CASE REPORT

Role of Neuroprotective Agents in the Anesthetic Management of Brain Tumors for Patients with Recidive Cystic Tumor with Signs of Intracranial Hypertension Underwent Re-Craniotomy Decompression Tumor Resection: Case Report

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ABSTRACT

Background: The management of brain tumor surgeries, particularly recurrent cystic tumors with cerebral edema, poses significant challenges. Elevated intracranial pressure (ICP) and the associated risk of ischemia necessitate a comprehensive neuroprotective approach during anesthesia to ensure optimal surgical and postoperative outcomes.

Case: A 54-year-old male presented with two weeks history of headaches and dizziness. He had previously undergone a craniotomy six months ago for the removal of a metastatic right parieto-occipital adenocarcinoma. Imaging revealed tumor recurrence, and the patient was scheduled for a re-craniotomy. The anesthetic plan included neuroprotective strategies: thiopental for metabolic suppression, sufentanil for hemodynamic stability, and sevoflurane for neuroprotection. The surgery lasted 3.5 hours, with minimal intraoperative blood loss and stable perioperative hemodynamics. Postoperatively, the patient recovered without complications and was discharged in stable condition.

Discussion: The anesthetic management prioritized maintaining ICP, cerebral perfusion pressure (CPP), and minimizing neuroinflammatory responses. Thiopental effectively reduced cerebral metabolic demands, sufentanil stabilized hemodynamics, and sevoflurane provided neuroprotective and anti-inflammatory benefits. hypothesis and principles. These strategies ensured cerebral autoregulation, controlled cerebral edema, and optimized recovery. The Monro-Kellie hypothesis and principles of neuroprotection were key guiding frameworks in this case.

Conclusion: This case highlights the critical role of neuroprotective agents in the anesthetic management of brain tumor surgeries. The combination of thiopental, sufentanil, and sevoflurane contributed to a stable intraoperative course and uneventful recovery. Integrating these strategies ensures improved surgical outcomes and patient safety in challenging neurosurgical cases.

Keywords: anesthetic management; intracranial pressure; neuroprotection; sevoflurane; sufentanil; thiopental

INTRODUCTION

A 54-year-old male presented with recurring headaches and dizziness persisting for six months before admission. Imaging revealed a solid cystic mass with significant perifocal edema in the right frontal lobe and the left occipital and bilateral parietal lobes, leading to increased intracranial pressure (ICP). The patient had undergone surgery one month earlier for a metastatic right parieto-occipital adenocarcinoma; however, the tumor had recurred. Over the past two weeks, symptoms of dizziness and nausea had returned.

The patient underwent a craniotomy and tumor excision under general anesthesia. The surgery lasted approximately 3.5 hours, with minimal intraoperative blood loss (100 cc) and no transfusion required. Postoperatively, the patient was monitored in the intensive care unit (ICU) for 24 hours before being transferred to the ward. Following one day of recovery, the patient was discharged in stable condition.

The goal of anesthesia in brain tumor surgery is to manage ICP, prevent cerebral edema, and protect the brain from ischemia or injury. A neuroprotective approach reduces intraoperative complications such as hypoxemia, hypercapnia, anemia, and hypotension, as well as addresses postoperative challenges. This strategy emphasizes maintaining adequate oxygenation and cerebral perfusion, stabilizing cerebral autoregulation, and minimizing the neuroinflammatory response. Neuroprotective agents like thiopental, sufentanil, and sevoflurane are effective in lowering the brain's metabolic demands, stabilizing blood flow and protecting cells from damage.

An essential part of neuroanesthesia is keeping cerebral blood flow (CBF) within safe limits by maintaining mean arterial pressure (MAP) between 50 and 150 mmHg. Lower pressures can cause ischemia, while higher pressures may result in swelling or bleeding. According to the Monro-Kellie hypothesis, the brain, cerebrospinal fluid (CSF), and blood share a fixed space inside the skull, so an increase in one must be offset by a decrease in another to maintain normal ICP. Neuroanesthetic techniques are designed to balance these factors, ensuring the brain functions well during and after surgery.

