Original Article

Histopathological Profile of Brain Tumors: A 12-year Retrospective Study from Madinah, Saudi Arabia

Albasri Abdulkader Mohammed, Almuhamdi Nawal Hamdan, Alqaidi Sara Homoud[1]

Department of Pathology, Taibah University, [1]Department of Surgery, Faculty of Medicine, Taibah University, Al-Madinah, Saudi Arabia

Abstract

Objectives: The objective of this study is to characterize the histopathological types and basic demographic parameters of brain tumors in the Madinah region of Saudi Arabia and to analyze and compare the findings with previously published literature. **Materials and Methods:** This retrospective study was conducted in the Department of Pathology, King Fahad Hospital, Madinah, Saudi Arabia, and comprised cases of brain tumors during 12 years (from January 2006 to December 2017). Basic demographic data, tumor site, and histopathological patterns were obtained from the medical records and further analyzed and graded according to the World Health Organization (WHO) 2007 classification. **Results:** A total of 227 brain tumors in 122 (53.7%) males and 105 (46.3%) female patients were recorded. Pediatric and adult patients accounted for 10.6% and 89.4% of the cases, respectively. The predominant age group affected was between 40 and 49 years (23.5%). The most common histopathological diagnosis in the present study was meningioma (30.8%), followed by astrocytic tumors (29.1%), metastatic tumors (7.7%), and embryonal tumors (6.6%). The meningothelial meningioma was the most common type of meningioma (48.5%). The majority of astrocytic tumors (52%) fell under the WHO Grade IV. **Conclusion:** This retrospective study established a baseline profile of brain tumors based primarily on the histopathological experience at a tertiary care hospital in the Madinah, Saudi Arabia, and provides an initiating platform to workup for future population targeted studies on brain tumors.

Keywords: *Brain tumors, histopathology, Madinah, World Health Organization 2007*

Introduction

Primary brain tumors are a diverse group of neoplasms. More than 120 histological types of these tumors have been classified by the World Health Organization (WHO). Unlike other tumors, they are not staged and WHO have assigned a Grade (I through IV) to predict their outcome. Conventionally, brain tumors are classified according to the cell of origin or the site of origin such as neuroepithelial origin (including astrocytic tumors, oligodendroglial tumors, oligoastrocytic tumors, ependymal tumors, choroid plexus tumors, neuronal and mixed neuronal-glial tumors, pineal tumors, and embryonal tumors), tumors of cranial nerves, tumors of the meninges, lymphomas and hematopoietic neoplasms, germ cell tumors, tumors of the sellar region, and metastases. A recent update in the WHO classification of brain tumor (2016) introduced a greater reliance on molecular markers.[1] With the introduction of newer diagnostic modalities, including molecular studies, the diagnostic accuracy has increased tremendously, and the exact histopathological diagnosis of brain tumors has played vital part in the diagnosis, management, and follow-up. The improvement in the diagnostic accuracy has played a major role in closing the performance gap between diagnostic centers, reduce subjectivity, and increase the standardization of diagnosis, which is crucial to plan an accurate treatment and predict the prognosis.

Brain tumor, which is one of the most important cancers causing death, represents the 17th most common cancer worldwide and accounts for 1%–2% of all tumors. Due to a significant increase in the incidence of, and death rates from, brain tumor in many developed countries, this type of tumor has special importance.[2] The peak rate of incidence of malignant brain tumors is seen in young children and in elderly individuals of the fifth and seventh decades. The prognosis of this tumor is relatively poor, and for all ages, the average survival period

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Address for correspondence:
Dr. Albasri Abdulkader Mohammed, Department of Pathology, Faculty of Medicine, Taibah University, Al-Madinah, Saudi Arabia.
E-mail: abdbasri@hotmail.com

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is 9 months, and the 5-year survival rate is low, especially for the glioblastoma multiforme (GBM). A benign neoplasm in the brain could have devastating effects and can turn lethal due to their location, space-occupying effects, and predisposition to undergo malignant transformation over a period of time.[3] Moreover, the incidence of brain tumors is increasing gradually throughout the world, and this is mainly attributed to the development of newer diagnostic technologies and the increased frequency of imaging tests.[4,5] The exact etiology of the brain tumor by enlarge remains unknown; however, genetic alterations, developmental abnormalities, and environmental factors have been reported to play a vital part in the etiopathogenesis of these tumors. The histopathological examinations are crucial for a definitive diagnosis and as a predictor of prognosis.[6]

