International Journal of Clinical and Diagnostic Pathology

ISSN (P): 2617-7226
ISSN (E): 2617-7234
www.patholjournal.com
2021; 4(2): 30-34
Received: 03-02-2021
Accepted: 17-03-2021

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Histopathological spectrum of astrocytoma in tertiary care hospital

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DOI: https://doi.org/10.33545/pathol.2021.v4.i2a.355

Abstract
Introduction: Astrocytoma is most common primary central nervous system (CNS) tumors that arise from the star-shaped cells (astrocytes) that form supportive tissue of the brain or from precursor cells. Astrocytoma is a subset of glial tumors. Glial tumors also known as gliomas referred to as the tumors that arise from supportive tissue of the brain which is formed by glial cells (astrocytes, oligodendrocytes, ependymal cells). Astrocytoma represent more than half of all primary brain tumors.
Aim: The aim of the study is an overview of most recent advancement regarding classification on astrocytoma, to evaluate the frequency and age, sex, site wise distribution and clinical presentation of the various types of astrocytic tumors and comparing it with national and international study.
Materials and Methods: The present histopathological study was undertaken in the department of Pathology, Civil hospital, Ahmedabad (CHA) on surgical specimens received from Department of Surgery, Civil hospital, Ahmedabad from January 2018 to October 2020. The superficial biopsy, biopsy with artefacts and inadequate material/history were excluded from the study. The specimens were fixed in 10% formalin, subsequently dehydration, clearing, embedding in paraffin wax were carried out. Blocks were made, sections of 5 um thickness were cut and stained with Harris Haematoxylin and eosin stain.
Results: Out of 100 cases of astrocytic tumors, most common tumors were WHO Grade II Diffuse Astrocytoma (54%) followed by Grade I Pilocytic astrocytoma (22%), Grade III Anaplastic astrocytoma (14%) and Grade IV Glioblastoma (6%). Most of the astrocytic tumors occur between 21-30 years of age in present study. Higher rates of astrocytic tumors located in supratentorial part of brain in which most common site was frontal lobe (28%).
Conclusion: The present study gives histopathological aspects of astrocytic tumors. Combining histopathological and molecular features helps in the definitive diagnosis and management of astrocytic tumors thus providing better quality of life to the patient.

Keywords: Diffuse astrocytoma, glioblastoma, anaplastic astrocytoma, pleomorphic

Introduction

Brain and Central nervous system (CNS) tumors are most common tumors in people under 20 years old [1, 11]. Glial tumors constitute 60% of CNS tumors. Glial tumors also known as gliomas referred to as the tumors that arise from supportive tissue of the brain which is formed by glial cells (astrocytes, oligodendrocytes, ependymal cells).

Astrocytoma is most common primary central nervous system (CNS) tumors that arise from the star-shaped cells (astrocytes) that form supportive tissue of the brain or from precursor cells. Astrocytoma is a subset of glial tumors [2], usually affecting the brain and sometimes the spinal cord.

Many classifications of gliomas have been suggested since the twenties of the last century [3, 12]. Currently, the 2016 World Health Organization classification is the most commonly used classification [12]. In the most updated version, molecular parameters were essential in classifying astrocytoma in addition to histopathologic appearance. Thus, astrocytoma includes many types that may differ on molecular basis and severity.

The two major categories of astrocytic tumors are the diffusely infiltrating astrocytoma (WHO grade II to IV) and the more localized astrocytoma which is pilocytic astrocytoma (WHO grade I). These two major categories are classified on the basis of how fast they are growing and the likelihood that they will spread (infiltrate) to nearby brain tissue.

The present study is an attempt to identify frequency of various histopathological types of astrocytoma, age group, gender distribution, site of lesion and clinical presentation in population attending our institution.

