Reduction of Blood Flow in the Brain Stem and Cerebellum Caused by Petroclival Tumors

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Abstract

Blood flow in the brain stem (BSBF) and cerebellum (CerBF) was investigated by positron emission tomography in 12 patients with petroclival tumors (study group) and 14 healthy volunteers (control group). 15O-labeled water was used as the radioisotope tracer. BSBF and ipsilateral CerBF were significantly lower in the study group compared with the control group (p < 0.005). Five of 12 patients in the study group exhibited more than 20% reduction of CerBF ipsilateral to the tumor, whereas no such asymmetry was disclosed in any subject in the control group (p < 0.01). Sex, age, and tumor histology had no statistically significant association with the level of BSBF. Ipsilateral CerBF was significantly lower in patients with vestibular schwannomas, compared to those with sphenopetocirical meningiomas (p < 0.025). No statistically significant association between BSBF and the type of postoperative course was found, whereas four of the five patients with more than 20% reduction of CerBF ipsilateral to the tumor had prominently increased cerebellar ataxia after removal of the neoplasm. Preoperative investigation of the cerebral blood flow may be important for the prediction of outcome after surgical resection of petroclival tumors.

Key words: petroclival tumor, cerebral blood flow, surgery, outcome

Introduction

Modern neurosurgical methods and tools now allow successful resection of virtually any skull base neoplasm, including those located in close proximity to the brain stem. However, the risk of postoperative morbidity remains high. Various risk factors of poor outcome have been identified, including advanced age and low preoperative performance status of the patient, large tumor size, presence of brain stem compression, invasion and/or edema, recurrence or regrowth of the neoplasm, previous radiation therapy, and ventriculoperitoneal shunting.1,5,13,16–18 The preoperative level of the blood flow in the brain stem (BSBF) and the cerebellum (CerBF) may also have some prognostic significance.9,11 The present study measured the BSBF and CerBF in patients with petroclival tumors which caused significant brain stem compression, and investigated the association with the severity of the postoperative course after surgical resection.

Materials and Methods

BSBF and CerBF were measured by positron emission tomography (PET) in 12 patients with petroclival tumors (study group), 10 women and two men aged 16 to 70 years (mean 48.7 ± 18.3 years), including six patients with vestibular schwannomas of whom one had bilateral neoplasms and one had recurrent tumor, four patients with meningiomas, one patient with trigeminal schwannoma, and one patient with epidermoid cyst (Table 1). All patients had significant compression of the brain stem caused by the tumor. The control group consisted of nine men and five women aged 18 to 49 years (mean 34.5 ± 14.2 years). The study protocol was approved by the Commission of Problems in Neurooncology of the Russian A.L. Polenov Neurosurgical Institute. Informed consent for investigation was obtained...
Table 1 Clinical characteristics of the study group

