Intracranial infection after neurosurgery is mainly caused by iatrogenic bacterial infection and is usually not fatal. Herpes simplex encephalitis is a rare postoperative infection, and it can be fatal if appropriate treatment is delayed. In several articles investigators have described HSE in relation to the surgical treatment of such brain tumors as craniopharyngioma, parasagittal meningioma, glioblastoma multiforme, oligodendroglioma, vestibular schwannoma, and sphenoid wing meningioma. In addition to being rare, HSE after craniopharyngioma surgery is not easy to detect because symptomatology can be masked by the effects of steroids, or confused with electrolyte imbalance related to extrapontine myelinolysis, surgical field retraction injury, or vascular insufficiency. Here, we report a unique case of HSE after craniopharyngioma resection and discuss the importance of the early diagnosis and treatment of HSE.

Case Report

History and Examination. This 13-year-old girl presented with a 1-year history of visual impairment and a 6-month history of intermittent headaches. The patient's height and weight were 139.5 cm (third percentile) and 38.6 kg (25th percentile). Neurological examination revealed decreased visual acuity (0.5/0.5) and bitemporal hemianopsia. Computed tomography scanning and MR imaging revealed a heterogeneous enhancing mass lesion with calcification on the suprasellar area (Fig. 1). There was no definite abnormality in serum hormonal levels; thus, hormonal replacement treatment was not given before surgery. Dexamethasone (3 mg intravenously every 6 hours) was administrated on the day of the operation to reduce cerebral edema.

Operation. We performed an anterior interhemispheric and subfrontal approach. The mass was radically resected except for portions that were attached to the optic chiasm and left optic nerve. The pituitary stalk was sacrificed during the procedure. An immediate postoperative brain CT scan showed pneumocephalus with some fluid collection in the operative bed (Fig. 2 left). Craniopharyngioma (adamantinomatous type, World Health Organization Grade I) was diagnosed based on histopathological examination.

Postoperative Course. The patient experienced drowsiness and fever (38.3°C) during the early postoperative period. Based on careful physical examination and laboratory findings, we, along with an infection specialist, concluded that her fever was caused by sinusitis and an upper respiratory tract infection rather than postoperative CNS infection. On the 6th postoperative day, the patient was transferred to a general ward with clear mental status. At that time, brain CT scanning showed that no new...
lesions had appeared (Fig. 2 right). On the 10th postoperative day the patient’s fever had subsided, although a low-grade fever (37.4°C) was observed intermittently. The peak and frequency of fever decreased without antibiotic administration, and on the 15th postoperative day the fever had subsided completely (36.9°C). Her CRP levels were elevated after surgery, decreased gradually, and normalized on the 6th postoperative day (Fig. 3). Because of central DI, desmopressin acetate was administered intermittently via subcutaneously during 4 days after surgery, and it was changed to oral form starting on the 5th postoperative day. Levothyroxine was administered starting the 7th postoperative day. Dexamethasone was replaced with oral prednisolone and this was maintained. The patient’s condition was gradually improving. She could ambulate with a walker and exhibited no limitations in conversation, although her speech and movement were slow.

On the 15th postoperative day, the patient experienced an episode of urinary incontinence during ambulation, after which her condition deteriorated. The next day she presented with the tendency to sleep and answered questions only briefly. There were no signs of seizure. An MR imaging study taken on the 17th postoperative day showed low signal intensity in the left frontal lobe and insula, and increased subdural fluid collection in both frontal areas (Fig. 4). Laboratory tests showed mild leukocytosis (white blood cell count 8800/µl, segmented neutrophils 73%, and lymphocytes 7%), hypernatremia (146 mmol/L), and elevation of liver enzymes (aspartate aminotransferase/alanine aminotransferase 52/84 IU/L). On the 18th postoperative day, the patient experienced tachypnea and semicomatose mentality. On chest radiography we noted a haziness of the entire...
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left lung field, and the patient was intubated and ventilator therapy was initiated. A chest radiograph taken after intubation and endotracheal suction showed improvement in the left lung field; therefore, we thought that the difficulty in expectoration was related to the deterioration in mental state, which triggered airway obstruction. On the same day, the patient underwent bur hole trephination, and subdural fluid was aspirated to relieve the mass effect of the subdural fluid collection. On the 19th postoperative day, a fever (37.8°C) was noticed for the first time since the 15th postoperative day. Intermittent fever was sustained until the 23rd postoperative day, after which it subsided. On the 22nd postoperative day, transcranial Doppler ultrasonography revealed that blood flow velocity was elevated in the bilateral MCAs and ACAs, suggesting vasospasm (right MCA 130 cm/second, left MCA 157 cm/second, right ACA 129 cm/second, and left ACA 149 cm/second). We continued triple-H therapy (hypervolemia, induced hypertension, and hemodilution), although vasospasm could not fully explain the cerebral infarction localized on the left side because elevated blood flow velocity occurred bilaterally.