This case report focuses on the use of neuroprotective agents in managing brain tumors during anesthesia. It highlights the importance of these strategies in improving patient outcomes, particularly in challenging cases with recurrent cystic tumors and cerebral edema.

CASE

The patient is a 54-year-old male, weighing 70 kg, height 165 cm, diagnosed with a recurrent cystic tumor and cerebral edema. He initially presented with a six-month history of headaches and dizziness. One month ago, he underwent a craniotomy for the removal of a metastatic right parieto-occipital adenocarcinoma. However, in the past two weeks, symptoms of dizziness and nausea reappeared. Evaluation revealed tumor regrowth.

Preoperative evaluation was conducted in the ward. The patient was alert and compos mentis, with a glasgow coma scale (GCS) score of E4V5M6. Pupils were round and isochoric, with intact pupillary reflexes in both eyes. Respiratory rate was 20 x/minute, with equal vesicular breath sounds in the

upper lungs bilaterally. No rhonchi or wheezing were detected. Oxygen saturation (SpO_2) was 98% on room air.

Vital signs were stable, with a blood pressure of 127/87 mmHg, pulse rate of 81 beats per minute (regular), and body temperature of 36.5°C. Head and neck examination revealed no abnormalities, and the thorax was symmetrical bilaterally. Heart sounds (S1 and S2) were single and regular, with no murmurs. Abdominal examination showed no distension, with normal bowel sounds. The patient reported normal spontaneous urination. Laboratory finding (Table 1). From the chest X-ray examination, the heart was within normal limits; the lung had increased perihilar patterns suggesting bronchitis or pneumonia. (Figure 1, Figure 2)

A head CT scan revealed multiple solid masses with associated perifocal edema in the right frontal lobe, left occipital lobe, and bilateral parietal lobes. The largest lesion, located in the left parietal lobe, measured 3 × 3.3 cm. Findings were consistent with signs of increased intracranial pressure (ICP). (Figure 3)

In the operating room, the patient was positioned in a neutral 30° head-up position. Voluntary hyperventilation was initiated by instructing the patient to breathe quickly and deeply at approximately 20 x/minute, while O_2 was administered through a face mask. Anesthetic induction included sufentanil (20 mcg), thiopental (200 mg), and rocuronium (50 mg). Ventilation was maintained with 100% O_2 and 2 vol% sevoflurane (MAC). Intubation was performed using a Macintosh laryngoscope with a 7.5 mm non-kinking endotracheal tube (ETT) with a balloon. Anesthesia was maintained with 2% sevoflurane (delivered in a 50:50 oxygen-to-air ratio), a sufentanil syringe pump (5 mcg/hour), and rocuronium (5 mg/hour/iv). Intraoperative monitoring included continuous evaluation of systolic, diastolic, and mean arterial blood pressure; end-tidal CO_2; oxygen saturation; electrocardiogram (ECG); and urine output via a urinary catheter. The surgery lasted for three and a half hours, with the patient in the supine position. Intraoperative blood loss was 100 cc, and urine output was 1,500 cc. The patient received 2,000 cc of crystalloid solution, 40 grams of mannitol, and 5 mg of dexamethasone (Figure 4). The duration of the operation was 3.5 hours, and after surgery, the patient was treated in the ICU and given analgesics in the form of Paracetamol 3 x 1 g IV and sufentanil 2 mcg/hour syringe pump.

Following the surgery, the patient was managed in the ICU for one day before being transferred to the general ward. Upon arrival in the ICU at 12:30 p.m., the patient was placed on ventilator support in pressure control mode with the following settings: FiO_2 50%, respiratory rate 12 x/minute, inspiratory pressure (P-insp) 12 cmH_2O, positive end-expiratory pressure (PEEP) 5 cmH_2O, tidal volume (TV) 490 cc, minute ventilation 6,200 mL, and SpO_2 100%.