Materials and Methods

The present histopathological study was undertaken in the Department of Pathology, Civil hospital, Ahmedabad on surgical specimens received from Department of Surgery, Civil hospital, Ahmedabad from January 2018 to October 2020. The materials were collected in the form of biopsy and resected specimens of Central Nervous System (CNS) along with the clinical profile of the patient with supportive investigations. The superficial biopsy, biopsy with artefacts, inadequate material and inadequate data were excluded from the study. This was correlated with gross and histopathological examination of respective surgical specimen. For histopathological study, the specimens were fixed in 10% formalin, subsequently dehydration, clearing, embedding in paraffin wax were carried out. Blocks were made, sections of 5 um thickness were cut and stained with Harris Haematoxylin and eosin stain. Special staining like PAS, ZN etc. may be used wherever necessary.

The slides were examined under microscope and histopathological findings were noted. All cases were confirmed applying WHO classification (2016). The histopathological diagnosis was categorised as the 2016 WHO grading system of Central Nervous System on Astrocytoma. In addition to histology, molecular parameters were also included in the 2016 WHO classification of CNS tumors on astrocytoma. Since the molecular testing and cytogenetic studies are not available in our institution the diagnosis is reclassified as tumour NOS. The relative frequency of tumors, their site and distribution of age and sex were analysed.

Results

The present study comprises histopathology of 100 Astrocytic lesions of Central Nervous System (CNS) studied in the Department of Pathology, Civil Hospital, Ahmedabad from January 2018 to October 2020.

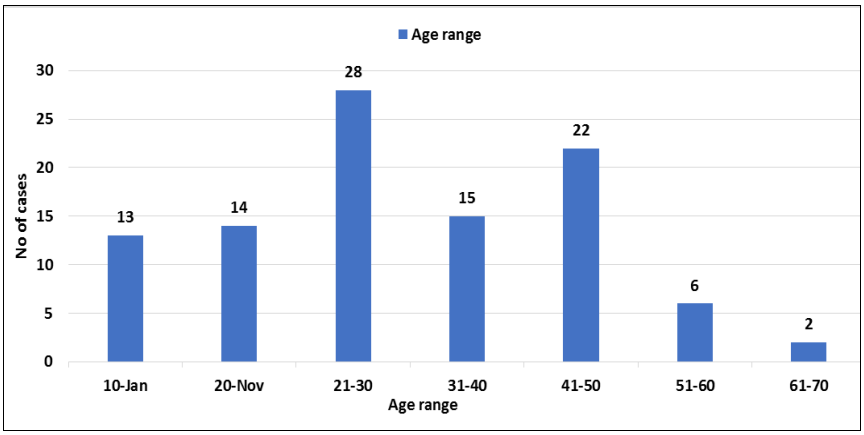

Fig 1: Age renge

Table 1: Age range in population of astrocytic tumors

Age range	No of cases
1-10	13
11-20	14
21-30	28
31-40	15
41-50	22
51-60	6
61-70	2

The patients age range 3 years to 65 years. The mean age was 33 years. Most cases belonged to 2nd decade of life followed by 4th decade. Astrocytic tumors in paediatric age group (≤ 18 years) were clinically diagnosed in 23 out of 100 cases. Of these 23 cases, 14 cases diagnosed to have Pilocytic astrocytoma.

Table 2: Distribution of astrocytic tumors according to gender

Grade	Type	Male	Female	M:F
I	Total cases	11	14	1:1.5
	Pilocytic Astrocytoma	11	11	
	Subependymal giant cell astrocytoma	0	3	
II	Total cases	37	17	2.62:1
	Diffuse Astrocytoma	34	16	
	a) Gemistocytic diffuse astrocytoma	7	2	
	b) Fibrillary diffuse astrocytoma	15	8	
	c) NOS	12	6	
	Pleomorphic Xanthoastrocytoma	3	1	
III	Total cases	9	6	1:1.1
	Anaplastic Astrocytoma	9	5	
	Anaplastic Pleomorphic Xanthoastrocytoma	0	1	
IV	Total cases	3	3	1:1
	Glioblastoma	3	3	

Out of 100 cases, 60 (60%) were males and 40 (40%) were females. The study showed male preponderance for all astrocytic tumors with male to female ratio 1.5:1.

