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Correspondence of Meningioma Orbital Grading and Clinicopathological Features among Indonesian Patients

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Abstract

BACKGROUND: Orbital meningiomas can cause visual disturbances, protrusion of the eyes, double vision, and optic nerve abnormalities that significantly decrease vision and eventually lead to blindness. To the best of our knowledge, data on the incidence and pathogenesis of orbital meningioma in Indonesia are non-existent.

AIM: This study aimed to analyze the clinicopathological relationship with orbital meningioma grading.

METHODS: It is a cross-sectional observational analysis on 44 orbital meningioma patients in Dr. Hasan Sadikin General Hospital and the National Eye Center, Cicendo Eye Hospital in 2017–2020. Chi-square analysis and logistic regression with statistical significance ($p < 0.05$) were engaged in the method.

RESULTS: Orbital meningioma mostly occurred in women aged 30–44 years. Meningioma Grade I was dominated by meningothelial meningioma found in 14 (31.8%) patients, Grade II was atypical meningioma in 9 (20.9%) patients, and Grade III was anaplastic meningioma in 3 patients (6.8%). Clinical symptoms in the form of papillary atrophy ($p = 0.046$), visual acuity ($p = 0.026$), proptosis ($p = 0.029$), and hyperostosis ($p = 0.024$) were statistically significant and there was a significant difference between Grade I, Grade II, and Grade III using the Chi-square test. Logistic regression results showed that hyperostosis is significantly related to grading the orbital meningioma ($p = 0.044$) with an odds ratio of 0.206 (IK95% 0.04–0.955).

CONCLUSION: Hyperostosis increases the grading of the orbital meningioma because it is related to the invasion of the tumor into the orbital bone and is a neoplastic process. The presence of hyperostosis which is more common in Grade III meningiomas can be used as one of the most important predictors of meningioma recurrence postoperatively. Nonetheless, our data add to the existing literature the potential points of anti-invasive adjuvant therapy attacks.

Introduction

Meningiomas are primary brain tumors originating from arachnoid cells, classified based on their anatomical location. They are divided into primary optic nerve (ON) sheath meningioma, primary intraorbital ectopic (Ob) meningioma, and sphenobarbital (Sph-Ob) meningioma [1]. Orbital meningiomas have a prevalence of 0.4–2% of all meningiomas prevalence [2], [3], [4], with a female predisposition more often than men in comparison 3:1 [3], [5].

Meningioma is known to have considerable risk factors. Risk factors for orbital meningioma have been reported in several conditions. The information in the literature database shows that prominent factors include hormonal contraception [6], [7], diabetes mellitus [8], hypertension [9], [10], and trauma [11]. Hormonal birth control is one of the risk factors that are reported to have strong strength with the incidence of this disease. According to research and meta-analysis studies, there is a significant relationship between the duration of exposure to exogenous hormones in women and increased risk of meningioma [6], [7]. Case–control studies in East and West Germany reported a positive relationship between diabetes and the risk of meningioma [8]. The previous studies reported a positive relationship between hypertension and increased risk of meningioma incidence because metabolic pathways are actively stimulated, thus affecting the growth of meningioma independently [9], [10]. It has been reported that the presence of head trauma increased the risk of meningioma, and a case–control study in West Washington confirmed this [11].

Orbital meningiomas are generally slow-growing and will cause symptoms when they overwhelm adjacent structures. Meningiomas are genetically related to neurofibromatosis (NF2) which is found on chromosome 22q12, causing multifocal meningiomas. NF2 is a gene that produces the protein merlin. Clinical symptoms of orbital meningioma include visual disturbances, proptosis, diplopia, and abnormal pupils, as well as ON atrophy which leads