After eight hours, the ventilator mode was switched to spontaneous mode with the following settings: FiO_2 60%, PEEP 5 cmH_2O, pressure support 6 cmH_2O, tidal volume ranging from 370 - 490 cc, minute ventilation ranging from 4,960 - 6,200 mL, and SpO_2 remaining at 100%. Gradual weaning was performed over the next 10 hours, and the patient was successfully extubated at 10:00 a.m. the following morning.

Post-craniotomy patients are not immediately extubated in the ICU due to critical neurological considerations. To maintain stable neurological conditions, reduce the risk of cerebral edema and increased ICP, ensure adequate cerebral perfusion, and safeguard airway patency and function.

On the first post-operative day, the patient's general condition was good with systolic blood pressure 100-136 mmHg / diastolic 61-83 mmHg. Heart rate 75 - 97 bpm, SpO_2 99- 100%, patient received ceftriaxone 2x1 g, pain score with visual analogue scale (VAS) 1-2 or mild pain. At 04.00 pm, the patient moved to the Amaryllis ward. (Table 3)

Table 1. Preoperative laboratory findings date 22/January/2024

Hemoglobin	15.8 g/dL
Hemathocrit	46.7 %
Leukocytes	22.200/mm^3
Thrombocyte	364x 10^3/µL
PT	12.8 second
APTT	26.6 second
Ureum	44.6 mg/dl
Natrium	136 mmol/L
Kalium	4.1 mmol/L
Chloride	101 mmol/L
Creatinine	0.91 mg/dL
SGOT	25.8 U/L
SGPT	74.4 U/L
GDS	118 mg/dl
Calcium	10.1 mmol/dl
HBSAG	Non-Reactive
ANTI-HIV	Non-Reactive
ANTI-HCV	Non-Reactive