The histopathological data on the brain tumor from our region is scant. Therefore, the aim of the present study was to look at the histopathological pattern of these tumors at King Fahad Hospital (KFH) in Madinah region over 12 years. The basic demographic data were collected, and the tumors were studied under the guidelines of the WHO 2007 classification.[7]

Materials and Methods

The present study was a retrospective analysis of the data on brain tumors, which involved the archival tumor blocks and clinicopathological data; and did not involve any patient's personal information or any implication on the management protocol. Hence, according to the principles of the Helsinki Declaration, no ethical approval was required in our study. The study included 227 consecutive cases of brain tumors diagnosed in the Pathology Department at a Tertiary Care Hospital in the Madinah region of Saudi Arabia, over 12 years (January 2006–December 2017). After receiving the specimen at our histopathology laboratory, the specimens were fixed for overnight in 10% buffered formalin. After fixation, the tissue is processed, and blocks were prepared using Leica automated tissue processor, and semithin (4-μm thick) sections were cut from the tumor blocks and mounted over a glass slide and stained with routine hematoxylin and eosin stains. Ancillary techniques such as special histochemical stain and immunohistochemistry were used in suitable patients. All the sections were examined by a consultant general pathologist and a second opinion was sought by a specialist neuropathologist in appropriate cases. The histopathological diagnosis, age, sex, and other relevant clinical data such as the site of tumor were collected from the patients' record. All the records which did not include any of the above-mentioned variables were excluded. Nonneoplastic and inflammatory lesions were also excluded. The tumors were reassessed and graded according to the WHO 2007 classification of tumors of the Central Nervous System (CNS).[7] We have very limited resources and could not expect all the standard diagnostic procedures, including molecular studies at our center. Thus, we have chosen the WHO classification 2007, which was not based on the molecular study. As the objective of this study was to address the histopathological pattern of brain tumors and basic demographic and information; hence, no comparison was indicated between the parameters. Thus, the statistical analysis was not performed in the present study. The findings were tabulated in Microsoft Excel Worksheet and analyzed on the basis of histopathological classification of the tumors, their frequencies, age, and sex distribution.

Results

A total of 227 consecutive patients with brain tumors were identified for 12 years; 122 (53.7%) patients were males, whereas 105 (46.3%) patients were females, with a male-to-female (M:F) ratio of 1.2:1. The ages ranged from 1 to 90 years, with a mean age of 42.9 years. In this study, the predominant age group affected was between 40 and 49 years (23.5%). There were only 24 (10.6%) cases of pediatric brain tumors (age <18 years) in our study.

Table 1 shows the number, percentage, mean ages, and sex distribution of our patients with brain tumors. There were 70 (30.8%) cases of meningiomas, 66 (29.1%) cases of astrocytic tumors, 17 (7.5%) cases of sellar tumors, 17 (7.5%) cases of metastatic carcinomas, 15 (6.6%) cases of medulloblastomas, 13 (5.7%) cases of oligodendroglial tumors, 9 (3.9%) cases of schwannomas, 7 (3.1%) cases of ependymal tumors, 4 (1.8%) cases of hemangioblastomas, 3 (1.3%) cases of cavernous hemangiomas, 2 (0.8%) cases of lymphomas, 2 (0.8%) cases of central neurocytomas, and 2 (0.8%) cases of plasma cell tumors. Among females, the most common diagnosis was meningiomas (40%); among males, it was astrocytic tumors (42.6%) [Table 1 and Figure 1].

Meningiomas showed a female predominance (M:F ratio of 1:1.5), with a mean age of 47.7 years [Table 1]. The most common sites were the dura overlying the temporal and parietal lobes of the cerebrum. The most common histological subtypes were the meningothelial type (24.2%) and fibroblastic type (6.6%). There were 61 (87.1%) cases of Grade I meningiomas, 6 (8.6%) cases of Grade II, and 3 (4.3%) cases of Grade III.