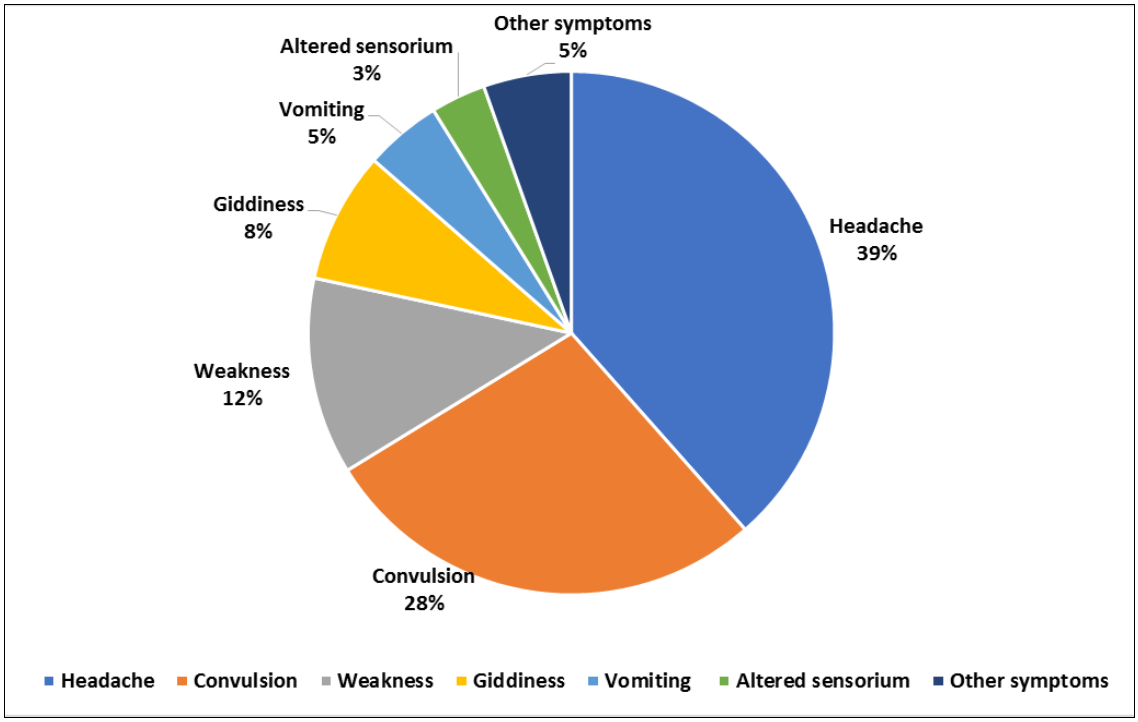

Fig 2: Show the co male preponderance

Table 3: Distribution of symptoms in astrocytic tumors

Symptoms	No of cases
Headache	39
Convulsion	28
Weakness	12
Giddiness	8
Altered sensorium	5
Vomiting	3
Other symptoms	5

In present study, most common presenting complaint in astrocytic tumors was headache which was present in 57 cases out of 100. Other symptoms in our study includes difficulty in walking, difficulty in swallowing, slurred speech and diminution of vision which was present in 8 cases out of 100.

Table 4: Distribution according to location of astrocytic tumors

Grade	Types	Location	
		Supratentorial	Infratentorial
I	Pilocytic Astrocytoma	11	11
	Subependymal giant cell astrocytoma	3	0
II	Diffuse Astrocytoma		
	a) Gemistocytic diffuse astrocytoma	9	0
	b) Fibrillary diffuse astrocytoma	20	3
	c) NOS	16	2
	Pleomorphic Xanthoastrocytoma	4	0
III	Anaplastic Astrocytoma	12	2
	Anaplastic Pleomorphic Xanthoastrocytoma	1	0
IV	Glioblastoma	6	0
Total Cases		**82**	**18**

Of all astrocytic tumour, 82% were of supratentorial origin and 18% were of infratentorial origin. In our study, Supratentorial site includes cerebrum, corpus callosum, insular region, thalamus, optic pathway, suprasellar region and Infratentorial site includes brain stem, spinal cord, cerebellum. Of all astrocytic tumors, most common location was frontal lobe (28%) of cerebrum.