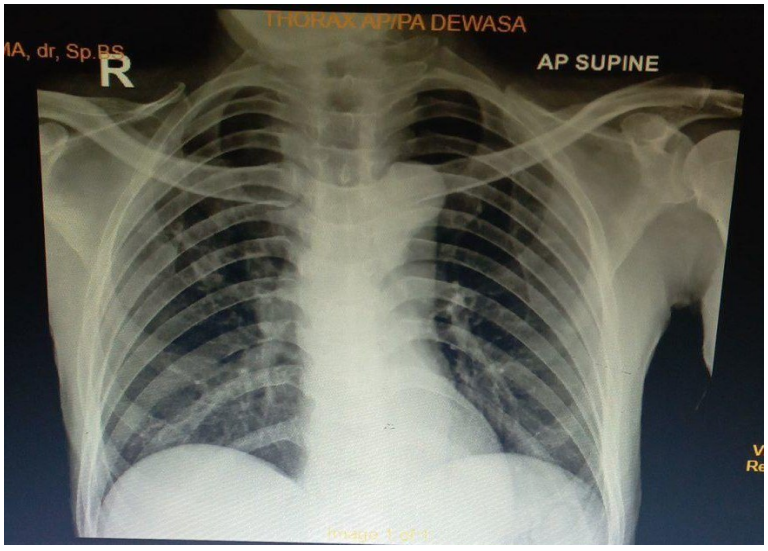

Figure 1. Chest X-ray

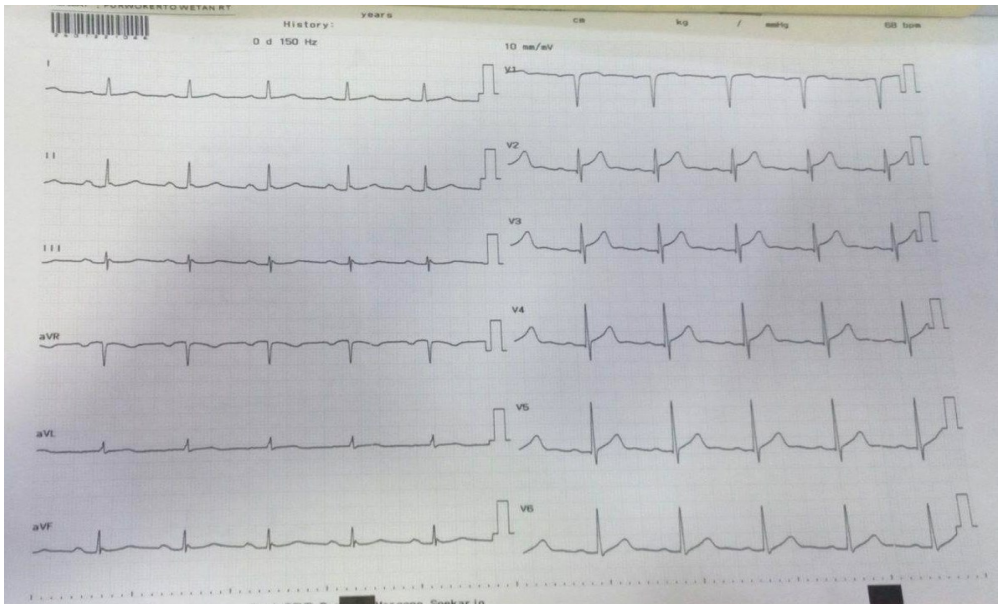

Figure 2. ECG examination (ST elevation v2-v4)

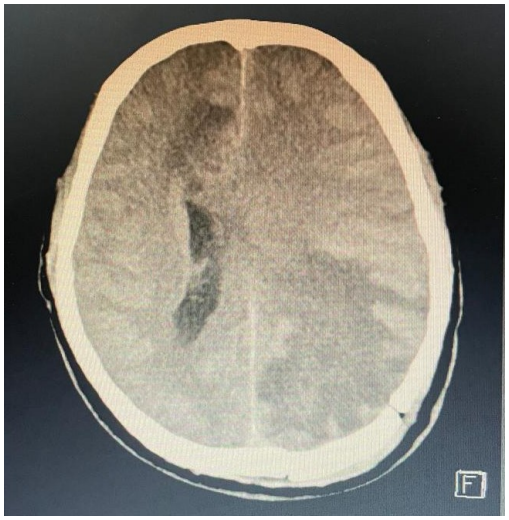

Figure 3. Head CT-scan

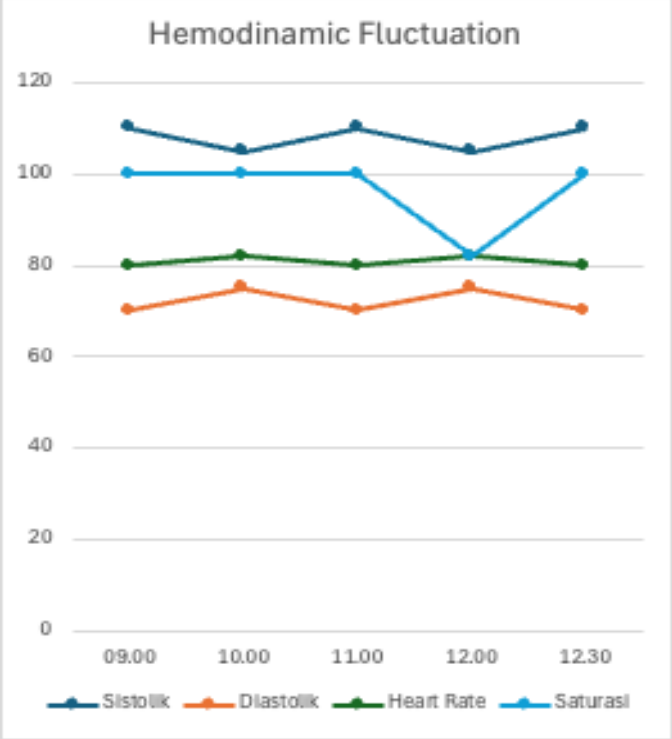

Figure 4. Hemodynamic fluctuation

Table 3. Post-operative laboratory examination profile in ICU on 08/28/2023

Blood Test	
Hemoglobin	14.0 mg/dL
Hematocrit	40.6 %
Leukocytes	23.700/mm^3
Thrombocyte	360,000/µL
Albumin	3.5 g/dl
Ureum	27.90 mg/dl
Creatinine	0.53 mg/dl
Glucose	120 mg/dl
Calcium	10 mmol/L
Natrium	135 mmol/L
Kalium	3.6 mmol/L
Chloride	110 mmol/L