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age/ Sex</th>
<th>Diagnosis (side of the tumor)</th>
<th>KPS score</th>
<th>BSBF*</th>
<th>Ipsilateral CerBF*</th>
<th>Extent of tumor removal</th>
<th>Postoperative course</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16/F</td>
<td>vestibular schwannoma (bil)</td>
<td>80</td>
<td>0.7214</td>
<td>0.7216</td>
<td>total/subtotal</td>
<td>uneventful/uneventful</td>
</tr>
<tr>
<td>2</td>
<td>20/F</td>
<td>vestibular schwannoma (lt)</td>
<td>90</td>
<td>0.6576</td>
<td>0.9822</td>
<td>total</td>
<td>uneventful</td>
</tr>
<tr>
<td>3</td>
<td>34/M</td>
<td>trigeminal schwannoma (lt)</td>
<td>80</td>
<td>0.8206</td>
<td>0.8615</td>
<td>total</td>
<td>uneventful</td>
</tr>
<tr>
<td>4</td>
<td>36/F</td>
<td>epidermoid cyst (rt)</td>
<td>80</td>
<td>0.8934</td>
<td>0.8623</td>
<td>total</td>
<td>uneventful</td>
</tr>
<tr>
<td>5</td>
<td>45/F</td>
<td>sphenopetrosclival meningioma (lt)</td>
<td>90</td>
<td>0.7153</td>
<td>1.0811</td>
<td>subtotal</td>
<td>uneventful</td>
</tr>
<tr>
<td>6</td>
<td>53/F</td>
<td>sphenopetrosclival meningioma (lt)</td>
<td>100</td>
<td>0.8473</td>
<td>0.9986</td>
<td>no surgery</td>
<td>no surgery</td>
</tr>
<tr>
<td>7</td>
<td>59/F</td>
<td>sphenopetrosclival meningioma (lt)</td>
<td>90</td>
<td>0.8419</td>
<td>1.1422</td>
<td>no surgery</td>
<td>no surgery</td>
</tr>
<tr>
<td>8</td>
<td>59/F</td>
<td>vestibular schwannoma (rt)</td>
<td>80</td>
<td>0.8683</td>
<td>0.9215</td>
<td>total</td>
<td>uneventful</td>
</tr>
<tr>
<td>9</td>
<td>63/F</td>
<td>vestibular schwannoma (lt)</td>
<td>80</td>
<td>0.6416</td>
<td>0.4022</td>
<td>subtotal</td>
<td>severe</td>
</tr>
<tr>
<td>10</td>
<td>63/F</td>
<td>sphenopetrosclival meningioma (lt)</td>
<td>90</td>
<td>0.7762</td>
<td>0.7465</td>
<td>subtotal</td>
<td>severe</td>
</tr>
<tr>
<td>11</td>
<td>66/F</td>
<td>vestibular schwannoma (rt)</td>
<td>80</td>
<td>0.6365</td>
<td>0.6453</td>
<td>total</td>
<td>severe</td>
</tr>
<tr>
<td>12</td>
<td>70/M</td>
<td>recurrent vestibular schwannoma (rt)</td>
<td>60</td>
<td>0.6342</td>
<td>0.1015</td>
<td>total</td>
<td>severe</td>
</tr>
</tbody>
</table>

*Expressed as relative isotope activity (see text). Bold: significant (more than 20%) reduction of the ipsilateral CerBF. BSBF: blood flow in the brain stem, CerBF: blood flow in the cerebellar hemisphere, KPS: Karnofsky performance status.

from each patient.

PET used a Scanditronix PC 2048 scanner (Scanditronix Medical AB, Uppsala, Sweden), which can obtain 15 axial slices simultaneously. 15O-labeled water was used as a radioisotope tracer. Blood flow was evaluated by PET adaptation of the autoradiographic method. All patients and volunteers were placed in the scanner with the head fixed in a molded head holder. Fast bolus intravenous injection of 30 mCi of 15O-labeled water dissolved in 5 ml of saline was followed by immediate start of the scanning. Images were acquired during 1 minute parallel to the orbitomeatal plane with a spacing of approximately 6.5 mm. Isotope activity was calculated in nCi/cm³. The region of interest was determined by alignment of the PET and magnetic resonance images. Blood flow was evaluated semiquantitatively by calculation of the relative isotope activity, defined for BSBF as the ratio between mean isotope activity in the brain stem at the level of maximum compression and mean isotope activity in the contralateral cerebellar hemisphere, and for CerBF as the ratio between mean isotope activity in the ipsilateral cerebellar hemisphere and mean isotope activity in the contralateral cerebellar hemisphere.

Ten patients underwent surgical removal of their tumors, whereas two rejected treatment. Both neoplasms were removed in the patient with bilateral vestibular schwannomas. Total resection was achieved in seven cases, and subtotal resection in four.

The early postoperative period was classified according to the previously proposed scheme.1) The postoperative course was characterized as uneventful if the patient had non-complicated awakening after anesthesia, had stable vital functions thereafter, had unchanged or slightly impaired neurological status which did not interfere with performance, and became completely independent in daily life by 2–3 days after surgery. The postoperative course was characterized as severe if the patient had non-complicated awakening after anesthesia with complete stabilization of the vital functions during 24 hours after surgery, possible transitory depression of consciousness, unchanged or impaired neurological status which interfered with performance, but with an evident trend for clinical improvement starting from the 1st week after tumor removal. The postoperative period was considered unfavorable if serious disturbances of the vital functions started immediately after surgery, associated with coma and signs of brain stem dysfunction. The postoperative period was called complicated if the patient had seemingly uneventful recovery during the initial hours or days after surgery, but experienced significant impairment due to neurological, regional, or systemic complications which interfered with performance and necessitated intensive therapy or urgent reoperation.

