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HEADACHE PROFILE OF BRAIN TUMOR PATIENTS IN MOHAMMAD HOESIN HOSPITAL PALEMBANG

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ABSTRACT

Headache is one of the most common complaint in population while a serious causative of underlying disease is very rare. Although headaches are rarely the result of a brain tumor, brain tumors are frequently associated with headaches. The challenges to the physician are to determine the specific feature of headache related to brain tumor. This is cross sectional study involved primary and metastatic brain tumor patient admitted in neurology ward of Mohammad Hoesin hospital from April 2018 to June 2019. The inclusion criteria including age > 18 years old and there was symptom of headache based on anamnesis. All were interviewed about their personal details (age, gender). The characteristic of headache was obtained based on questionnaire designed in our department. Various neurological symptoms related to the tumor were also recorded. Information of the tumor was obtained from the patient's chart (histopathology of the tumor) and from characteristic of neuroradiological finding (magnetic resonance imaging or computed tomography). Headache and tumor characteristics were compared between primary and metastatic tumor by contrasting frequencies. We also analysed the correlation between tumor characteristics (location, hidrocephalus, vasogenic edema and tumor type) with headache intensity. A total of 95 of 199 patients (48%) with headache symptom were studied in this series. Most patients were complained of chronic headache. Headache was mostly throbbing in both primary and metastatic brain tumors. Progressively headache was dominant in this study and more than half patients report the quality of headache as moderate at the onset. In 35,8% patients, headache was the patient's first complaint. Headache as the isolated symptom of brain tumor was found in only 3,2% and only 28,4% of patients fulfilled the three 'classic criteria' of the brain tumor headache. A great localizing value of the headache was found in 63 cases of 95 patients. Of the 61 patients with single tumor and unilateral side, the unilateral headache was on 48 cases (78,8%). Of the 26 patients with strictly bilateral headache, 10 cases (38,5%) had bilateral sided tumors. The incidence of brain tumor headache in this study is similar to previous reports although the classic brain tumor headache features was found in a small portion of the patients.

Keyword: brain tumor, classic brain tumor headache, headache

1. INTRODUCTION

Headache is one of the most common somatic complaint of patients seeking medical care. Most headaches are not of serious cause and can be diagnosed easily with a good history and physical examination. In a primary care setting, approximately 90% of headaches are classified as primary headache, such as tension headache or migraine. Of the remaining 10%, some are related to other causes, including brain tumors.

The challenges to the physician are to determine when underlying intracranial pathology may be causing the symptoms and to identify the few patients in whom a tumor is the cause of the headache [1].

Although headaches are rarely the result of a brain tumor, brain tumors are frequently associated with headaches. Up to 70% of patients have a headache during the course of their illness, particularly in the

final stages of their disease [2]. In approximately 60% of supratentorial tumors and 50% of metastatic brain tumors, the headache is one of the cardinal presenting symptoms [3]. However, isolated headache as the initial clinical manifestation of brain tumors is uncommon. A case controlled study reported the risk of primary tumour with a presentation of headache in primary care as 0.09% [4]. More often, patients with brain tumors will present with headache associated with other neurologic symptom, such as nausea, vomiting, papilledema, blurred vision, personality changes, seizures, and/or other focal neurological signs.

Although, there is no specific headache features of brain tumor, it is said that brain tumor headache tends to be non-throbbing, deep aching and intermittent in nature. It is worse on exertion, changing posture and may be associated with vomiting or aggravated by coughing or sneezing. However, brain tumor can cause headache which in some instances mimics migraine, tension-type or cluster headache.[5,2] Good clinical judgment, based on history taking and physical examination remains the cornerstone in the differential diagnosis of headache. The other reason to study headaches in brain tumor patients is trying to see if there are unique opportunities to understand something about the location and pathophysiology of headache pain in general, as well as the overlap between the traditional categories of primary and secondary headache. The purpose of this study is to determine the incidence of headache among patients with brain tumor and to describe common characteristics of headaches in brain tumor patients.

2. METHODS

This is cross sectional study involved primary and metastatic brain tumor patient admitted in neurology ward of Mohammad Hoesin Hospital from April 2018 to June 2019. This study was approved by ethical comitte of Mohammad Hoesin Hospital and Faculty of Medicine of Sriwijaya University No 066/kepkrsmhfkunsri/2018.