DISCUSSION

Anesthetic management in brain tumor surgery, especially that caused by recurrent cystic tumors and cerebral edema, requires a comprehensive strategy, especially to properly manage tumor volume, vasogenic edema, and ICP that occurs during and after surgery. In this context, neuroprotective agents are very important because they are considered to help protect brain tissue from ischemic injury, maintain hemodynamic stability, and improve surgical outcomes. Several studies have analyzed and explained the nature and mechanism of action of neuroprotective agents such as thiopental, sufentanil, and sevoflurane.

The choice of anesthesia is a critical factor in neuroprotection during brain tumor surgery, as it directly impacts postoperative outcomes. Fundamental principles of brain protection during anesthesia include maintaining CPP, reducing metabolic demands, stabilizing the blood-brain barrier (BBB), and mitigating inflammatory responses.[1] Anesthetic management should be tailored to optimize CBF autoregulation and minimize ischemic events, aligning with the Monro-Kellie doctrine, which emphasizes maintaining constant intracranial volume by carefully balancing the brain parenchyma, blood, and CSF.[2] Effective collaboration among anesthesiologists, neurosurgeons, and intensive care teams is essential to prevent intracranial hypertension and enhance patient outcomes.

Thiopental, a highly lipid-soluble barbiturate, plays a crucial role in neuroprotective anesthesia due to its ability to significantly reduce the cerebral metabolic rate of oxygen consumption ($CMRO_2$) and its potent anti-ischemic properties. By lowering $CMRO_2$, thiopental decreases oxygen demand in brain tissue, thereby providing an effective protective barrier against ischemia.

Thiopental's neuroprotective effects are primarily mediated through the reduction of $CMRO_2$ and CBF. By decreasing metabolic demand, thiopental protects the brain from ischemic damage during periods of compromised blood flow.[3] Additionally, it attenuates excitotoxicity by inhibiting glutamate release and calcium influx, further enhancing its neuroprotective properties. This mechanism makes thiopental particularly advantageous in neurosurgical settings where the risk of ischemia is heightened, such as during tumor resection or periods of elevated ICP.[4]

Thiopental is widely used in neurosurgical procedures to manage ICP and achieve optimal brain relaxation. Studies have demonstrated its efficacy in reducing ICP and CBF, correlating with improved outcomes in patients undergoing brain tumor surgery. In one study, intraoperative administration of thiopental significantly reduced the incidence of postoperative neurological complications, with an odds ratio of 0.26 (95% confidence interval: 0.13 to 0.51, $p < 0.001$). The analysis also identified aneurysm size (≥ 10 mm) and hyperlipidemia as independent risk factors for postoperative complications, emphasizing the protective role of thiopental in high-risk cases.[5,6]

A notable case study involved a 32-year-old female patient undergoing meningioma resection. The patient received an induction regimen consisting of thiopental (5 mg/kg), followed by a continuous infusion of thiopental (1–3 mg/kg/h) combined with

dexmedetomidine (0.4–0.7 μg/kg/h). This combination achieved optimal brain relaxation, facilitated tumor removal, and maintained hemodynamic stability throughout the 11-hour surgical procedure. Such cases underscore the practicality and effectiveness of thiopental in complex neurosurgical settings.[7]