Non-parametric statistical methods, namely the chi-square test, Mann-Whitney-Wilcoxon test (t), and Spearman correlation (Rs), were used as appropriate for data analysis. The level of significance was p < 0.05.

Results

In the present series, five patients including one with bilateral tumors had an uneventful postopera-
Fig. 1 Comparison of blood flow in the brain stem (BSBF) and ipsilateral cerebellar hemisphere (CerBF), expressed as relative isotope activity, in the control (circles) and study (diamonds) groups. Several patients with petroclival neoplasms had hypoperfusion of the brain stem and ipsilateral cerebellar hemisphere. Bars indicate medians. *p < 0.005.

Fig. 2 T1-weighted magnetic resonance image (A) and positron emission tomography scan (B) in a patient with sphenopetroclival meningioma causing brain stem compression (Case 10) showing reduction of blood flow in the brain stem (arrowheads) and ipsilateral cerebellar hemisphere (arrows).

Sex (t = 1.338; p > 0.1) and age (R = −0.439; p > 0.05) showed no statistically significant association with the ipsilateral CerBF. However, patients with vestibular schwannomas had significantly (t = 2.535; p < 0.025) lower ipsilateral CerBF than those with sphenopetroclival meningiomas. Mean relative isotope activity was 0.73 ± 0.23 and 0.99 ± 0.17, respectively.

Ipsilateral CerBF had a statistically significant association with the type of postoperative period (t = 2.500; p < 0.025). Mean values of the relative isotope activity in the ipsilateral cerebellar hemisphere in patients with uneventful and severe postoperative courses were 0.91 ± 0.13 and 0.55 ± 0.30, respectively. Four of the five patients with more than 20% reduction of CerBF ipsilateral to the tumor had a severe postoperative course.

Discussion

Intracranial neoplasm may cause significant hypoperfusion in the peritumoral brain tissue, ipsilateral hemisphere, and even distant areas of the brain, frequently associated with alterations of the autoregulation of cerebral blood flow.2−4,6−12,14,15 Scintigraphy disclosed reduced blood flow in the ipsilateral cerebellar hemisphere in five of nine patients with cerebellopontine angle tumors.14 Xenon-enhanced computed tomography showed that in patients with vestibular schwannomas, the ipsilateral CerBF was 45 ± 13 ml/100 g/min compared with contralateral CerBF of 58 ± 15 ml/100 g/min.9,11 Our PET-based study also demonstrated significant ipsilateral reduction of CerBF in five of 12 patients with various petroclival tumors.
Moreover, brain stem compression caused by the tumor was associated with reduction of BSBF in several patients, in contrast to previous findings in only a few patients with large cerebellopontine angle tumors.6,10)

Intracranial neoplasms could reduce cerebral blood flow by various pathophysiological mechanisms. Firstly, direct compression of the cerebral structures by the tumor may cause pressure-induced ischemia with associated atrophy.2–4,9,15) Cerebral blood flow values lower than 10 ml/100 g/min have been reported in the vicinity of intracranial meningiomas.15) In the present study, the ipsilateral CerBF was reduced in patients with vestibular schwannomas, compared to those with sphenopetrosclival meningiomas, which probably reflects the more posterior location of the former with more prominent compression of the cerebellar hemisphere. Secondly, accumulation of edematous fluid in the peritumoral brain may result in increased tissue pressure and hypoperfusion.3,4,7,6,15) Peritumoral edema is negatively correlated with the regional cerebral blood flow.6) Thirdly, brain areas distant from the tumor may suffer from hypoperfusion due to diaschisis, which is believed to be caused by transneural mechanisms.9,14) In the posterior fossa, this effect can be initiated by deactivation of the corticopontocerebellar pathway due to compression of the middle cerebellar peduncle.14) Fourthly, the brain tumor may secrete metabolically active substances, which can diffuse into the peritumoral brain and directly alter the microvasculature.4)

Fifthly, hypoperfusion may be caused by compression or encasement of the arteries on the base of the brain.9) Finally, significant increases of intracranial pressure with concomitant decreases of cerebral perfusion pressure may augment reduction of the cerebral blood flow in the affected peritumoral brain areas.4,12) Any of these mechanisms can influence the BSBF and CerBF in patients with petroclival tumors.