The inclusion criteria including age > 18 years old and there was symptom of headache based on anamnesis. Patients with no history of headache underwent no further evaluation. Thus, 95 patients took part. All were interviewed about their personal details (age, gender). The characteristic of headache was obtained based on questionnaire designed in our department. Various neurological symptoms related to the tumor were also recorded.

We recorded the course, frequency, duration, quality, intensity and location of headache. We also recorded timing of headache, trigger by valsava manuevers or not, response to drugs (painkillers and steroids) as well as occurrence of associated symptoms and neurology signs. Current headache was categorized according to course (less than a month, 1-3 month, > 3-6 month, > 6-12 month, > 12 month) frequency (daily, 1-3 day/week, 1 day/week, 1-3 day/month), duration of the event (<30 min, 30 min–1 h, h1-4 h, > 24h) location (frontal, temporal, parietal, occipital, vertex, unilateral, bilateral), intensity (on a numeric pain range scale (NPRS) from 1 to 10 with 1-4 for mild, 5-7 moderate and 8-10 severe , quality of pain (dull, pulsating, stabbing, pressing, other), association with blurry vision, vomiting, photophobia.

The terminology 'progressive headache' was used, when there was an increase in intensity, frequency, and duration of the pain. The change of pattern was defined as an alteration of headache frequency, localization, severity or quality. In each case, an attempt was made to classify the tumor-attributed headache (i.e. duration of attack, pain characteristics and associated symptoms) in line with the ICHD-II and categorizing it as migraine-like, tension-type-like, or cluster headache-like.

Information of the tumor was obtained from the patient's chart (histopathology of the tumor) and from characteristic of neuroradiological finding (magnetic resonance imaging or computed tomography). Tumor type was categorized as primary and metastatic. Based on lateralization, tumors were divided into unilateral and bilateral. Tumors were grouped into four categories by location: supratentorial, infratentorial, midline and supratentorial and infratentorial. Midline tumor included tumors in the midline structures such as pineal region, thalamus and third and fourth ventricle. Multiple tumors was categorized if there was more than one tumor according to CT or MRI. We also recorded hydrocephalus and vasogenic edema based on radiological characteristic impression by radiologist.

Statistical analysis was performed using SPSS 23.0 for Windows. Data were statistically evaluated using for univariate and bivariat analysis. The level of significance was set at $P< 0.05$. Headache and tumor characteristics were compared between primary and metastatic tumor by contrasting frequencies. We used Coefficient contingency to evaluate the correlation between tumor characteristics (location, hidrocephalus, vasogenic edema and tumor type) with headache intensity. We also compared the concordance between headache location and tumor location.

3. RESULTS

There were 199 patients were diagnosed with brain tumor during April 2018 to June 2019 in Mohammad Hoesin hospital.

Table 1. Clinical charackteristic of the patients (n=95)

Characteristic	Frequency (n)	Percentage (%)
Sex		
- Male	38	40,0
- Female	57	60,0
Ages (years)		
- 18-30	11	11,6
- 31-40	11	11,6
- 41-50	31	32,6
- 51-60	26	27,4
- >60	16	16,8
Tumour type		
- Primary	67	70,5
- Metastatic	28	29,5

A total of 95 patients with headache symptom were studied in this series. The female to male ratio was 1.2:1. The average age was 47,83±12,56 years, ranging from 20 year to 79 years. Finally, more than half patients had adult age at presentation (> 40 year). Primary brain tumor was higher compared to metastatic brain tumors. The clinical characteristics of patient are shown in Table 1.

In table 2, characteristic of patients according to headache status are presented. Most patients were complained of chronic headache (> 3 month) while the course of headache most common more than a year both of primary and metastatic. Fifty-four percent or 51 patients with headache had intermittent pain whereas continuous headache was noted in 46%. Only 44,2% patients reported headache on nocturnal and early morning. Headache was mostly throbbing in both primary and metastatic brain tumors. In this study more than half patients report the quality of headache as moderate at the onset.

Progressively headache was dominant in this study. Based on headache intensity, there was increasing severity of headache intensity from onset to hospitalized, while the number in moderate and severe headache increased when the patients were hospitalized (both in primary and metastatic). According to headache location, unilateral headache was pronounced in primary brain tumor. Contras to metastatic brain tumor, the headache location were equally distributed between unilateral and bilateral.