Astrocytic tumors were the second-most common histological type in our analysis, representing 29.1% of the total percentages of cases. In contrast to meningiomas, astrocytic tumors were more common in males than in females (M: F ratio of 2.3:1). The mean age of the patients was 45.2 years. There were 3 (4.5%) cases of Grade I astrocytomas, 7 (10.6%) cases of Grade II, 13 (19.7%) cases of Grade III, and 43 (65.2%) cases of glioblastomas (Grade IV). The most common sites involved were the temporal and parietal lobes of the cerebrum.

Table 1: The number, percentage, mean ages, and sex distribution of our patients with brain tumors

Histopathological diagnoses	Frequency, *n* (%)	Mean age (years)	Male/female
Neuroepithelial tumors (*n*=101)			
Astrocytic tumors	66 (29.1)	45.2	53/13
Oligodendroglial tumors	13 (5.7)	43.2	12/1
Ependymal tumors	7 (3.1)	28.5	3/4
Embryonal tumors	15 (6.6)	16.5	9/6
Tumors of the meninges (*n*=70)			
Meningothelial (34%-48.5%)	55 (24.2)	48.2	24/31
Fibroblasdtic (14%-20%)	15 (6.6)	47	4/11
Mesenchymal tumors (*n*=7)			
Hemangioblastoma	4 (1.8)	12	1/3
Hemangioma	3 (1.3)	43.1	1/2
Sellar tumors (*n*=17)			
Pituitary adenoma	14 (6.2)	42.6	8/9
Craniopharyngioma	3 (1.3)	53	2/1
Tumors of cranial and paraspinal nerves (*n*=9)			
Schwannoma	9 (3.9)	39.3	5/4
Lymphomas and hematopoietic neoplasms (*n*=4)			
Lymphoma	2 (0.8)	58.5	0/2
Plasmacytoma	2 (0.8)	37	0/2
Neuronal and mixed neuronal-glial tumors (*n*=2)			
Central neurocytoma	2 (0.8)	29	1/1
Metastatic carcinoma (*n*=17)	17 (7.5)	47.3	2/15
Total	227 (100)		122/105

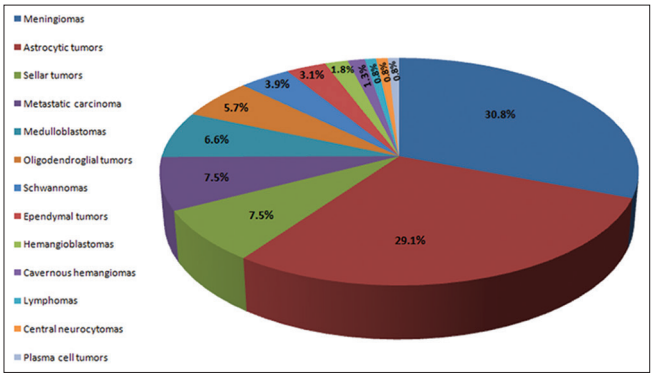

Figure 1: Pie chart showing the incidence of various brain tumors

The third-most common histological diagnosis was for sellar tumors, of which 82.4% were pituitary adenomas. The mean age of the patients with sellar tumors was 42.6 years, and the M:F ratio was 7:10. Craniopharyngiomas were less frequent sellar tumors, accounting for 17.6% of the cases. Medulloblastomas showed a male predominance (M:F ratio of 1.5:1) with a mean age of 16.5 years. The most common site was the cerebellum (81.3%). Other less frequent brain tumors seen in our series were oligodendroglial tumors, schwannomas, and ependymal tumors, which represented 5.7%, 3.9%, and 3.1% of the total percentages of cases, respectively. Among mesenchymal tumors and hematopoietic tumors, there were three cases of cavernous hemangiomas and two cases of CNS lymphomas, respectively.

Of the 17 metastatic tumors, the most common histological type was adenocarcinomas (14 cases, 82.3%). There were 2 (11.8%) cases of metastatic hepatocellular carcinomas and 1 (5.9%) case of metastatic thyroid cancer.