to fundus abnormalities, headaches, seizures, and hemiparesis [12], [13], [14]. Primary orbital meningioma with progressive clinical symptoms, namely, unilateral vision loss, axial proptosis caused by hyperostosis of the bone and is a neoplastic process, ON atrophy. Besides seizures, papilledema, nausea, vomiting, and headache, the clinical symptoms of spheno-orbital meningioma/secondary orbital meningioma include visual disturbances due to pressure on the ON, and diplopia due to compression of cranial nerves III, IV, and VI [4], [15]. Several studies have proven a significant relationship between grade and risk of recurrence. At higher tumor grades (Grades II and III), increased cellularity, higher mitosis, and necrosis predict increased recurrence. Overall, the most important prognostic factor regarding recurrence is related to the histopathological grade of orbital meningioma. The recurrence is more common in high-grade orbital meningiomas which, according to the WHO, are 29–59% in Grade II and 60–94% in Grade III, but rarely present in benign case or Grade I, that is, 7–25% [16], [17], [18].

One of the causes of blindness in Indonesia is tumors in the orbit, such as orbital meningioma tumor. To date, we have not found a robust data on national epidemiology (Indonesia) for all types of meningiomas, especially orbital meningioma. Therefore, the present research is of great importance to bring impact on blindness rates in Indonesia. This study fills a gap in clinicopathology in predisposing grading of orbital meningioma by analyzing the clinicopathological relationship with predisposing orbital meningioma grading.

Materials and Methods

An observational analytic study in form of cross-sectional investigated the secondary data from medical records of patients with confirmed orbital meningioma clinically, radiologically, and histopathologically at Dr. Hasan Sadikin General Hospital and the National Eye Center, Cicendo Eye Hospital. The primary data were obtained from the results of the re-evaluation of orbital meningioma subtypes and grading and secondary data such as gender, age, clinical symptoms (papillary atrophy, visual acuity, headache, proptosis, and hyperostosis), risk factor meningioma (diabetes mellitus, head trauma, history hormonal contraception, and hypertension), and radiology investigation without changing the existing diagnosis at the Dr. Hasan Sadikin General Hospital and the National Eye Center, Cicendo Eye Hospital between 2017 and 2020. Data sampling was conducted using a Chi-square analysis ($p < 0.05$), selecting 44 samples of the entire medical records which met the inclusion criteria in the secondary such as papillary atrophy, visual acuity, headache, proptosis, and hyperostosis and primary data such us subtypes and grading. The exclusion is secondary data incomplete, and the paraffin block is exhausted, so it cannot be re-evaluated for orbital meningioma subtype and grading. Predictive logistic regression test with $p < 0.05$ to determine which clinicopathological relationship is a risk factor for meningioma orbital grading.

Results

The results of histopathological analysis of subtype of meningioma according to the WHO 2016 showed that patients with histopathological types in Grade I consisted of 14 (31.8%) meningothelial meningioma, 2 (4.5%) fibrous meningioma, 4 (9.1%) transitional meningioma, 2 (4.5%) psammomatous meningioma, 2 (4.5%) angiomatous meningioma, and 2 (4.5%) microcystic meningioma. Orbital meningioma subtypes in Grade II consisted of 9 (20.5%) atypical meningiomas, 1 (2.3%) clear cell meningioma, and 1 (2.3%) chordoid meningioma. Grade III orbital meningioma resulted in 2 (4.5%) rhabdoid meningiomas, 2 (4.5%) papillary meningiomas, and 3 (6.8%) anaplastic meningiomas. Accordingly, the highest proportion of histopathological subtypes in Grade I included 14 (31.8%) meningothelial meningiomas, 4 (9.1%) transitional meningiomas, and 9 (20.5%). There were 9 (20.5%) atypical meningiomas in Grade II and 3 (6.8%) anaplastic meningioma in Grade III.