Table 2. Headache characteristic of the patients

Characteristic	Primary (n=67)	Metastatic (n=28)	p value
Intensity (onset)			
- mild	18 (26,9)	8 (28,6)	0,942[a]
- moderate	44 (65,7)	17 (60,7)	
- severe	5 (7,4)	3 (10,7)	
Intensity (hospitalized)			
- mild	7 (10,4)	4 (14,3)	0,957[a]
- moderate	31 (46,3)	11 (39,3)	
- severe	29 (43,3)	13 (46,4)	
Progresivity			
- Yes	53 (79,1)	18 (64,3)	0,130[b]
- No	14 (20,9)	10 (35,7)	
Course of headache			
- ≤ 1 month	13 (19,4)	2 (7,1)	0,176[a]
- 1-3 month	15 (22,4)	5 (17,9)	
- >3-6 month	15 (22,4)	6 (21,4)	
- >6-12 month	4 (6,0)	7 (25,0)	
- >12 month	20 (29,9)	8 (28,6)	
Duration			
- < 30 minute	34 (50,7)	12 (42,9)	0,451[a]
- 30 minute-1hour	14 (20,9)	7 (25,0)	
- >1minute-4 hour	14 (20,9)	5 (17,9)	
- > 24 hour	5 (7,5)	4 (14,3)	

Frequency			
- Daily	31 (46,3)	13 (46,4)	0,719[a]
- >1-3 day per week	20 (29,9)	10 (35,7)	
- 1 day per week	9 (13,4)	4 (14,3)	
- 1-3 day/month	7 (10,4)	1 (3,6)	
Timing of headache			
- Morning	25 (37,3)	4 (14,3)	0,001[a]
- Day	1 (1,5)	0 (0,0)	
- Night	12 (17,9)	1 (3,6)	
- Uncertain	29 (43,3)	23 (82,1)	
Quality			
- Pulsating	50 (74,6)	20 (71,4)	0,820[a]
- pressing	7 (10,4)	5 (17,9)	
- dull	1 (1,5)	0 (0,00)	
- stabbing	6 (9,0)	1 (3,6)	
- Other	3 (4,5)	2 (7,1)	
Laterality (onset)			
- Unilateral	47 (70,1)	14 (50,0)	0,062[b]
- Bilateral	20 (29,9)	14 (50,0)	
Laterality (hospitalized)	47 (70,1)	13 (46,4)	0,029[b]
- Unilateral	20 (29,9)	15 (53,6)	
- Bilateral			
Change of headache location			
- Yes	6 (9,0)	1 (3,6)	0,670[c]
- No	61 (91,0)	27 (96,4)	
Change of headache type			
- Yes	5 (7,5)	1 (3,6)	0,667[c]
- No	62 (92,5)	27 (96,4)	
Associated symtomps*			
- Blurry vision	13 (19,4)	3 (10,7)	0,169[a]
- Vomiting	15 (22,4)	4 (14,3)	
- Photofobia	1 (1,5)	1 (3,6)	
- Blurry vision, vomiting	3 (4,5)	1 (3,6)	
- Blurry vision, Fotofobia	3 (4,5)	2 (7,1)	
- Blurry vision,vomitung, photofobia	2 (3,0)	1 (3,6)	
- None	30 (44,8)	16 (57,1)	
Neurologic dysfunction			
- Yes	66 (98,5)	26 (92,9)	0,207[c]
- No	1 (1,5)	2 (7,1)	
Neurologic dysfunction*			
- Counsiousness disorder	24 (35,8)	10 (35,7)	0,992[b]
- Motorik	58 (86,6)	19 (67,9)	0,034[b]
- seizure	22 (32,8)	7 (25,0)	0,450[b]
- cranial nerves	56 (83,6)	19 (67,9)	0,087[b]
- higher cortical function	4 (6,0)	2 (7,1)	1,000[c]
Trigger by valsava			
- Yes	42 (62,7)	11 (39,3)	0,036[b]
- No	25 (37,3)	17 (60,7)	
ICD classification			
- Migrain	34 (50,7)	11 (39,3)	0,475[a]
	32 (47,8)	16 (57,1)	

- Tension	1 (1,5)	1 (3,6)	
- unspecific			
Medication			
- NSAID	1 (1,5)	2 (7,1)	0,004[a]
- Opioid	0 (0,0)	1 (3,6)	
- Steroid	16 (23,9)	12 (42,9)	
- Steroid + NSAID	47 (70,1)	13 (46,4)	
- Steroid + NSAID + Opioid	3 (4,5)	0 (0,0)	
Respons to drugs			
- Yes	64 (95,5)	27 (96,4)	1,000[c]
- No	3 (4,5)	1 (3,6)	
Headache location			
- Frontal	21 (31,3)	7 (25,0)	0,658[a]
- Oksipital	12 (17,9)	8 (28,6)	
- Parietal	15 (22,4)	3 (10,7)	
- Temporal	18 (26,9)	9 (32,1)	
- Vertex	1 (1,5)	1 (3,6)	

