The identification of factors affecting intracranial meningioma recurrence two years postoperatively

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Abstract. The study objective was to determine the recurrence rate of intracranial meningioma and the risk factors that are contributory to an increase in the incidence of recurrence. A prospective design was used in this study on meningioma patients treated at Cipto Mangunkusumo Hospital between 2010 and mid-2015. Data on the subjects were collected from the Departments of Neurology, Neurology, and Pathology, at the Universitas Indonesia/Cipto Mangunkusumo Hospital. The subjects were adults who had been previously diagnosed with meningioma. Follow-up was performed to assess the patients in relation to their initial clinical presentation. Neuroimaging was carried out to determine recurrence. The histopathological findings, extent of tumor resection (using Simpson’s criteria), and World Health Organization grade, were also determined. Immunohistochemistry was performed to evaluate the expression of progesterone receptor (PR), Ki-67, and vascular endothelial growth factor (VEGF). The recurrence rate was then analyzed to determine any correlation with the aforementioned risk factors. The recurrence rate was found to be 13%. Ki67, VEGF, and PR expression was positive in 9%, 73%, and 50% of the subjects, respectively. A significant correlation was not found between the study variables (tumor location, the scope of resection based on Simpson’s criteria, histopathologic grade, mitotic index, i.e., Ki-67, and PR and VEGF expression in the meningioma tissue) and the recurrence of meningioma.

1. Introduction
Meningioma was identified as the most frequently found primary intracranial tumor (58%) at Cipto Mangunkusumo Hospital, Jakarta, Indonesia, followed by glioma (24%), according to 2011 data from the Pathology Anatomy Department, Faculty of Medicine, Universitas Indonesia [1]. Globally, meningioma is the second most frequently identified intracranial tumor (21%) after glioma (50%). Most of these tumors (90%) are histologically benign (i.e., grade I, World Health Organization [WHO]) and have a good prognosis following resection [2]. Thus, Simpson’s criteria and the degree of tumor malignancy, based on the WHO tumor classification grading system, are the main benchmarks for predicting postoperative recurrence [3-5]. Recurrence is difficult to predict in a real clinical scenario, even for tumors that have been totally resected macroscopically, and that involve the dura and bone (grade I, Simpson’s criteria). Recurrence, with unknown mechanisms, of 4–15%, was demonstrated in one study [6]. Globally, prognostic factors have been sought and analyzed in relation to their impact on the recurrence of intracranial meningioma. Comprehensive data on the recurrence of meningioma in patients in Indonesia is not yet available.
Thus, the objective of the current study was to determine the recurrence level of intracranial meningioma in patients in the country and to identify risk factors that could lead to recurrence and/or an associated increase therein. Specifically, the study aims were to determine: (1) the prevalence of meningioma recurrence two years postoperatively; (2) the relationship between WHO grade and Simpson’s criteria and the recurrence rate of intracranial meningioma; (3) The relationship between progesterone receptor (PR), vascular endothelial growth factor (VEGF), and Ki67 expression in relation to intracranial meningioma recurrence.

2. Materials and Methods
A cross-sectional study design was used. The level of recurrence of intracranial meningioma and contributing factors were analyzed in this study. The assessed variables included tumor location, the scope of resection (based on Simpson’s criteria), histopathologic grade, mitotic index (Ki-67), and PR and VEGF expression in the meningioma tissue. The study was conducted at Cipto Mangunkusumo Hospital, Indonesia. The study population was adult patients diagnosed with intracranial meningioma between January 2010 and May 2015. A method of consecutive non-random sampling was employed.

The inclusion criteria were patients aged >18 years, who agreed to participate in the study, who could be followed-up directly, who were able to undergo neuroimaging two years postoperatively, and for whom immunohistochemistry (IHC) of tissue samples from the previous surgery was possible. The exclusion criteria were unsuccessful IHC staining using the coloring method (≥2 attempts), and patients for whom direct follow-up was not feasible or who had demised.

3. Results and Discussion
Meningioma was the most frequently identified intracranial tumor in Cipto Mangunkusumo Hospital, Jakarta, Indonesia. This was in line with previous study that stated males have generally higher rates of primary malignant brain tumors while females have higher rates of non-malignant tumors, primarily meningiomas [7]. Data from several national cancer registries support differences in the epidemiology of brain tumors in children versus adults. For example, in Sweden, medulloblastoma and low grade glioma are the most common type of tumors in pediatric cases aged 15 years and younger; this is very different compared to the adult cases, in whom high-grade glioma and meningioma are the most common types of adult primary brain tumors. Data from CBTRUS support these differences in the United States as well [7].

Certain biological behavior has been found to play an important role in prognosis. Prognostic factors for the recurrence of postoperative meningioma are yet to be described in Indonesia. Two hundred and eight-two patients with intracranial meningioma were identified. Follow-ups could feasibly be conducted for 32 patients (11%), who also agreed to provide informed consent. The subjects were mostly women (27 subjects, 32%). There is a paucity of research on treatment outcome and patients’ survival as well as demographic and clinicopathological variables and prognostic factors in patients receiving radiation therapy. Previous study suggested the tumor grade as the most important prognostic factor in meningioma outcome [8]. As shown in previous reports, the extent of surgical resection is a critical prognostic factor determining the meningioma treatment outcome. The risk of recurrence and progression-free survival is largely dependent on the extent of tumor removal during surgery [9,10].

Convexity meningiomas were the most common type identified (13 subjects, 41%). The tumors of 14 subjects (44%) were classified as grade IV using Simpson’s criteria, and those of 19 subjects (59%) were categorized as grade I using the WHO tumor classification grading system. Recurrence occurred in four subjects (13%). Twenty-two of the 32 subjects could be tested immunohistochemically. Positive Ki67 expression was observed in 2 cases (9%), VEGF expression in 16 cases (73%), and PR expression in 11 cases (50%). A significant correlation was not established between intracranial meningioma recurrence and the WHO classification (p = 0.60) or between its recurrence and Simpson’s criteria. A significant association was also not found between PR, VEGF, and Ki67 expression, and intracranial meningioma recurrence.
4. Conclusion
The majority of the intracranial meningiomas were histologically benign and were located on the convexity in the current study, with a Simpson’s grade of IV or V. Only a few patients could be followed-up to determine recurrence. The prevalence of intracranial meningioma recurrence two years postoperatively was found to be 13%. A significant correlation was not established between the identified factors and recurrence, or with the key factor, i.e. WHO classification (p > 0.005). A more thorough follow-up in relation to recurrence is warranted in future studies on the identified factors to determine significant risk factors for meningioma in Indonesia.

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