Discussion

Brain tumors are a heterogeneous group of neoplasm, and the predominant types in the adult population are glial neoplasms, meningioma, and metastasis. Globally, there is a large variability in the trends of brain tumor diagnoses given the vast different histological subtypes interpretation criteria and potential artifacts linked to newer diagnostic modalities, therapeutic approaches, and registries practiced in different countries. High morbidity and mortality are associated with these tumors, irrespective of their nature and histological grades. The GLOBOCAN Project (2012) reported the incidence of CNS tumors at 1.8% and the mortality rate at 2.3% worldwide (total incidence age-standardized rate [ASR] of 3.4/100,000 and a mortality ASR of 2.5/100,000 worldwide). In the developing countries, the incidence ASR of CNS tumors was reported to be 3.0/100,000, and for mortality ASR, the estimate was 2.2/100,000. In addition, GLOBOCAN has also described the sex-related data and showed that males have a higher CNS tumor incidence ASR (3.9) compared with that of females (3.0) throughout the world.[8,9]

Despite the growing burden of brain tumors throughout the world, the published data available on the histopathological

profile of brain tumors from our region in Saudi Arabia is scant. Hence, in this baseline study, the author has tried to highlight the frequency, demographic features, and histopathological profile of brain tumors in a large cohort of 227 Saudi patients. The present study being a retrospective histopathology laboratory-based research, it has the limitation of dependence on the data collection efficacy and lack of statistical analysis. However, it has served the purpose of providing basic demographic and clinicopathological data, which can be compared with available studies in the literature. This study provides a primary baseline tool to workup for future population targeted studies on brain tumors.

Saudi Arabia is the largest nation in the Middle East and the 12th largest nation in the world, with an estimated population of 33 million. According to the most recent Saudi Cancer Registry report showed that there are 329 new cases of brain cancer diagnosed in 2014, accounting for 2.8% of total cancer patients and making it the 10th most frequent cancer among males and females in the Saudi population. The five regions with the highest brain cancer ASR were Riyadh region, followed by Jouf region, then the Northern region, then the Eastern region, and Qassim region. Madinah region had the lowest brain cancer ASR after Jazan, Hail, and Asir regions.[10]

An extensive search of the literature did not yield any independently published study from our region; hence, no regional data are available for the comparison of our findings. However, an article on the same topic from KFH, Dammam, Saudi Arabia, had a comparable number of neuroepithelial brain tumor cases. In their study, the authors reported all the neuroepithelial tumors according to the 2007 edition of the WHO classifications of CNS tumors. They analyzed all the neuroepithelial tumor cases of the Eastern province retrospectively from 2007. After excluding other brain tumors, such as metastases, meningiomas, lymphomas, and tumors located in the pituitary gland, a total of 149 cases of neuroepithelial tumors were reported. We found similarities in the prevalence of GBM cases in our study (43 cases) when correlated with the above study (48 cases).[11]

In this study, the predominant age group affected by brain tumors was between 40 and 49 years (23.5%). Regarding the pediatric population (age <18 years) in our study, there were only 24 (10.6%) cases of pediatric brain tumors, of which 15 (6.6%) were medulloblastomas, with a mean age of 16.5 years, and 3 (1.3%) were cavernous hemangiomas, with a mean age of 12 years. However, when compared with data reported from the Central Brain Tumor Registry of the United States (CBTRUS) between 2010 and 2014, the age groups affected by brain and other brain tumors were older, only 14% <20 years, 28% from 20 to 49 years, 31% from 50 to 69 years, and 27% >70 years.[12] Males were affected more than females in the current study (M:F was 1.2:1), and this was in coherence with other studies.[13,14] However, in meningiomas females outnumbered the males in our series (M:F 1:1.5). A similar female preponderance was observed by Yeole,[15] Ghanghoria *et al*.,[16] and Masoodi *et al*.[17]

In the present study, the most frequently encountered intracranial tumor was meningiomas which were accounted for 30.8% (70/227) of a total number of cases, followed by astrocytic tumors 29.1% (66/227), metastatic tumors 7.5% (17/227), and pituitary adenomas at 6.2% (14/227). The high prevalence of meningiomas in our study is comparable with findings of the CBTRUS[11] in the United States (35%), Das *et al*.[18] in Singapore (35.1%). Idowu *et al*.[19] in Nigeria (35%), Dho *et al*.[20] in the Republic of Korea (37.3%), and Nakamura *et al*.[21] in Japan (36.8%) where all of them reported meningiomas as the most commonly occurring brain tumor in their series.