[*] *subjek may had more than one symtomps or neurologic dysfunction*
[a] *Mann Whitney*
[b] *Chi square pearson*
[c] *Fischer exact test*

Blurry vision and vomiting were most common association symptoms. Headache was more frequently accompanied by vomiting in the group of patients affected by tumors in supratentorial (19 patients). Only 2 patients complained of vomiting among 8 patients in infratentorial tumor. In most cases, motoric and cranial nerve disfunction were found in more than half patients of all clinical signs. In 35,8% patients, headache was the patient's first complaint. Headache as the isolated symptom of brain tumor was found in only 3,2% (1 primary and 2 metastatic patients). Only 28,4% of patients fulfilled the three 'classic criteria' of the brain tumor headache, i.e. severe pain intensity, morning occurrence and association with nausea or vomiting.

Valsava manuver (e.g Straining and movements) aggravated headache was found in 62,6% patients. The headache mostly responded to medication such as corticosteroid or acetaminophen in 95,7% patients. The headache citeria mimicked migraine and tension were met almost in equal proportion both in primary and metastatic brain tumor.

We also explored the tumors characteristic related to headache (table 3). Primary brain tumors were detected more than two folds compared to metastatic respectively. Supratentorial location was the most common both in primary and metastatic brain tumor. Unilateral sided and single lesion mostly found in primary brain tumor while multiple lesion dan vasogenic edema was dominant in metastatic brain tumor.

Table 3. Tumor characteristic

Characteristic	Primary (n=67)	Metastatic (n=28)	p value
Location			
- Supratentorial	53 (79,1)	19 (67,9)	0,086[a]
- Infratentorial	7 (10,4)	1 (3,6)	
- Midline	7 (10,4)	0 (0)	
- Supra+infra	0 (0,0)	7 (24,9)	
- Infra+midline	0(0,0)	1 (3,6)	
Sided			
- Unilateral	59 (88,1)	13 (46,4)	0,000[b]
- Bilateral	8 (11,9)	15 (53,6)	
Number			
- Single	65 (97,0)	6 (21,4)	0,000[b]
- Multiple	2 (3,0)	22 (78,6)	
Vasogenic edema			
- Yes	40 (58,2)	22 (78,6)	0,078[b]
- No	27 (41,8)	6 (21,4)	
Hydrocephalus			
- Yes	14 (20,9)	3 (10,7)	0,379[c]
- No	53 (79.1)	25 (89,3)	

[a]*Mann whitney*
[b]*Chi square pearson*
[c]*Fischer exact test*

When hospitalized, mostly patient suffered from moderate and severe intensity of headache with equal proportion. Based on tumor location, midline and infratentorial tumor tended to have severe headache when hospitalized. Statistical analysis showed that no significant difference between tumor characteristic and headache intensity (table 4).

Table 4. Correlation between tumor characteristic and headache intensity (hospitalized)

Tumour characteristic		Headache intensity			Total N	Coefficient correlation (r*)	p value
		Mild	Moderate	Severe			
Location	supratentorial	8	33	31	72	0,263	0,528
	infratentorial	0	3	5	8		
	midline	1	2	4	7		
	Supra+infra	2	4	1	7		
	Infra+midline	0	0	1	1		
Type	Primary	7	31	29	67	0,073	0,774
	Metastatic	4	11	13	28		
Vasogenic edema	Yes	7	25	30	62	0,117	0,515
	No	4	17	12	33		

Hydrocephalus	Yes	0	9	8	17	0,169	0,248
	No	11	33	34	78		
Total		11	42	42	95		

*****Coefisien Contingency*

We compared the concordance between tumor sided and headache lateralization. Tumor in midline location (8 patients) was excluded for this analysis as well as single tumor with bihemisfer location (3 patients) A great localizing value of the headache was found in 63 cases of 95 patients.