Table 1: Demographic mapping of the respondents to grading meningioma orbital

S. No.	Characteristic	Grade I (%)	Grade II (%)	Grade III (%)	Total (%)
1.	Age (n, %)				
	0–14 years old	2 (4 5)	0 (0)	0 (0)	2 (4.5)
	30–44 years old	11 (25)	7 (15.9)	4 (9.1)	22 (50)
	45–59 years old	11 (25)	3 (6.8)	2 (4.)	16 (36.4)
	60–74 years old	1 (2.3)	1 (2.3)	1 (2.3)	3 (6.8)
	75–89 years old	1 (2.3)	0 (0)	0 (0)	1 (2.3)
	Total (n = 44)	26 (59.1)	11 (25)	7 (15.9)	44 (100)
2.	Jenis Kelamin (n, %)				
	Male	1 (2.3)	1 (2.3)	2 (4.5)	4 (9.1)
	Female	25 (56.8)	10 (22.7)	5 (11.4)	40 (90.9)
	Total (n = 44)	26 (59.1)	11 (25)	7 (15.4)	44 (100)
3.	Education level (n, %)				
	Senior high school	3 (6.8)	0 (0)	2 (4.5)	5 (11.4)
	Junior high school	1 (2.3)	0 (0)	1 (2.3)	2 (4.5)
	Elementary school	22 (50)	11 (25)	4 (9.1)	37 (84.1)
	Total (n = 44)	26 (59.1)	11 (25)	7 (9.1)	44 (100)
4.	Employment status (n, %)				
	Unemployed	2 (4.5)	0 (0)	0 (0)	2 (4.5)
	Retired civil servant	1 (2.3)	0 (0)	0 (0)	1 (2.3)
	Farmers	1 (2.3)	1 (2.3)	1 (2.3)	3 (6.9)
	Entrepreneurs	2 (4.5)	2 (4.5)	2 (4.5)	6 (13.6)
	Housewife	20 (45.5)	8 (18.2)	4 (9.1)	32 (72.7)
	Total (n = 44)	26 (59.1)	11 (25)	7 (9.1)	44 (100)
5.	Province (n, %)				
	Other province	3 (6.8)	0 (0)	1 (2.3)	4 (9.1)
	West Java	23 (52,3)	11 (25)	6 (12.6)	40 (90.9)
	Total (n = 44)	26 (59)	11 (25)	7 (9.1)	44 (100)

In this study, there were more respondents with a history of hormonal birth control who suffered from meningioma, namely, 18 (40.9%) in Grade I, 10 (22.7%) in Grade II, and 4 (12.5%) in Grade III. Meanwhile, the number of patients without history of hormonal birth

control was 8 (18.2%) in Grade I, 1 (2.3%) in Grade II, and 3 (6.8%) in Grade III. Therefore, most orbital meningioma patients (32 individuals, 72.7%) have used hormonal contraception. Regarding head trauma, patients across grades showed no risk factors for head trauma, except for 1 patient (2.3%) in Grade II. The number of patients with DM risk factors in this study was 1 (2.3%) in Grades I and II, and 0 in Grade III. Meanwhile, a total of 3 patients (6.9%) with hypertension risk factors suffered from orbital meningiomas, one individual in Grades I, II, and III. Those without the risk factors were accounted for 25 (56.7%) in Grade I, 10 (22.7%) in Grade II, and 6 (13.6%) in Grade III.

This study found that the number of patients with orbital meningioma Grades I, II, and III in the right retrobulbar ocular in was 11 (25%), 4 (9.1%), and 3 (6.8%), respectively, while those in the left retrobulbar ocular was 5 (11.4%), 1 (2.3%), and 1 (2.3%), respectively. Patients with orbital meningioma Grades I, II, and III in the left spheno-orbital were 6 (13.6%), 2 (4.5%), and 0, respectively, while in the right spheno-orbital was 4 (9.1%), 4 (9.1%), and 3 (6.8%), respectively. The results of radiological investigations showed that ocular nerve sheath meningioma in Grade I was 9 (20.5%), Grade II was 3 (6.8%), and Grade III was 2 (4.5%). Furthermore, spheno-orbital meningioma (Sph-Ob) in Grade I was 17 (59.1%), Grade II was 8 (25%), and Grade III was 5 (11.4%). The recurrence rate of orbital meningioma patients in Grade I was 4 (9.1%), in Grade II was 0, and Grade III was 1 (2.3%).