Thiopental's pharmacokinetics are characterized by a rapid onset and redistribution, making it an ideal choice for induction in patients with brain tumors. However, prolonged infusion can lead to drug accumulation due to its long context-sensitive half-life. The context-sensitive half-life increases with the duration of infusion, meaning the time required for the plasma concentration to decrease by half becomes longer with extended administration. Careful monitoring is essential to avoid prolonged recovery times and potential side effects.[8]

Studies consistently highlight thiopental's role in reducing postoperative neurological complications and enhancing patient outcomes. By reducing neuronal activity and metabolic demand, thiopental minimizes the risk of ischemia and protects the brain during neurosurgical procedures. Its ability to achieve brain relaxation and support hemodynamic stability further solidifies its utility in managing complex cases.

Sufentanil is a highly potent synthetic opioid widely recognized for its superior analgesic properties and minimal hemodynamic disturbance, making it an essential component in the anesthetic management of brain tumor surgery. Its high affinity for opioid receptors allows for effective pain relief at lower doses, thereby reducing the risk of side effects such as respiratory depression or excessive sedation.

One of the most critical aspects of neurosurgical anesthesia is maintaining hemodynamic stability to ensure adequate CPP and oxygen delivery to the brain. Sufentanil has demonstrated a significant ability to maintain stable hemodynamics during neurosurgical procedures. A study comparing the combination of propofol and sufentanil to propofol and remifentanil found that the sufentanil combination resulted in improved hemodynamic stability and higher cerebral tissue oxygenation. This aligns with another study that demonstrated the combination of sufentanil and nitrous oxide effectively maintained hemodynamic stability during brain tumor surgery.

Intravenous administration of sufentanil at doses of 0.5, 1.0, and 2.0 μg/kg did not significantly alter ICP in neurosurgical patients. However, higher doses led to a reduction in MAP, which in turn decreased CPP. Despite this, the findings concluded that while sufentanil itself does not directly affect ICP, its hemodynamic effects, particularly on MAP, are crucial for maintaining adequate CPP during neurosurgical procedures.[9]

Although the direct neuroprotective effects of sufentanil are less well-documented compared to agents such as thiopental, its ability to maintain stable hemodynamics plays a key role in supporting neuroprotection. Hemodynamic stability ensures consistent CPP, which is essential for adequate oxygen delivery to the brain.[10] Additionally, sufentanil exhibits anti-inflammatory properties that contribute to neuroprotection by reducing cytokine-mediated disruption of the BBB and mitigating vasogenic edema.[11]

Sufentanil's pharmacodynamic profile is characterized by its rapid onset and short duration of action, enabling precise titration during surgery. This allows for optimal analgesia while facilitating postoperative neurological assessment. By allowing for lower inspired concentrations of volatile agents, sufentanil also supports superior cardiocirculatory stability, further highlighting its suitability for neurosurgical anesthetic management.[12]

A recent study examined the opioid-sparing effects of a perioperative dexmedetomidine and sufentanil infusion. This combination reduced overall opioid requirements, thereby accelerating postoperative recovery. These findings further support the appropriateness of sufentanil in the anesthetic management of brain tumor surgery.[13]

Sevoflurane is widely regarded as an anesthetic of choice in neurosurgical procedures due to its minimal impact on cerebral hemodynamics and its neuroprotective effects. Unlike other volatile anesthetics, sevoflurane has a reduced tendency to elevate CBF, thereby minimizing the risk of exacerbating ICP in patients with cerebral edema. Additionally, sevoflurane decreases $CMRO_2$ and helps protect the brain from ischemic injury through modulation of apoptotic pathways and reduction in excitotoxicity. These mechanisms prepare the brain resilience to potential damage during surgery.