Table 5. The degree of correspondence of headache lateralization at the onset to the location of the tumor (Single tumor n = 61)

		Tumor Location		Total
		Unilateral	**Bilateral**	
Laterality of headache	**Unilateral**	48 (78,7)	0 (0,0)	48 (78,7)
	Bilateral	13 (21,3)	0 (0,0)	13 (21,3)
Total		61 (100)	0	63 (100.0)

Of the 61 patients with single tumor and unilateral side, the unilateral headache was on 48 cases (78,8%). Of the 26 patients with strictly bilateral headache, 10 cases (38,5%) had bilateral sided tumors (table 5 & 6). Supratentorial tumors were associated with ipsilateral headache in only 62,3% patients with single tumor while bilateral headache was found 26,7% patients with multiple tumor (data not shown).

Table 6. The degree of correspondence of headache lateralization at the onset to the location of the tumor (Multiple tumor n = 23)

		Tumor Location		Total
		Unilateral	**Bilateral**	
Laterality	**Unilateral**	5 (21.7)	5 (21.7)	10 (43.5)
	Bilateral	3 (13.0)	10 (43.5)	13 (56.5)
Total		8 (34.8)	15 (65.2)	23 (100.0)

4. DISCUSSION

Although the great majority of headache patients do not have intracranial abnormalities, it is important to exclude such causes. The physician as well as the patient, is likely to experience anxiety that headache will be falsely diagnosed as functional but will eventually prove to be due to brain tumor.

In brain tumor the clinical picture is characterised by two levels of symptoms consist of general symptoms associated with increased intracranial pressure and focal symptoms related to tumor location. Based on retrospective cohort study in population with headache symptom,

malignant brain tumors were identified in 0.22% of individual based on (0.19–0.26%; n = 178) after the incident headache visit.[6]

In our study the incidence of headache in brain tumor was 48%. This rate seems a little higher in primary than metastatic brain tumors (51% vs 40%). Headache as a symptom at the onset was found in 35,75% patients. In 42,1 % patients, headache became a chief complain to be hospitalized. (data not shown).

The incidence of headache in brain tumor in our study are similar with previous study, that reported about 20–71%.[9,2,7,8] A prospective study of 111 patients with both primary and metastatic brain tumors revealed an equal incidence of headache of 48% [10]. The other study showed that headache at presentation was reported in 37–62% of patient, with 60–90% of patients developing headaches over the course of their illness [11]. A prospective study reported approximately 58.78% of patients with brain tumor had headaches and half of them declared headaches to be their first complaint[12]. Case control study in primary care setting showed that headache as symptom of primary brain tumor in 10,2% compared to 2,6% in controlled group [4].

As a brain tumor symptom, headache could be appeared at the early or late course of the disease. Traction to pain sensitive structure role a major portion in pathophysiology of brain tumor headache. Brain parenchyma is insensitive to pain, and headache from intracranial tumors is often caused by traction and displacement of pain-sensitive intracranial structures located in the blood vessels, venous sinuses, cranial nerves, dura and the periosteum of the cranium. In brain tumor, traction results from the expansion of tumoral tissue, edema, and/or hemorrhage.[1,5,14,13]

The growth rate of space-occupying lesions also plays an important role in predicting the occurrence of traction and headache pain. Tumors that increase rapidly in size can cause sharp, intense pain because the intracranial space does not have a chance to adapt to the increased pressure. This is thought to result from the sudden irritation of pain-sensitive structures. Slow-growing tumors, on the other hand, produce headaches that are transitory and occur only later in the course of disease, principally because protracted mechanical adaptation to the expanding tumor is possible. Progressive headaches have been associated with more rapid growing tumors, the presence of hydrocephalus, midline tumor location, and the extent of edema. In the setting of presence hydrocephalus, the pain could be localized or distant depending on the degree or displacement of the brain that might cause traction on distant structures. [13]

Approximately 86–95% of patients with increased intracranial pressure have headaches [14]. These headaches can be distinguished from other types of brain tumor headaches due to their severity, association with nausea or vomiting and resistance to common analgesics, rather than their quality or location. The common signs and symptoms associated with increased intracranial pressure are headache, nausea, vomiting, lethargy, papilledema, visual obscuration, diplopia, tinnitus, and somnolence. Etiologies for the development of increased intracranial pressure include intracranial mass effect due to tumor, cerebral edema, intratumoral hemorrhage, obstructive hydrocephalus, communicating hydrocephalus, and leptomeningeal spread of the tumor. In the presence of elevated intracranial pressure, headaches tend to be more severe and constant

Patients with brain tumor usually suffer from chronic headache which headache lasting more than 3 months. Our study showed that 61,86% patients suffer with chronic headache. About 29,9 % patient reported duration of headache was more than twelve months which similar proportion between primary and metastatic. Only 15,7% reported new onset headache which is duration of headache less than 4 weeks. When the patients were hospitalized, it showed that most patients came with moderate and severe headache. Our study found that severe headache more pronounces with tumor in midline location even the number was smaller compared to other location. The presence of high intracranial pressure was note with sign such as vasogenic edema and hydrocephalus that correlated with higher intensity of headache even it was not significant in statistical analysis.