Table 5: Distribution of Various Astrocytic lesion according to WHO grading

Grade	Types	No. of cases	Percentage (%)
I	Total cases	25	25%
	Pilocytic Astrocytoma	22	22%
	Subependymal giant cell astrocytoma	3	3%
II	Total cases	54	54%
	Diffuse Astrocytoma	50	50%
	a) Gemistocytic diffuse astrocytoma	9	9%
	b) Fibrillary diffuse astrocytoma	23	23%
	c) NOS	18	18%
	Pleomorphic Xanthoastrocytoma	4	4%
III	Total cases	15	15%
	Anaplastic Astrocytoma	14	14%
	Anaplastic Pleomorphic Xanthoastrocytoma	1	1%
IV	Total cases	6	6%
	Glioblastoma	6	6%
Total Cases		100	100%

Amongst 100 cases, there were 25 (25%) cases of Grade I astrocytic tumors. Out of 54 cases of Grade II astrocytic tumors, diffuse astrocytoma constituted 50 (50%) cases and Pleomorphic Xanthoastrocytoma constituted 4 (4%). Total 15 cases of Grade III astrocytic tumors in which 14 (14%) were Anaplastic astrocytoma. Grade IV Glioblastoma

constituted 6 (6%) cases out of 100 cases of astrocytic tumors. Diffuse astrocytoma (50%) were most common astrocytic tumors followed by Pilocytic astrocytoma (22%) and Anaplastic astrocytoma (14%).

Discussion

Astrocytoma is a subset of glial tumors [2]. Glial tumors comprise 60% of the brain tumors. In present study, most common astrocytic tumour was diffuse astrocytoma (50%). Pilocytic astrocytoma comprises 22% of cases and Anaplastic astrocytoma comprises of 14% cases. Damir *et al* study had 19.9% of pilocytic astrocytoma and 18.2% of anaplastic astrocytoma cases [2].

In present study, most cases belonged to age group between 21-30 years followed by 41-50. Mean age at diagnosis in present study 33 years. Damir *et al*. had 35.4 years as mean age at diagnosis in their study [2]. The median age group of different histological subtypes of astrocytic tumors in this study was intermediate between those from international (CBTRUS) and national (NIMHANS) data [7, 8]. The median age group of pilocytic astrocytoma and glioblastoma were 13 years and 50 years respectively in present study compared to 12 years and 65 years respectively in CBTRUS and 14 years and 50 years in NIMHANS [7, 8].

Many studies showed that the incidence of astrocytic tumour was more in the male population than the female [2, 5-11]. In our study too, 60% of the cases were males and the rest were females.

In present study, 82% of astrocytic tumors were supratentorial origin and 18% were infratentorial origin. The most common site of tumors in present study was frontal lobe followed by temporal lobe of brain similar to CBTRUS study [7]. Temporal lobe followed by frontal lobe was common site of astrocytic tumors in Damir *et al* study [2].

Grading of CNS tumors are based on 4 morphologic criteria: Cytological atypia, Mitotic activity, Microvascular proliferation and Necrosis.

Grade I astrocytoma include Pilocytic and subependymal giant cell astrocytoma, those are slow growing.

Pilocytic astrocytoma is most common in male children and adolescent. Most commonly occur in site of cerebellum and cerebral midline structure. Pilocytic astrocytoma is most commonly associated with Neurofibromatosis I. Subependymal giant cell astrocytoma most commonly associated with Tuberous Sclerosis and involves wall of lateral ventricle.