Clinical studies support the advantages of sevoflurane in neurosurgical settings. For example, one study demonstrated shorter anesthesia and extubation times in patients receiving sevoflurane, which contributed to reduced intraoperative blood loss and a lower incidence of postoperative complications such as agitation and urinary tract infections. Patients under sevoflurane anesthesia also exhibited faster recovery of orientation and cognitive function postoperatively.[14] Another study highlighted its neuroprotective potential, showing significantly lower serum S100B protein levels in patients administered sevoflurane compared to isoflurane, suggesting that sevoflurane effectively minimizes cerebral ischemia during brain tumor surgery.[15]

Sevoflurane's neuroprotective effects are attributed to several mechanisms. It reduces neuronal apoptosis by modulating intrinsic apoptotic pathways and decreasing excitotoxicity. Additionally, sevoflurane stabilizes the BBB by regulating inflammatory pathways and mitigating permeability changes linked to tumor-induced vasogenic edema. Its favorable cardiovascular profile ensures stable CPP during surgery by maintaining cardiac output and systemic vascular resistance. Moreover, the rapid elimination of sevoflurane facilitates early postoperative neurological assessments, critical for neurosurgical patients.

Despite its benefits, sevoflurane may have dose-dependent neurodegenerative effects, particularly in the developing brain. Research has demonstrated that sevoflurane administration can induce neuronal apoptosis in immature brains through intrinsic apoptotic pathways, highlighting potential neurotoxic effects. Thus, careful consideration of dosage and patient selection is crucial when using sevoflurane in neurosurgical procedures.[16]

The management of a 54-year-old male patient with a recurrent cystic tumor and associated cerebral edema was guided by a comprehensive neuroprotective approach.

The primary focus was on optimizing neurological and systemic stability. The patient presented with significant leukocytosis, imaging evidence of cerebral edema, and increased ICP. To address these, dexamethasone was administered to reduce vasogenic edema, and controlled hyperventilation was employed to effectively lower ICP. These measures ensured the patient was in optimal condition for surgical intervention.

The anesthetic plan aimed to maintain CPP, minimize ischemic risk, and promote cerebral relaxation. A combination of thiopental (200 mg), sufentanil (20 mcg), and sevoflurane (2 vol% MAC) was selected for their complementary neuroprotective effects. Thiopental reduced $CMRO_2$ and inhibited excitotoxic pathways, providing robust ischemic protection. Sufentanil ensured effective analgesia while maintaining hemodynamic stability to support adequate CPP. Sevoflurane contributed to neuroprotection by stabilizing the BBB, reducing $CMRO_2$, and modulating CBF. Mannitol was administered intraoperatively to control ICP, alongside careful fluid management to maintain hemodynamic balance. Continuous monitoring of key parameters—including blood pressure, end-tidal CO_2, and oxygen saturation—was performed throughout the procedure to ensure stability.

Postoperatively, the neuroprotective strategy focused on consolidating the intraoperative gains. The patient was managed in the ICU with close monitoring. Ventilator support was gradually weaned, and analgesia was maintained with paracetamol and a sufentanil infusion to control postoperative pain while preserving hemodynamic stability. Dexamethasone was continued to manage vasogenic edema, and prophylactic antibiotics were administered to prevent infection. The patient demonstrated stable recovery with no significant laboratory or clinical complications and was discharged from the ICU within 24 hours.

This case highlights the importance of an integrated neuroprotective strategy in brain tumor surgery. By addressing critical factors such as ICP, CBF, and CPP during the perioperative period, this approach facilitated optimal neurological outcomes. The successful outcome underscores the role of tailored anesthetic management in ensuring patient safety and promoting recovery in neurosurgical care.

CONCLUSION

The successful management of a patient undergoing surgery for a recurrent cystic brain tumor with cerebral edema underscores the importance of neuroprotective anesthetics in optimizing perioperative care. The combined use of thiopental, sufentanil, and sevoflurane effectively maintained intracranial pressure and cerebral perfusion while reducing brain metabolic demands. Thiopental suppressed cerebral oxygen consumption, sufentanil provided hemodynamic stability, and sevoflurane offered neuroprotective and anti-inflammatory benefits. These strategies helped prevent ischemic injury and cerebral edema, leading to a stable surgery and smooth recovery, marked by rapid extubation, stable vitals, and early ICU discharge.

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