These finding literature was unlikely with our study**.** The previous study reported 29% headache lasting than 1 month while 45% case lasting more than 6 months [3]. The other study found that the risk of a malignant brain tumour with new undifferentiated headache was 0.15%, rising from 0.08 to 0.28% below and above the age of 50 years. Tumours were diagnosed within 3 months in 74% patients and in 90% patients by 6 months [15]. In a cross-sectional study of 171 patients, reported the duration of the headache was from 3 days to 10 years (Suwanwela et al, 1994). In addition, the proportion of patients with headache duration of less than 10 weeks was greater among those with newly diagnosed cerebral metastatic [10].

Brain tumor related headaches are usually intermittent in nature, generally lasting hours and tends to progressive by the time. Headaches associated with a mass lesion are often worse in the morning because brain edema increases overnight from the effects of gravity in the supine position (because of a lack of gravity-assisted drainage of the venous system) and because sleep normally increases arterial PCO_2 (high PCO_2 levels cause vasodilation, which, together with the effects of disease, increases intracranial pressure).

Classic brain tumor headache describes as moderate in intensity, throbbing and shooting in nature, associated with nausea and vomiting and usually progressive. The headache appears weeks and/or months before the diagnosis, lasts for hours, and occurring at night, often awakening the patient from sleep, or upon awakening in the morning. They may be exacerbated by valsalva maneuvers, such as lifting heavy objects, sneezing or coughing. In reality, however, that brain tumor uncommon presents with classic brain tumor headache. Often, headaches may be indistinguishable from primary headache category such as tension or migraine headaches [10].

Several previous studies had reported about headache characteristic in brain tumor. A study reported the headaches accompanying brain tumors were characterized as a throbbing headache, lasting for hours, increasing for weeks or months and moderate to severe in intensity [12]. However, another prospective study found that the pain was usually described as shooting or throbbing which was fairly nonspecific but progressively severe headache in 79.1% which was more characteristic [10]. In a prospective study of 111 patients with brain tumors, the “classic” brain tumor type headache occurred in a meager 17% of patients. 67% patients of this subtype of “classic” brain tumor headaches had evidence of increased intracranial pressure. Headaches were worse in the morning in 36%, worse with

bending over in 32%, worse with Valsalva in 23% and woke patients from sleep or interfered with falling sleep in 32% of the patients with headache. Headaches were described as similar to tension type in 77% of these patients; the second most common headache type is typically migraine like (5-10%), a finding duplicated in a prospective study [3]. Unlikely, in other prospective study, only 5.1% had classic brain tumor headache and when present was more commonly seen in patients with posterior fossa tumors (42.3%) (Valentinis et al, 2010).

In this study, brain tumor headache tended to intermitten, daily occurance, lasting for months and moderate to severe intensity**.** Contras to others study, the classic brain tumor headache was found in 28,49%. The characteristic describes as a throbbing with moderate intensity was the most common. 55,79% patient reported that headache was trigger by valsava manuver. Throbbing headache in this study fairly consistent with a study, but the others study reported the majority type was dull and aching.[7,2,12] Contrast to previous study, the characteristic headache mimicking tension and migrain (49,5% & 46,4%) was found nearly in a similar proportion. Another study found that in population with migrain headache, there was increasing risk of brain tumor while there were significant differences between cases and controls in the prevalence of prior migraines (4.89% vs. 2.08%, $p<0.001$) [16]. Migrain headache have moderate to severe intensity pain, in some instance makes the patiens curiuos about the dangerous underlying causative.

