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Investigating the Clinico-Pathological Parameters in Astrocytoma

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ABSTRACT

Background and Objective: Astrocytoma is a tumor of neurological origin, arising from special supportive cells in the brain and spinal cord called the astrocytes. Astrocytoma is classified according to grade, site, and molecular features. The aim of this study is to investigate the relationship between histopathological and clinical parameters and gender, age, location and different grades.

Methods: This cross-sectional study included 36 cases of astrocytoma from April 2017 to June 2020 from the archive of AL Shaheed Gazi AL Hariri Hospital. The cases reached the final diagnosis by H&E staining with 16 cases stained by immunohistochemical stain for confirmation of diagnosis. SPSS was used for analysis.

Findings: Thirty-six cases of astrocytoma were included in this study. Their ages were ranging from 1 to 56 years, with a mean age of 31.43±0.015 years. Assessment of age reveals that the most frequent age (25%) was in the 3rd decade of life. The predominant grades were grade I and grade IV with 11 cases for each (32.5%). Whereas patients of grade II and III compose 10 (27%), and 4 (11%) cases, respectively. The relationship between the age of the patients and their grades shows a positive significant correlation between age and grade ($p<0.001$), and tumor grade increases with the increase in the age of the patients.

Conclusion: The results of the study show that there is a significant relationship between tumor grade and clinical-pathological characteristics, because tumor grade increases with age and is more aggressive in female patients.

Keywords: *Astrocytoma, Histopathological, Grading, WHO Classification.*

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Introduction

Astrocytoma are primary brain tumors originating from a special type called the supportive cells of the brain (astrocytes), which form the bulk of the cellular part of the brain (1). Astrocytoma in adults represents the most common type of primary malignant brain tumors (80%) (2). Glioblastoma multiform is the most aggressive and the most common type of astrocytoma (grade IV WHO classification) associated with just 13 months' median survival (3) based on statistics in Iraq. Brain tumors represent 1\5 of most common tumors in adults and are the 2nd most common tumor in pediatric age group with approximate male to female percentage of 5%:3% (2). Astrocytoma (as part of glioma) classification by the World Health Organization (WHO) classification system of CNS tumors are in 1979, 2000, 2007, 2016 and finally 2021 (3). All the old WHO classifications used the histopathological features for grading, and the 5th WHO classification system considered the molecular features as an important point in grading (4). The histological features include the cellularity, atypia, number of mitosis, the increased vascularity and the presence of absence of necrosis at the level of light microscope with or without the use of immunohistochemistry (5). The most important molecular features involved in the 5th edition include *IDH1, IDH2, TP53, TERT, BRAF, ATRX* (6). According to 2022 classification system (7), the astrocytoma is broadly divided into 4 grades: Grade 1 represents the localized tumors occurring in young patients with well demarcated tumors (pilocytic astrocytoma), Grade II (diffuse astrocytoma) occurs mostly in adults with increased ability to invade adjacent parenchyma with high cellularity and atypia of well-differentiated fibrillary, protoplasmic, or gemistocytic astrocytes without necrosis or vascular proliferation. Grade III (anaplastic astrocytoma) has more atypia and mitosis and diffuse location; and Grade IV (Glioblastoma Multiform= GBM) which is the most aggressive one, is highly cellular, pleomorphic with high mitosis and endothelial proliferations and necrosis (8, 9). GBM is either primary without precursor tumor in more than 90% or secondary (less than 10%) from other grades of astrocytoma (10, 11). This study's aim is to clarify the relationship between histopathological and clinical parameters age, sex, site of various grades.

Methods

In this retrospective study, a total of 36 formalin-fixed paraffin-embedded brain excisional biopsies were collected from Iraqi patients from January 2019 to December 2020. The study included 10 cases of Diffuse fibrillary astrocytomas, 11 cases of Glioblastomas, 11 cases of Pilocytic astrocytomas and 4 cases of Anaplastic astrocytomas, retrieved from the archival materials in AL Shaheed Ghazi Alhariri Hospital. All the data was collected according to the ethical code of AL Shaheed Gazi AL Hariri Hospital (AL:SGH 2020/188). Data analysis was done by application of t-test, chi-square. Values are assumed to be significant by $p<0.05$.

Results

Age distribution: Thirty-six cases of astrocytoma were included in this study. Their ages were ranging from 1 to 56 years, with mean age of 31.4 years. Assessment of age presentation reveals that the most frequent age (25%) was in the 3rd decade of life.