The results of the analysis Chi Square in Table 2 showed statistically significant ($p < 0.05$) differences in clinical symptoms of papilledema, visual atrophy, proptosis, and hyperostosis among the groups of meningioma Grades I, II and III.

Table 2: Results of clinical pathology analysis with meningioma grading

S. No.	Variables	Grade I (%)	Grade II (%)	Grade III (%)	Total (%)	p
1.	Papillary atrophy	25.0	18.2	2.3	45.5	0.046
	Yes	15 (34.1)	3 (6.8)	6 (13.6)	24 (54.5)	
	No	11 (25)	8 (18.2)	1 (2.3)	20 (45.5)	
	Total (n = 44)	26 (59.1)	11 (25)	7 (15.9)	44 (100)	
2.	Headache	31.8	9.1	6.8	47.7	0.599
	Yes	12 (27.3)	7 (15.9)	4 (9.1)	23 (52.3)	
	No	14 (31.8)	4 (9.1)	3 (6.8)	21 (47.7)	
	Total (n = 44)	26 (59.1)	11 (25)	7 (15.9)	44 (100)	
3.	Vision					0.026
	Light perception (LP)	7 (15.9)	8 (18.2)	4 (9.1)	19 (43.2)	
	No light perception (NLP)	19 (43.2)	3 (6.8)	3 (6.8)	25 (56.8)	
	Total (n = 44)	26 (59.1)	11 (25)	7 (15.9)	44 (100)	
4.	Proptosis					0.029
	Yes	21 (47.7)	4 (9.1)	4 (9.1)	29 (65.9)	
	No	5 (11.4)	7 (15.9)	3 (6.8)		
	Total (n = 44)	26 (59.1)	11 (25)	7 (15.9)	44 (100)	
5.	Hyperostosis					0.024
	Yes	11 (25)	9 (20.5)	6 (13.6)	26 (59.1)	
	No	15 (34.1)	2 (4.5)	1 (2.3)	18 (40.9)	
	Total (n = 44)	26 (59.1)	11 (25)	7 (15.9)	44 (100)	

Chi-square $p < 0.05$.

The results of the logistic regression analysis in Table 3 showed that hyperostosis was meaningfully related to orbital meningioma grading ($p = 0.044$) with an odds ratio (OR) of 0.206 (IK95% 0.04–0.955). The odds ratio of 0.206 means that orbital meningiomas with hyperostosis have a 0.2 times risk of getting a higher meningioma rating. We can draw the conclusion that variable hyperostosis is meaningfully related to orbital meningioma grading as a risk factor.

Discussion

The results of the demographic analysis of orbital meningioma (Table 1) showed that the disease was most prevalent among respondents aged 30-44 years. Orbital meningiomas usually occur in the 3–4 decades of life, as reported in recent findings that it was common in people aged 30–50 years [19], [20]. In this study, female respondents occupied the highest proportion or 90.9%, which confirmed the previous studies that 75.6% of orbital meningiomas happened to adult women [4], [21]. The incidence ratio of orbital meningioma in female to male is 3:1. The higher prevalence of meningioma is observed among postmenopausal women received exogenous hormone replacement therapy (e.g., contraception) compared to those without the therapy [20], [22].

Trauma in the development of meningiomas remains controversial [23]. This study showed a 2.3% history of head trauma in Grade II which is in line with the case–control studies that reported an increased risk of meningioma in patients with a history of head trauma such as in men during sports activities. A long history of head trauma (10–19 years) and frequent head trauma has been reported to associate with a higher risk of meningiomas. However, a cohort study in Sweden reported that traumatic brain injury was not associated with primary brain tumors, including meningiomas [24].

