al. Agrotóxicos: uma revisão de suas consequências para a saúde pública. Rev Eletrônica Gest Educ Tecnol Ambient. 2014;18(1):437-45. doi: https://doi.org/10.5902/2236117012498
32. Louis LM, Lerro CC, Friesen MC, et al. A prospective study of cancer risk among agricultural health study farm spouses associated with personal use of organochlorine insecticides. Environ Health. 2017;16:95. doi: https://doi.org/10.1186/s12940-017-0298-1

Recebido em 3/11/2020
Aprovado em 3/2/2021