Gender distribution: Out of 36 studied cases, 19 (53%) were females and 17 (47%) were males, with female to male ratio of (1.11) as shown in the figure 1.

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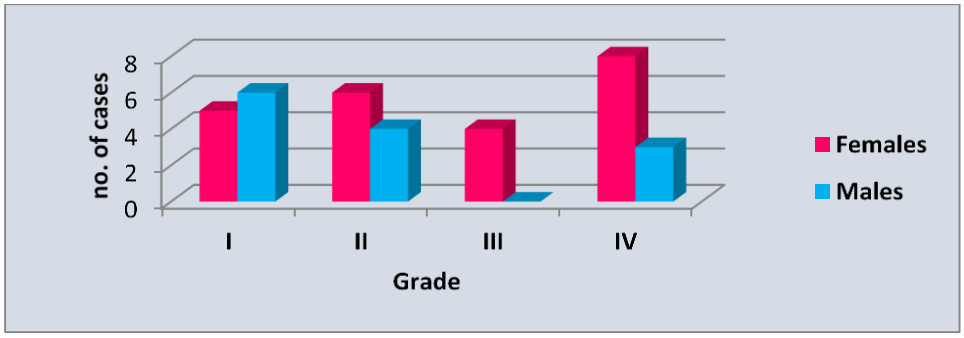

Figure 1. Distribution of sex in collected astrocytic cases

Grade distribution: The predominant grades were grade I and grade IV with 11 cases for each (32.5%). Patients of grade II and III compose 10 (27%), 4 (11%) cases respectively, as shown in figure 2.

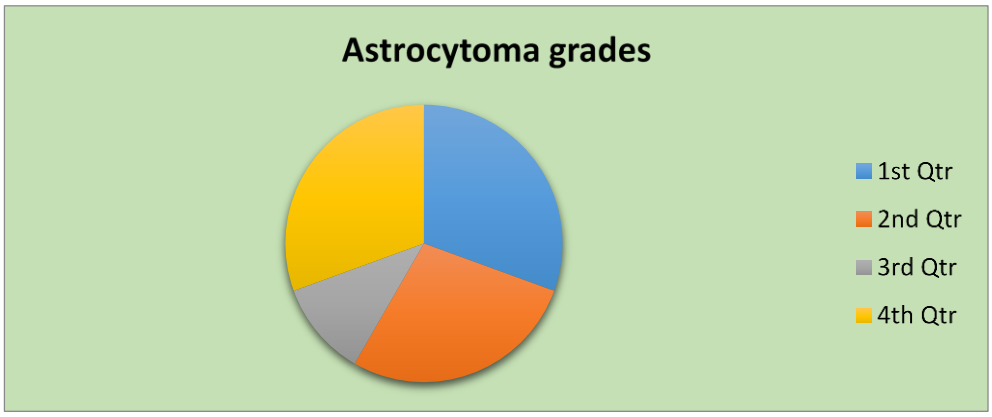

Figure 2. Distribution of collected cases. Blue color for grade I (30.5%), Orange color represent grade II (27%), Gray color for grade III (11%) and yellow color for grade IV (30.5%)

Baseline characteristics of studied cases in regard to grade, age and gender: Table 1 shows baseline characteristics in terms of age, sex and grade. Young age predominates in grade I, while grade IV has mostly the older age and female patients.

Table 1. Baseline characteristics of cases

Grade	No.	Age (Years)		Gender	
		Mean±SD	Range	Male Number(%)	Female Number(%)
I	11	9.923±7.065	1.0-20	6(69.231)	5(30.769)
II	10	31.1±9.159	5.0-39.0	4(60)	6(40)
III	4	48.75±4.65698	42.0-55.0	0(0)	4(100)
IV	11	47.846±7.284	30.0-56.0	3(30.769)	8(69.231)
Total	36	31.425±18.0151	1-56	17(47)	19(53)

The age and grade distribution relationship: The relationship between the age of the patients and their grades are shown in the figure 3, showing a positive significant correlation between age and grade ($p<0.001$); tumor grade increased with the increased age of the patients.