The results of orbital meningioma in this study showed a 2.3% history of hypertension in each Grade I, II, and III, which is in accordance with the statement that an increased blood pressure is associated with the risk of brain tumors including meningiomas despite the unclear mechanism. The metabolic syndrome is estimated to have around 15% prevalence among non-diabetic European adults and is associated with an increased incidence of gliomas and meningiomas [9]. The present study showed that Grades I and II orbital meningiomas had a history of diabetes mellitus of 2.3% each, which confirmed Schneider that there was a positive relationship between people with diabetes mellitus and the risk of meningioma [8], [25]. However, there remains conflicting evidence as to whether diabetes is positively, unrelated, or inversely associated with meningioma risk.

In this study, the history of using hormonal contraceptives was 32 (72.7%). It is in accordance with the previous studies that the history of contraceptive use is based on the underlying factor of the relationship between exogenous hormones and the incidence of orbitocranial meningiomas because meningiomas

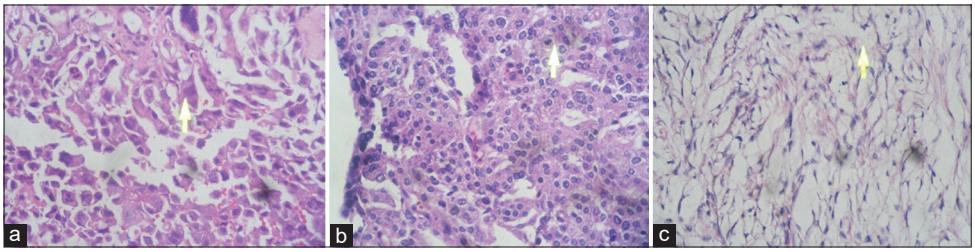

Figure 1: Histopathology (HE, ×400): (a) Orbital meningioma Grade III and (b) orbital meningioma Grade II. (c) Orbital meningioma Grade I

have progesterone and estrogen receptors, which if activated with the appropriate hormone will trigger the proliferation of meningioma cells. The pathophysiology of orbitocranial meningioma is also associated with the duration of hormonal contraceptive use, in which with the result that the use of hormonal contraceptives for more than 10 years increased the risk factors for meningioma. The mechanism underlying the relationship between the exposure duration to exogenous hormones and the development of meningiomas is that exogenous progesterone, in the long term, can change progesterone levels and progesterone receptor expression and has impact at the genetic level, namely, Merlin tumor suppressor gene, especially in meningeal tissue, specific for the NF-2 gene protein which regulates the growth of nervous tissue, including meningeal tissue [22], [26].

The results showed that most orbital meningioma Grade I was found in the right retrobulbar ocular. Based on the radiological examination, the most common spheno-orbital meningioma and its recurrence was in Grade I. This is consistent with the fact that spheno-orbital meningioma is the third most common location for meningiomas. En plaque meningiomas with extension to the orbit represent only 2–9% of meningiomas. Spheno-orbital meningiomas are diagnosed based on their growth pattern and their radiographic appearance but not on their histological morphology. They tend to induce bone hyperostosis and the extent of hyperostosis is usually disproportionate to the size of the meningioma [27], [28]. In this study, there was a recurrence of four subjects in Grade I meningioma and one subject in Grade III meningioma. Patients with meningiomas were grouped into three recurrences or risk groups based on the WHO's grading by class, resection rate, and recurrence status. Group I patients have a low risk of recurrence with Grade I meningioma, either by subtotal or total resection. Group II patients are at moderate risk with Grade II meningioma after crude resection or recurrent Grade I meningioma. Group III patients are at high risk and include those diagnosed with Grade III meningioma, Grade II recurrent meningioma, and newly diagnosed Grade II meningioma who undergo subtotal resection [20].