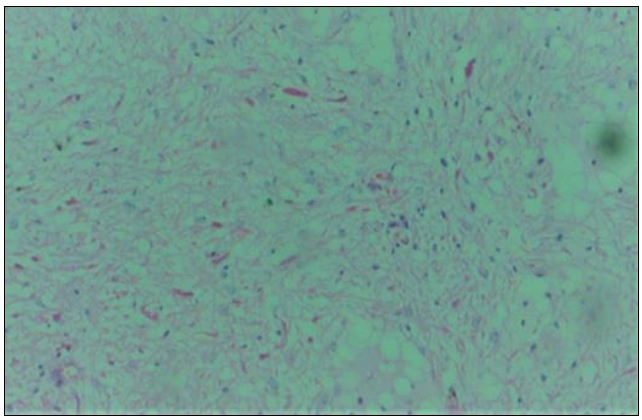

Fig 3: Pilocytic Astrocytoma: Spindle cells in a compacted fibrillary background with Rosenthal fiber

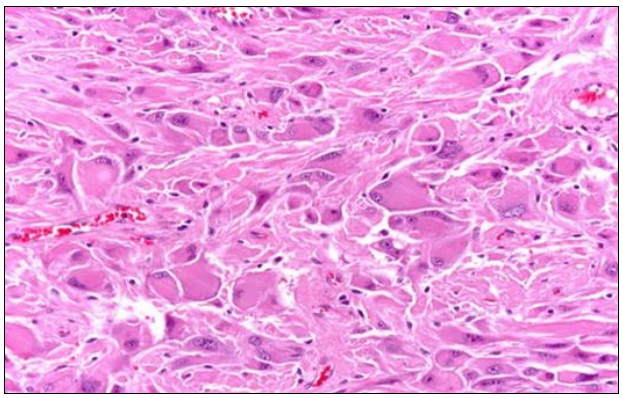

Fig 4: Subependymal giant cell astrocytoma: Large ganglion cell like nuclei with prominent nucleoli with pink glassy astrocyte like cytoplasm

Grade II astrocytoma include Diffuse astrocytoma and Pleomorphic xanthoastrocytoma in which grading according to cytological atypia.

Diffuse astrocytoma includes IDH mutant type, IDH wild type and NOS type. Diffuse astrocytoma IDH mutant type common in young male and in frontal lobe. Gemistocytic diffuse astrocytoma is variant of diffuse astrocytoma IDH mutant type and occur most commonly in adult male and in frontal and temporal lobes. Pleomorphic xanthoastrocytoma is rare and seen in children and young adults. Most commonly involving temporal lobe. Mitoses is < 5 per 10 high power field in Pleomorphic xanthoastrocytoma.

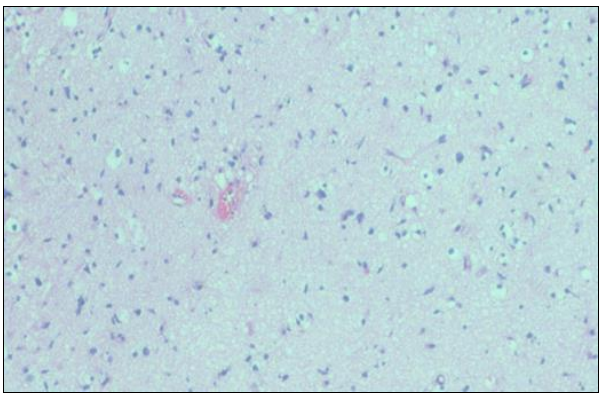

Fig 5: Diffuse Astrocytoma: Neoplastic fibrillary astrocytic cells in a background of a loosely structured matrix