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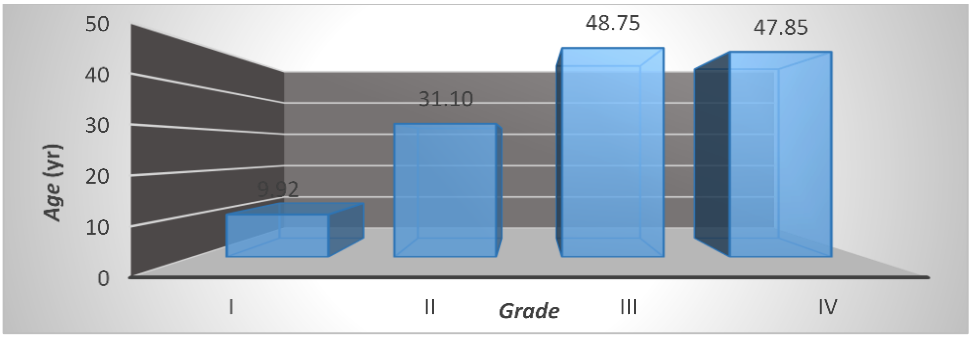

Figure 3. Relationship between the age of the patients and the grade of astrocytoma, which show positive correlation

The distribution of sex in relation to grade: Table 2 shows the relationship between sex and grade which document that there is no significant correlation between them. The Relative risk with CI 95% women-to-men for incident grade 3 and 4 were 2.45 (95% CI 1.3-4.5) and 2.66 (95% CI 1.4-5.1) respectively, which shows that the women are more likely to be in the high grades compared to men. In other words, females predominate in grade IV while males predominate in grade I.

Table 2. Distribution of patient sex relative to tumor grade

Grade	Number(%)	Mean±SD	RR (95% CI)	p-value*
I				
Females (n=23)	5(22)	43.01±15.98	0.51 (0.1-2.1)	0.018
Males (n=14)	6(43)	42.22±16.02		
II				
Females (n=23)	6(26)	8.12±1.66	0.89 (0.2-3.2)	0.019
Males (n=14)	4(29)	8.22±1.62		
III				
Females (n=23)	4(17)	31.25±7.25	2.45 (1.3-4.5)	0.05
Males (n=14)	1(7)	29.55±4.14		
IV				
Females (n=23)	8(35)	8.22±10.25	2.66 (1.4-5.1)	0.017
Males (n=14)	3(21)	7.99±11.02		

***Yate's chi square**

Discussion

The results of our study about the clinical and pathological behavior of astrocytoma is similar to many studies and research results on different types of astrocytoma; showing a positive relationship between the age and the grade of tumor. In their study, Almenawer et al. (12) show that the incidence of astrocytic tumors is generally high in pediatric age group (35%) from the total brain tumor percentage. Lin et al. (13) confirm our result by defining the age group for pilocytic astrocytoma (0-14); our results showed age below 20 y as the upper limit of age. Lin et al. found that it is spreading in wider range 15-64 y, which is against our range 30-57 y and may be due to the large population selected by him (1502) (13). The result of Saadoon et al. is the same for pilocytic astrocytoma; all cases were<14 y, while the other types began in middle age group (14). Other studies to support our results include the findings by Jia et al. (15), in which all cases of GBM

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were above 45 y the same as ours. According to the results of Ladomersky et al., (16) the same findings could be seen; positive correlation between age and grade of astrocytoma with the more aggressive GBM in older age groups. Regarding the Sex of cases collected in our work, the female predominantly covers all the types except for the grade I pilocytic astrocytoma, in which there was male > female result, which is exactly the same result found by (17). Mojahed et al., (18) show that at pediatric age groups, the male sex has more incidence for astrocytoma and the feature will change with increasing age to become of female predominance. Against our results is the study of Métais et al. that confirm the male predominance in all types of astrocytic cases (19). There may be hormonal effect on astrocytic tumor incidence and progression as done by Bello-Alvarez et al. (20), who show the protective progesterone effect in women and the promoter testosterone effect. Another study to support our work is the result by Soon et al. (21) who found no significant relationship between sex and grade of astrocytoma. The results of Cancer Genome Atlas Research Network show that male patients represent the largest group of astrocytic patients (7, 22). The difference in all the results above may be due to the number of collected data, the race of the patients as we work in Iraqi pt. only; or may be due to environmental factors which require detailed future works. Regarding the types and grades of astrocytoma, all the clinical data and WHO classifications (5^{th} edition) is the same and not included here and require follow up, and we are working on a retrospective study.

Overall, this research found that age is an important prognostic factor in astrocytoma, and that there is a positive, statistically significant link between age and tumor grade. All pilocytic astrocytoma occurrences occur in the first two decades of life, but the most aggressive GBM occurs in the fourth decade as a minimum age.

Conflict of interest: The authors declare there is no conflict of interest.

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