The results showed that the histopathological subtype of orbital meningioma Grade I had the highest proportion of 14 (31.8%) meningiothelial meningiomas (Figure 1). The highest subtype in Grade II was atypical

Table 3: Multivariate clinical pathology analysis with meningioma orbital grading

Steps	Variables	Coefficient	Standard error	p	OR	IK 95%	
						Min	Max
Step 1	Papillary atrophy (1)	–1.929	1.187	0.104	0.145	0.014	1.489
	NLP vision (1)	1.607	0.894	0.072	4.987	0.864	28.772
	Proptosis (1)	1.259	1.044	0.228	3.524	0.455	27.259
	Hyperostosis (1)	–1.905	0.948	0.044	0.149	0.023	0.954
	Constant	–.035	0.705	0.960	0.966		
Step 2	Papillary atrophy (1)	–1.322	0.947	0.163	0.267	0.042	1.706
	NLP vision (1)	1.845	0.850	0.030	6.329	1.197	33.468
	Hyperostosis (1)	–2.090	0.911	0.022	0.124	0.021	0.737
	Constant	0.096	0.683	0.888	1.101		
Step 3	NLP vision (1)	1.325	0.712	0.063	3.762	0.932	15.186
	Hyperostosis (1)	–1.581	0.783	0.044	0.206	0.044	0.955
	Constant	–0.427	0.568	0.452	0.652		

Logistic regression test p < 0.05; Hosmer and Lemeshow test step 3 p = 0.863; area under curve IK (95%) step 5 = 0.777 (0.634–0.920).

meningioma, detected in 9 participants (20.5%) while the Grade III orbital meningioma subtype was anaplastic meningioma in 3 participants (6.8%). In line with the previous studies, meningothelial is the most common histopathological type [21]. Histopathological appearance of meningothelial cells is round, oval nuclei, uniform, lobes of medium size, pale eosinophilic cytoplasm with indistinct cell boundaries, forming a whorl structure.

A study reported that there were significant differences in clinical symptoms of papilledema, visual disturbances, proptosis, and hyperostosis between meningiomas Grades I, II, and III. It is in line with the previous studies that the main complaint of primary orbital ON meningioma usually includes ON compression, extension of subdural space and is more progressive, can be in the form of loss of one-sided vision, proptosis, or ON atrophy [4], [23], [29]. Proptosis (45–100%) and progressive visual impairment (30–77%) are the two most common complaints in patients with orbital meningiomas. Proptosis occurs because of the invasion of the tumor bone in the orbital wall, the mass effect pressing the intraorbital soft-tissue component of the tumor, and the reduction of venous drainage from the orbit [25], [27]. ON abnormalities may be due to intracranial hypertension causing papilledema or direct compression of the ON causing papillary atrophy and the presence of optociliary shunt vessels on the surface of the optic disk. The common symptom is progressive loss of one-sided vision accompanied by painless exophthalmos. Gradual loss of visual acuity is common but there are reports that acute visual acuity loss occurs in 2–5% intracanalicular and 8–12% intracranial. Common clinical symptoms include optic disk changes, diplopia due to cranial neuropathy, or

direct disturbance of the rectus muscle, headache, nausea, and vomiting [23].

Meningioma orbital, especially the type of spheno-orbital meningioma (Sph-Ob), is often associated with eye disorders, namely, compression of the afferent and efferent ON s, proptosis caused by hyperostosis in the orbital cavity. In this study, the results showed that there was a significant relationship between hyperostosis and orbital meningioma grading, with an OR of 0.206. This is because hyperostosis can cause compression of the ON [30]. Spheno-orbital meningiomas are usually low grade (Grade I). High-grade meningiomas, such as Grades II and III, in the spheno-orbital region are usually rare [31]. The exact cause and mechanism of bone hyperostosis in spheno-orbital meningioma remain unclear and subjected to debate. The current consensus is the existence of histologic tumor invasion in respected bone specimens. It suggests that hyperostosis is essentially a part of the neoplastic process. Changes in signal intensity on MRI reveal increased vascularity of these tumors, essentially from the external carotid supply [27]. Hyperostosis of orbital meningiomas is may be associated with expression matrix metalloproteinases (MMPs). MMPs capable of destroying these ECM components are required for skull tumor infiltration. MMP is a calcium-dependent zinc-containing endopeptidase that degrades extracellular matrix (ECM) and is involved in the penetration of tumor cells into adjacent tissues. This molecule initiates angiogenesis and the bioactive processes of proteins such as cytokines, chemokines, and cell surface receptors [32]. Bone is mainly composed of type I, type V, and type VI collagen. MMP-1, also known as interstitial collagenase, degrades type I collagen and may be associated with malignancy. Mutations in the promoter region of the functionally acquired MMP-1 gene are not associated with stronger infiltration of adjacent structures by meningiomas. The above mechanism means that the expression of MMP 1 can be associated with the occurrence of hyperostosis in orbital meningiomas. Less frequent use of MMP-1 was associated with studies in meningiomas unlike MMP-2 and MMP-9. MMP-2 (gelatinase A) and MMP-9 (gelatinase B) degrade basement membrane type I, type IV, and type V collagen. These proteases are responsible for the development of peritumoral edema, grade meningioma, recurrence rate, and brain infiltration associated with meningioma. MMP-2 expression depends on the histological subtype of meningioma, and it has been observed that MMP-2 expression is the weakest in meningioma and the highest production in fibroblastic meningioma. Both MMP-2 and MMP-9 are involved in angiogenesis. Expression of MMP9 was correlated with expression of VEGF in meningiomas. The combined data of MMP-2, MMP-9, and VEGF expressions in the meningioma with skull infiltration may reveal the critical role of angiogenesis in determining bone invasiveness of these tumors [32], [33], [34], [35], [36].

