

Analysis of the influencing factors of neurological dysfunction after surgery of cerebral arteriovenous malformations

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Keywords: Cerebral arteriovenous malformation; Postoperative; Neurological dysfunction; influencing actors

Abstract: **Objective** To investigate the influencing factors of postoperative neurological dysfunction in patients with cerebral arteriovenous malformation (CAVM). **Methods** From March 2012 to March 2017, 106 patients with CAVM who received surgical treatment in the department of neurosurgery of the first hospital of Jilin University in Changchun city were analyzed. Neurological function of the patients was assessed by modified Rankin score (mRS) before and 7 days after surgery. **Results** 28 of 106 patients (26.42%) had postoperative nerve dysfunction. **Conclusion** CAVM patients are prone to neurological dysfunction after surgery.

Cerebral arteriovenous malformation (CAVM) is one of the most common cerebral arterial malformation (CAVM), which is a congenital disease caused by abnormal cerebral vascular development during embryonic period. Bleeding is the most common symptom of CAVM, accounting for 43 percent to 69.6 percent. The annual bleeding rate of untreated CAVM is 2%~4%, and the CFR of the first hemorrhage is about 10%. The CFR of the second hemorrhage would be increased. The incidence of neurological impairment after each hemorrhage is about 50%, and the annual mortality and disability rate caused by hemorrhage is 2.7%. Treatment depends on a comparison with CAVM's natural history and treatment risk. Unfortunately, they are still not fully understood until now.

CAVM therapy includes microsurgery, endovascular embolization, stereotactic radiotherapy, combined therapy and clinical observation. Microsurgical excision can immediately remove the lesion and eradicate blood theft, and it is recognized as an ideal treatment for CAVM. The mortality of operation is 0% ~12.5%, the morbidity and disability rate is 3% ~ 30%, which is higher. In order to explore the clinical factors influencing the efficacy of CAVM microsurgery, the author retrospectively analyzed the clinical data of 106 CAVM patients who were treated with microsurgery in neurosurgery department of the first hospital of Jilin University from March 2012 to March 2017.

1. Materials and methods

1.1 General information

From March 2012 to March 2017, 106 CAVM patients, including 69 males and 37 females, were admitted to the neurosurgery department of our hospital and received surgical treatment. The patients' age was between 4 and 55 years old. 72 cases had intracranial hemorrhage before operation, while 34 cases had no intracranial hemorrhage. There were 67 cases with malformed vascular masses less than 3cm, 34 cases with 3-6cm, and 5 cases with larger than 6cm. The lesions were located in the functional area in 47 cases, and in the non-functional area in 59 cases. There were 24 cases with deep vein drainage and 82 cases without deep vein drainage. There were 20 cases of malformed vessels with aneurysms and 86 cases without aneurysms. And 33 cases of Spetzler - Martin class I, 41 cases of II level, 20 cases of III level, 7 cases of IV level, 5 cases of V grade.

1.2 Inclusion criteria

Those who meet the following three criteria are selected.

- 1) CAVM patients admitted and treated by Digital subtraction angiography DSA and CTA in the department of neurosurgery of the first hospital of Jilin University from March 2012 to March 2017;
- 2) Complete medical records; 3) The operation was successful.

1.3 Exclusion criteria-except for any one of the following six points.

- 1) Received embolization and gamma knife treatment before surgery; 2) Preoperative radiotherapy; 3) Insufficiency of heart, lung, liver, kidney and other important organs before operation; 4) Preoperative stress ulcer; 5) Intracranial hemorrhage unrelated to CAVM was observed before surgery; 6) Preoperative detection of lesions with other properties (e.g., intracranial tumors, intracranial infections, abnormal brain development, etc.)

2. Treatment

All patients received microsurgical treatment under general anesthesia, and the operative position were selected according to the lesion location. Resection of malformed vascular masses should follow the principle of first cutting off the blood supply artery and then cutting off the draining vein. Routine electrophysiological monitoring was performed intraoperatively, and intraoperative indorqual fluorescence imaging was used to determine arterial and postoperative CAVM resection. After surgery, the patients were admitted to the neurosurgical ICU for close observation, and the systolic blood pressure was controlled at about 120mmHg 24h after surgery. Pathological examination and immunohistochemical analysis were performed on the intraoperative specimens.

3. Efficacy evaluation

The modified Rankin Scale (mRS) was used to evaluate the neurological status of patients, and the grading criteria were as follows. 0 point, completely asymptomatic; 1 point, with symptoms, but no obvious dysfunction, the patient can complete daily work and life; 2 points: mildly disabled, unable to complete all activities before illness, but able to independently take care of daily affairs without help; 3 points: moderate disability, partial help needed, but able to walk independently; 4 points: moderately and severely disabled, unable to walk independently, and in need of help in daily life; 5 points: severe disability, bed rest, incontinence; Six points, death.

4. Statistical methods

Binary Logistic regression model was used to examine the relationship between gender, age, preoperative intracranial hemorrhage, CAVM size, venous drainage, CAVM site and early postoperative new neurological defects. Spetzler-Martin classification and early postoperative neuro-functional deficits were evaluated by chi-square test. P<0.05 was considered statistically significant. All statistical analysis was performed by SSPS 19.0 statistical software.