Although headache is a common feature of brain tumours, it very seldom occurs as a single symptom. Ussually patient with brain tumor have additional symptom and neurologic deficit. In our data showed only 3,2% came with isolated headache. 51,6% patients had associated symptoms and the most common were vomiting and blurry vision as well as motoric disfunction and cranial nerve palsy for the neurologic sign. Consistent with the previous study that reported the isolated headache as symptom of brain tumor was found in less than 10%(Schankin et al, 2007; Suwanwela et al, 1994; Vázquez-Barquero et al, 1994). Another work pointed out in their retrospective review of headache and brain tumor that headache can be present in 50% to 60% of cases [3]. Headaches more often occur with other symptoms and in approximately 33-71% of brain tumor patients [10]. Additional symptoms found in 54.1% included focal neurological (hemiparesis, unsteady gate, visual field defect, etc.) and in 37.6%, neuropsychological (memory deficit, dysphasia, change of personality, etc.). Symptomatic epileptic seizures occurred in 27.1%. In the study population vertigo, blurred vision, nausea/vomiting and tinnitus were also frequent (36.5%) [3]. Several previous studies estimated a differ result in headache number as a symptomps at hospital presentation. Study about brain tumor symptomps found that 39,82% patients of brain tumor came to emergency while headache as a symtomp about 20,8% (Ozawa et al, 2018). Headache as a symptom at emergency was 14,6% in previous [18]. In other study, headache was the most common first symptom in patients with single intracerebral tumor 23,5% and was present in 46,5% at hospital presentation. However, by the time of hospital presentation 86% of patients had other symptoms [19].

Historically, it was thought that the topographic distribution of headaches could have some predictive value in determining the location of underlying mass lesions. The most frequently cited cause of brain tumor headache is the presence of traction on intra- and extracranial pain-sensitive structures. In the absence of distal traction,

headaches occur regionally and are thus more predictive of tumor location. When intracranial pressure is high, however, headache pain has very limited localizing/lateralizing value, mostly because the distal traction produced by increased pressure activates pain-sensitive structures in widespread areas. The presence of increased intracranial pressure may slightly decrease the localizing value of ipsilateral headaches.[2] The headache may localize to the same side of the tumor or be generalized**.** Location of headache in brain tumor patients can have localizing value, especially in the early course of the disease. In this study showed the was concordance between tumor location and headache location in 66,3% patients. Unilateral headache mostly in single tumor with unilateral sided location while bilateral headache mostly found in multip tumor with bilateral location. Bilateral headache was also found in single tumor with hydrocephalus with vasogenic edema with less persentage. Contrast to midline tumor, mostly patients had bilateral headache even the tumor was single.

Previous study has reported value of headache in localization of brain tumors. A cross-sectional study from Thailand did evaluation of laterality while headache and the side of the tumor coincided in one third of patients [2]. Fairly consistent other study, that in the absence of increased intracranial pressure, headache correctly predicted the side of the supratentorial tumor 100% of the time.[2] Furthermore, among patients with unilateral headaches, the tumor was always on the ipsilateral side. In patients with clinical evidence of increased intracranial pressure, correct lateralization of the tumors was noted in 80% of supratentorial and 62.5% of infratentorial lesions. In patients without papilledema or other clinical signs of increased intracranial pressures, correct lateralization was possible in 100% of supratentorial and 80% of infratentorial lesions. Therefore, patients with supratentorial tumors had headaches that corresponded to the side of the tumor more often than patients with infratentorial tumors but there was no statistically significant difference.[2] Contrast with previous study while hemispheric tumors were associated with ipsilateral headache in only 41% of the patients, while the headache was contralateral in 11.7%, bilateral in 17.6%, diffuse in 20.7%, and central in 9% [12]. While the other study other studies headaches occurred on the same side as the tumor more commonly. The pain was most often hemispheric and was as likely to be bilateral (49.0%) as unilateral (21.6% or 29.4%).[7] A prospective study reported, of the 60 patients with strictly bilateral headache, 53.3% had hemispheric tumours and only 25% had midline or bilateral tumours [8]. Similarly, another study noted that bilateral headaches occurred in patients with elevated intracranial pressure with midline or bilateral tumors. Only infratentorial tumours were associated with headache location, and predominantly with occipital but rarely frontal pain while no other localizing or lateralizing value for headache as regards tumour location was found.[7]

5. CONCLUSION

The prevalence of headache pain in neuro-oncology patients is insufficiently high and its presentation too diverse to justify using this symptom as a diagnostic index. The classic brain tumor headache feature is not always found in brain tumor patient. A careful clinical workup and a thorough examination of the patient remain, to date, the most valuable way to establish the etiological significance of headache pain and the necessity for physicians to conduct additional tests.

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