On the other hand, we know that the inflammatory process is a promoting factor for tumor growth in research by Gunadarma found a high expression of IL-6 in meningiomas with hyperostosis. IL-6 is produced by meningioma cells but does not stimulate tumor growth, whereas IL-6 mediates the differentiation of osteoblast and osteocytes into osteoclasts. Therefore, the role of IL-6 in hyperostosis in meningiomas is attributed to the effect of bone resorption rather than to tumor cell growth [32], [37]. The limitation of our study is that it did not examine IL-6 expression associated with the mechanism of hyperostosis.

Conclusion

Orbital meningiomas are more common in women aged 30–40 years. History of using hormonal birth control is a risk factor for the occurrence of orbitocranial meningiomas because meningiomas have progesterone and estrogen receptors which, when activated with the appropriate hormones, will trigger the proliferation of meningioma cells. The duration of using hormonal contraceptives above 10 years increases the risk factors for meningioma. The relationship between the exposure duration to exogenous hormones and the development of meningiomas that exogenous progesterone in a long term can change progesterone levels and progesterone receptor expression and have impact at the genetic level the Merlin tumor suppressor gene, especially in meningeal tissue, specific for the NF-2 gene protein which regulates the growth of nervous tissue, including meningeal tissue. Based on radiological examination, the most common spheno-orbital meningioma and recurrence was found in Grade I. The most common histopathological type of orbital meningioma was meningothelial meningioma. There is a significant relationship between the clinical symptoms in the form of papillary atrophy, visual acuity, proptosis, and hyperostosis with the grade of orbital meningioma. Hyperostosis is found to be the most influential risk factor with the predisposition of orbital meningioma grading. It shows that hyperostosis is indeed a part of the neoplastic process, which may be associated with EGVR expression, MMPs, EGFR, and IL-6. The presence of hyperostosis which is more common in Grade III meningiomas can be used as is one of the most important predictors of meningioma recurrence postoperatively. Nonetheless, our data add to the existing literature the potential points of anti-invasive adjuvant therapy attacks.

Statement of ethics

This study has been approved by the Research Ethics Commission of the Dr. Hasan Sadikin Bandung

(LB.02.01/X.6.5/201/2020), and the research permit was issued by the Research Ethics Committee of Dr. Hasan Sadikin General Hospital and the National Eye Center, Cicendo Eye Hospital. The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. No written informed consent was obtained as this was a retrospective observational study (2017–2020).

Authors' Contributions

Raudatul Janah devised the project, the main conceptual ideas, proof outline, and drafted the manuscript. Lantip Rujito and Daniel Joko Wahyono reviewed the manuscript.

Data availability statement

All data generated or analyzed during this study are included in this. Further enquiries can be directed to the corresponding author.

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