5. Results

5.1. Comparison of imaging and laboratory test indexes of patients

Among the 106 patients, 28 patients (26.42%, 28/106) developed new neurological dysfunction (including 2 patients who died of brain stem failure, 1.89%). The relative expression of VEGF in the abnormal vascular masses was 0.032~0.815, with an average (0.059 + 0.015) and a median value of 0.057. The relative expression of ang-1 was 0.027~0.071, with an average (0.041 + 0.007) and a median value of 0.041. The relative expression of ang-2 was 0.014~0.080, with an average (0.038 + 0.007) and a median value of 0.032. In patients with recent postoperative neurological dysfunction, RI in CAVM blood supply artery was lower, VEGF expression was higher in abnormal vascular tissue, ang-1 expression was lower, and ang-2 expression was higher, and the difference

was statistically significant ($P<0.05$).

5.2 Logistic regression analysis of influencing factors of postoperative neurological dysfunction in patients

Indicators with statistically significant differences between groups included in the univariate analysis, taking intracranial hemorrhage, deep venous drainage, lesion location, the lesion size and grade of Spetzler - Martin, concomitant aneurysm, blood supply artery RI, deformity arteriolar VEGF, Ang - 1, Ang - 2 as the independent variable, and taking recent nerve dysfunction as the dependent variable to carry out the logistic regression analysis. The results showed that the high expression of ang-1 in preoperative intracranial hemorrhage malformed vascular mass was a protective factor for the recent postoperative neurological dysfunction ($P<0.05$), and the high expression of VEGF and ang-2 in the vascular mass with deep venous drainage lesion located in the functional area with larger lesions Spetzler-Martin grade III~ grade V was a risk factor for the vascular mass with aneurysm hyperri malformation ($P<0.05$).

6. Discussion

CAVM's main therapeutic objective is to prevent and treat bleeding, also remove hematoma, as well as improve blood stealing, and control epileptic symptoms. Although microsurgical regimens can effectively reduce the disability rate, the postoperative recovery of patients still needs to be improved.

In this study, postoperative mRS score was increased in 43 of the 213 patients, indicating that new neurological defects occurred, accounting for 27.19%, suggesting that it is necessary to explore the factors affecting the recovery of neurological function of patients. This study showed that deep venous drainage, the location of the lesion in the functional area and the large size of the lesion were risk factors for postoperative neurological dysfunction. The above indexes were all components of Spetzler-Martin classification, indicating that Spetzler-Martin classification is an important indicator for predicting the short-term prognosis of patients.

CAVM deep vein drainage is very fragile, and it is difficult to hemostasis and easy to retract after rupture, also bleeding is easy to enter the brain parenchyma and ventricle. At the same time, such blood vessels are often located near the brain line, which may lead to intraoperative damage to the thalamus, basal ganglia, brain stem, etc.. The larger the vascular malformation is, the more difficult the intraoperative separation is, and the more likely it is to damage the surrounding brain tissue, prolonging the operation time, and increasing the risk of surgical complications. At the same time, the larger the malformed vascular masses are, the greater the blood flow through CAVM is, the more blood is stolen, and the risk of postoperative normal perfusion pressure breakthrough increases correspondingly, increasing the risk of postoperative neurological dysfunction.

In this study, it was also found that patients with aneurysms were more likely to suffer from postoperative neurological dysfunction, which may be related to factors such as the need to simultaneously treat aneurysms during the operation, the vulnerability of aneurysms to rupture and bleed during the operation, and the increased difficulty of the operation. This study found that patients with intracranial hemorrhage are not prone to new neurological dysfunction after surgery, which may be because intracranial hemorrhage itself can lead to severe neurological dysfunction in patients, and the surgery will not further aggravate the above disorders, and may help improve such disorders. Therefore, patients with intracranial hemorrhage have a lower risk of new nerve function injury after surgery. In this study, it was found that the mechanical parameters of blood supply arterial blood flow are helpful to predict postoperative neurological dysfunction, which may be because this index is related to vascular rupture, and the smaller the resistance index is, the lower the blood flow velocity is, and the blood supply to brain tissue in functional areas may therefore decline, affecting the recovery of neurological function. VEGF, ang-1 and ang-2 are all related to abnormal angiogenesis and are important indicators reflecting patients' conditions.

This study also found that increased VEGF, ang-2 and decreased ang-1 are independent factors influencing postoperative neurological dysfunction of patients, which may be related to the decrease

of vascular stability and endothelial permeability caused by the above changes. In conclusion, patients with CAVM are prone to neurological dysfunction after surgery. High expression of ang-1 in preoperative intracranial hemorrhage and malformed blood vessels may reduce the risk of postoperative neurological function. Deep venous drainage, lesions located in functional area, larger lesions, Spetzler - Martin class III ~ V, concomitant aneurysm, low blood supply artery RI, abnormal blood vessels VEGF and Ang - 2 high expression may increase the risk of postoperative nerve dysfunction.

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