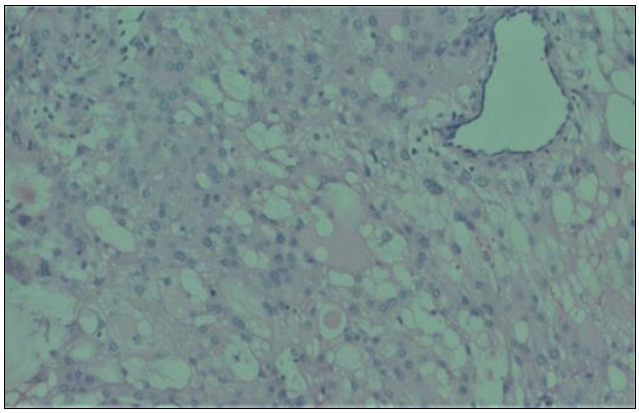

Fig 6: Pleomorphic astrocytoma: Large pleomorphic cells, spindle cells and lipidized cells.

Grade III astrocytoma include Anaplastic astrocytoma and Anaplastic pleomorphic xanthoastrocytoma with anaplasia

and mitotic activity.

Anaplastic astrocytoma includes IDH mutant type, IDH wild type and NOS type. Anaplastic astrocytoma most commonly involves frontal lobe in adult male. In Anaplastic pleomorphic xanthoastrocytoma, mitoses are > 5 per 10 high power field and have significantly worse survival then pleomorphic xanthoastrocytoma.

Grade IV astrocytoma include Glioblastoma according to anaplasia, mitotic activity, microvascular proliferation and/ or necrosis.

Glioblastoma include IDH mutant type (10%), IDH wild type (90%) and NOS type. Glioblastoma occur most commonly in older age group male. Most commonly involves supratentorial region in which most common in temporal lobe more than parietal and frontal lobe.

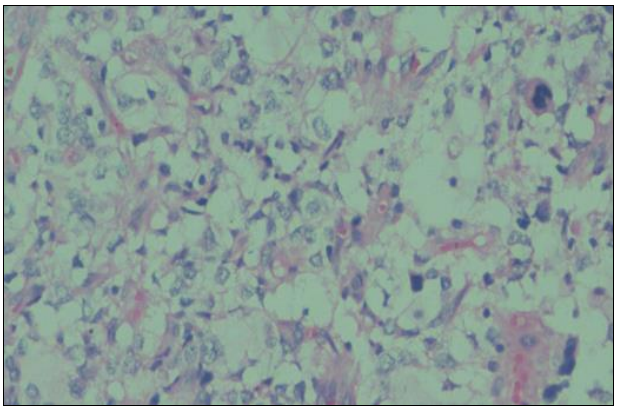

Fig 7: Anaplastic Astrocytoma: Elongated astrocytic nuclei with varying cytoplasm with significant pleomorphism and scattered mitotic figures with prominent atypical mitoses.

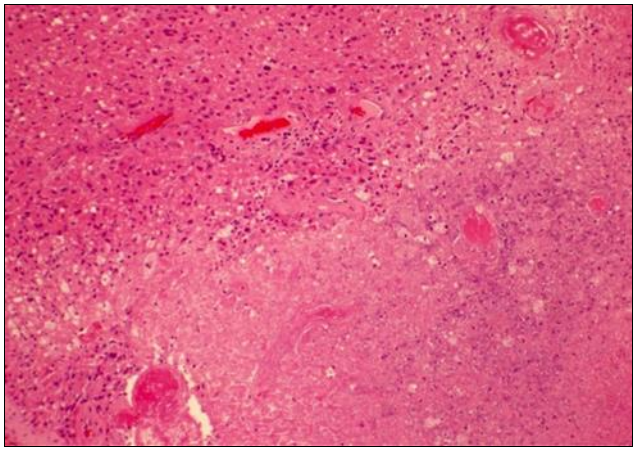

Fig 8: Glioblastoma: Highly cellular glioma, poorly differentiated tumor cells with nuclear atypia, areas of microvascular proliferation and necrosis

Conclusion

The present study provides histopathological aspects of astrocytic tumors. Over all the histology pattern of astrocytic tumors in present study paralleled with national and international data. Combining histopathological and molecular features helps in the definitive diagnosis and management of astrocytic tumors thus providing better quality of life to the patient.

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