Contrary to our findings, few differences were observed with the studies from Croatia, Italy, and Canada, which showed that glioblastomas were the most common tumor among intracranial neoplasms.[22-24] Our findings also contrast with the study by Bangash[25] in Saudi Arabia, who reported that the most common tumors affecting adult Saudis at King Abdul-Aziz University Hospital were metastatic brain tumors (28.5%), followed by astrocytomas (20.7%), and pituitary adenomas (15.5%). Another less frequently occurring tumor is our study was a pituitary adenoma. We found 14 (6.2%) cases of pituitary adenoma in the present study. The frequency of pituitary adenoma was reported to be lower than what observed by Masoodi *et al*.,[17] Das *et al*.,[18] and Bangash[25] they noted 11.3%, 11.8%, and 15.5% of cases, respectively.

In our series, the metastatic spread from a distant primary to the brain is 7.5% (17/227) of total cases. The frequency of metastasis in our study is lower than that of various previous studies. Bangash[25] from Western Saudi Arabia has reported a very high rate (28.5%) of metastatic tumors in his study; in fact, metastatic tumors were the most common brain neoplasm in his cohort. It has been postulated that the increase in the diagnosis of metastatic brain tumors could be in part attributed to the presence of a well-established oncology service at his institute. Among the 17 metastatic tumors, the most common histological type noted was adenocarcinoma (14 cases, 82.3%), our findings are comparable to studies done in Nepal and Korea.[26,27] A detailed comparison of our demographic findings and histopathological types of brain tumors with the previous national and international publishes literature is summarized in Table 2.

This study has a few limitations. First, the sample was restricted to one tertiary care government hospital, which might limit the extension of results to the general population and provide a rough estimate of primary

Table 2: Comparison of our findings of brain tumors with the previous national and international publishes literature

Study	Place	Number of cases	Male (%)	Female (%)	Age (years)	Most common histopathological type
Das *et al*.[18]	Singapore	655	42.1	57.9	40-69	Meningioma Pituitary adenoma
Bauchet *et al*.[4]	France	10,000	46.4	53.6	56	Astrocytic tumors Meningioma
Idowu *et al*.[19]	Nigeria	113	54.8	45.2	46	Glioma Meningioma
Aryal[26]	Nepal	57	49.1	49.9	40-60	Astrocytoma Meningioma
Bangash[25]	Jeddah Saudi Arabia	112	55.8	44.2	46	Metastasis Astrocytoma
Chen *et al*.[28]	China	34,140	Male>female	Female<male	40-59	Neuroepithelial tumors Meningioma
Ghanghoria *et al*.[16]	India	65	53.8	46.2	31-40	Meningioma Astrocytoma
Taha *et al*.[11]	Eastern Province, Saudi Arabia	149	58	42	<5 26-45	GBM Medulloblastoma
Walker and Davis[29]	Canada	12,515	56.6	43.4		Glioblastoma Embryonal tumors
Present study (2019)	Madinah Saudi Arabia	227	53.7	46.3	40-49	Meningioma Astrocytic tumors

GBM – Glioblastoma multiforme

brain tumors in the Madinah region. Second, being a retrospective histopathology laboratory-based research, it has the limitation of dependence on the data collection efficacy and lack of a proper statistical analysis. Finally, the sample size is relatively small, and it has not included the recent WHO 2016 classification for the categorization of brain tumors.

Conclusion

This retrospective study on 227 consecutive Saudi patients established a baseline of brain tumor pattern on the basis of histopathological experience at a tertiary care hospital in Madinah, Saudi Arabia, and provides a platform to workup for future population targeted studies. The highest incidence of brain tumors was observed in patients between 40 and 49 years with a male preponderance (M:F = 1.2:1). The most common histopathological type seen in our study of brain tumors were meningiomas, astrocytic tumors, embryonal tumors, pituitary adenomas, and metastatic tumors. Our recorded data match with that of the world literature and Saudi national studies with some variations.

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Conflicts of interest

There are no conflicts of interest.

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