Patients with lower preoperative BSBF values require longer hospital stays and have higher risks of neurological impairment after removal of cerebellopontine angle tumors.9,11) In the present series, ipsilateral decrease of CerBF was associated with severe postoperative course due to increased cerebellar ataxia. Therefore, preoperative investigation of the cerebral blood flow may be important for prediction of the outcome after surgical removal of posterior fossa tumors causing brain stem or cerebellar compression. However, further studies with more patients and use of cerebral metabolism mapping are definitely needed to define the exact role of peritumoral hemodynamic abnormalities in the development of neurological signs and postoperative complications.

**Acknowledgment**

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Dr. M.F. Chernov is presently a Clinical and Research Fellow at the Department of Neurosurgery of the Tokyo Women’s Medical University under the sponsorship of the Ministry of Education of Japan.

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Commentary on this paper appears on the next page.
Commentary

The authors should be commended for studying this important problem, connected with displacement and compression of the brain stem and cerebellum by tumors growing from the petroclival region. Reduced blood flow through the brain stem and cerebellum on the ipsilateral side to the tumor should be an additional warning sign that surgery on such patients should be extremely carefully planned and executed in order not to aggravate the clinical status. As the authors pointed out, several causes may exist for reduced blood flow through the compressed brain stem and cerebellum. Any damage to the veins does have an important negative effect on the local circulation. Most probably the most important is still gentle handling of the neural and vascular tissues at surgery. If the surgeon succeeds in preserving the petrous vein with all its branches, as well as the veins on the surface of the brain stem, and in addition, if the tumor is removed without any surgical retraction of the cerebellum and the brain stem, this is a guarantee that the surgical outcome will be good and the final result of treatment optimal.

The authors claim that there was no difference regarding the nature of the tumor, however, it is well known that different tumors have a different cleavage line between the tumor and the brain tissues. And it is also clear that the size of a tumor and displacement of the brain stem and the cerebellum is less important than the (non) existence of the pial membrane, since when it is destroyed, complete resection of tumor from the brain stem is extremely difficult and never without affecting the corresponding functions.

Further studies will be necessary in order to prove useful in the grading of possible damage of blood circulation in the brain stem and cerebellum prior to surgery in cases of large PCA tumorous lesions. Any decrease in cerebellar and/or brain stem circulation should be a serious warning prior to surgery, that the PCA tumors should be treated by somebody who has vast experience in surgical treatment with these pathologies.

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The authors presented the outcome of their analysis of blood flow studies in the brainstem and in the cerebellum adjoining the tumors located in the cerebellopontine angle and petroclival region. I believe that such an evaluation may form an important preoperative study in the future. As discussed by the authors, surgery on petroclival and cerebellopontine angle tumors is a challenging endeavor. The surgeon looks for all the possible information regarding the nature of the tumor, the difficulties that he will encounter during the surgery and to prognosticate the outcome from the preoperative studies.

MRI gives considerable information regarding the size, consistency and vascularity of the tumor, nature of the arachnoid plane, anatomical extensions, encasement/displacement of the blood vessels and the effects of the tumor on the adjoining brainstem. All these factors mentioned have significant bearing on the conduct and outcome of the surgery. It would have been worthwhile if the authors could have included the radiological parameters and related them to the findings of blood flow.

The other important issue that affects the surgery in the region is the clinical symptoms. Surgery in patients with long standing symptoms and gross neurological deficits is different from surgery in tumors with shorter duration of symptoms and minimal neurological deficits. It would have been worthwhile if the authors could have included the clinical presentation in their overall analysis.

In the petroclival region, surgery for a meningioma is entirely different from surgery on a vestibular schwannoma or an epidermoid tumor. It is surprising to note in this study that the cerebral blood flow is affected almost equally in a meningioma and a vestibular neurinoma. This feature has discouraged me regarding the efficacy of blood flow study in the presented group. Further studies on this subject are warranted to critically evaluate the efficacy of the presented investigation.

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