A follow-up CT scan on the same day revealed an increased low-attenuated lesion on the left frontotemporal lobe (Fig. 5 left). Although HSV infection had not been confirmed in our patient’s medical history, herpes encephalitis was suspected based on the location of the lesion and the rapid progression of the disease. A CSF study was done, and antiviral therapy with high-dose acyclovir11 (10 mg/kg every 8 hours) was started immediately. The CSF study detected several white blood cells (2 neutrophils/ml and 3 lymphocytes/ml), slightly decreased glucose (39 mg/dl), and an increased protein level (113.9 mg/dl). All bacteriological and fungal culture studies of CSF samples obtained during a lumbar puncture were negative, but the results of the CSF PCR for HSV DNA were positive. The normalized CRP levels increased again. After acyclovir treatment, the serum level of CRP started to decrease and normalized on the 25th postoperative day (Fig. 3). The CT scan acquired on the 25th postoperative day showed more diffuse and prominent low-attenuation lesions in the left hemisphere (Fig. 5 right). After antiviral therapy for 3 weeks, the patient recovered enough to speak short sentences; however, dysphasia and right hemiplegia remained.

A follow-up MR imaging study obtained 2 months later showed diffuse extensive loss of cerebral parenchymal tissue in the left hemisphere, including the medial side of the left thalamus. At follow-up 1 year after surgery in an outpatient clinic, the patient was alert and her speech had improved enough to communicate. An MR imaging study taken 13 months after surgery showed a small enhancing lesion in the tuberculum sellae, an enlarged ventricle, and progressive tissue loss (Fig. 6). The enhancing lesion was small and seemed to have slightly decreased in size. We planned a short-term follow-up without adjuvant treatment.

Discussion

After resection of the craniopharyngioma, neurological deterioration might be induced by direct injury or brain retraction during surgery, postoperative CNS infection, electrolyte imbalance due to DI and related extrapontine myelinolysis, hormonal insufficiency, or vasospasm, among others. In addition, herpes viral infection involving the CNS should be considered, especially when other possible causes do not explain the clinical status. In the present case report, we considered several possible causes of our patient’s altered mental status based on clinical course and neuroimaging findings. First, we suspected that a brain retraction injury had occurred intraoperatively. Because both frontal lobes were retracted during the anterior interhemispheric approach, the infarction in the left frontal lobe could have occurred. However, the unilateral nature of the lesion and the chronological changes in our patient’s neurological status did not support the notion that a retraction injury had occurred. Second, a bacterial CNS infection was considered, and during a subdural drainage operation, some subdural fluid was collected and examined. The laboratory investigation then revealed that the possibility of bacterial CNS infection was low. Therefore, we did not give our patient...
antibiotics to target bacterial CNS infection. Third, vasospasm might have been the cause of our patient’s deterioration. There are several reports about delayed cerebral infarction after skull base surgery, suggesting that vasospasm induced by variable factors can cause infarction. Although transcranial Doppler ultrasonography did not prove that vasospasm had occurred, empirical triple-H therapy was begun. Fourth, subdural fluid collection in the frontal area was suspected to produce a mass effect resulting in a semicomatose mentality. However, no significant interval change occurred in our patient’s mentality after subdural fluid drainage. Fifth, electrolyte imbalance related to DI and extrapontine myelinolysis caused by rapid electrolyte correction were examined thoroughly as a possible cause of altered mentality. During postoperative days, DI was well controlled in our patient under the administration of desmopressin, and serum electrolyte levels were stable. Thus, electrolyte imbalance and extrapontine myelinolysis could not be the cause of the altered mentality in our patient. Last, we focused on the location of lesions, the rapid progression of the disease state, and elevated CRP. We started antiviral therapy before the final report of HSV was received because of our patient’s rapid deterioration and the time lag for diagnostic confirmation of HSV.

Herpes encephalitis is the most common sporadic form of acute encephalitis, and its annual prevalence is 1–4 individuals per million population. It is thought to result from primary HSV infection of brain parenchyma or trigeminal nerve ganglia, or latent reactivation of HSV. The mechanism of HSV reactivation is unclear, but studies show that immune suppression, certain stresses, trauma, and radiation are possible causes. Therefore, steroid treatment for hormonal replacement might suppress a patient’s immunity, subsequently leading to HSV reactivation.

Herpes simplex encephalitis progresses rapidly and commonly results in grave consequences; early diagnosis and treatment are essential. However, a clinical suspicion is not always easy to prove because of HSE’s nonspecific symptoms. Fever, headache, and alteration of mentality are typical clinical symptoms of HSE, but these symptoms are also common in other postoperative complications that occur more frequently than HSE. Previous reports indicate that HSE should be considered to be a cause of fever of unknown origin after a neurological procedure. In particular, a latent period of 4–10 days after neurosurgery is a typical finding for the onset of HSE. Our patient, fever was not observed when her condition worsened, but CRP levels had gradually elevated. Fever is one of the most important signs of infection, although it is not always present and can be masked by the effects of steroid treatment. In this situation, the CRP level can be predictive of covert infection. Brain MR imaging is the most sensitive modality for detecting early lesions and is the imaging method of choice in HSE. It can reveal focal edema in the medial region of the temporal lobe and the orbital surface of the frontal lobe, the insular cortex, and angular gyrus. Cerebrospinal fluid PCR for HSV DNA, which is rapid, sensitive, specific, and minimally invasive, is essential for the diagnosis of herpes encephalitis. In our patient, herpes encephalitis was proven by PCR.

Considering the very high mortality and morbidity rates associated with HSE and the time lag before diagnostic confirmation, specific antiviral therapy must be started before confirmation of diagnosis if HSE is clinically suspected.

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**Disclaimer**

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**References**


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