Jurnal Healthsains
Printed ISSN: 2722-7782
Electronic ISSN:2722-5356
jurnal.healthsains.co.id

Anesthetic Management in Cerebellopontine Angle Tumor (CPA) Removal Patients

Taufiq Gemawan,Adelia Handoko,Rizal Hadi Pratama,Renaldi Wibisono
Department of Anesthesiologist and Intensive Care, Medical Faculty University of Jember – Dr. Soebandi Regional Hospital Jember, Indonesia, Physiology Department, Laboratorium Fisiologi, Medical Faculty University of Jember, Indonesia, Student of Medical Faculity University of Jember – Dr. Soebandi Regional Hospital Jember, Indonesia
Email: adelia.fk@unej.ac.id

Keywords:
Cerebellopontine Angle Tumor, Anesthetic Management, Total Intravenous Anesthesia

Introduction : Cerebellopontine Angle Tumor (CPA) is the most common type of tumor found in the posterior fossa. Without a proper anesthetic approach, this can increase the risk of brain edema and hemorrhage due to surgical manipulation. Case Illustration : A 46-year-old woman was diagnosed with a meningioma type CPA tumor, CT-Scan found meningioma in the left petrous tentorial tubercullum sellae with perifocal edema in the pons and left cerebellum. The patient was planned to get tumor excision surgery in a supine position. General anesthesia was performed, induced using propofol, fentanyl and rocuronium. The patient had a good hemodynamic profile while in the ICU postopertively. Discussion : Proper patient positioning during CPA tumor surgery is one of the important factors in the success or failure of the procedure. TIVA technique uses propofol and fentanyl, can reduce CBF reduce intracranial pressure, maintain brain perfusion pressure and reduce CMRO2 to protect brain tissue from damage. Conclusion: Several things that must be evaluated routinely in these patients are maintaining hemodynamic stability by maintaining adequate cerebral perfusion pressure, reducing cerebral blood flow, maintaining normal autoregulation, reducing the rate of cerebral metabolic oxygen, and maintaining an adequate cerebral oxygen supply.

INTRODUCTION

The Cerebellopontine Angle (CPA) is a triangular space in the posterior fossa bounded by the tentorium superiorly, the brainstem posteromedially and the petrous portion of the temporal bone posterolaterally. Anatomically, the CPA contains cranial nerves V, VI, VII, and VIII along with the anterior inferior cerebellar artery. CPA tumors are the most common type of tumor found in the posterior fossa, 5-10% of intracranial tumors. Based on histology, the most common types of CPA tumors are vestibular schwannoma, meningioma, and epidermoid cysts. CPA tumors are mostly benign, slow growing with low malignancy potential. Based on its anatomical location, CPA tumors cause hearing loss, tinnitus, dizziness, vertigo, headaches, and gait disturbances. Hearing loss is mostly unilateral sensorineural and is caused by involvement of the cochlear nerve. Other cranial nerve deficits, symptoms of brainstem compression, and hydrocephalus may also be seen with larger tumors (Yasmin et al., 2021)

Surgery of the posterior fossa especially CPA tumors give significant challenges to anesthesiologists and surgeons with a wider range of complications

than surgery to the supratentorial compartment. Apart from general perioperative considerations involving intracranial lesions, posterior fossa surgery includes unusual surgical positions and complications, potential brainstem injuries, lengthy surgical procedures, perioperative cardiovascular and respiratory compromise, and acute obstructive hydrocephalus. In addition, things that need attention in performing neuroanesthesia are controlling Intracranial Pressure (ICP) and brain volume, protecting nerve tissue from injury and ischemia, and reducing bleeding during surgery (Suryadi, Zulfan, & Kulsum, 2021)

The Total Intravenous Anesthesia (TIVA) technique uses propofol and fentanyl, can reduce Cerebral Blood Flow (CBF), reduce intracranial pressure, maintain brain perfusion pressure and reduce Cerebral Metabolism Oxygen Rate (CMRO2) to protect brain tissue from damage. The inhalation anesthetic technique that is often used in the management of intracranial surgery can reduce vascular resistance, especially cerebral vascular resistance, thereby increasing CBF and intracranial pressure. In cases with increased intracranial pressure, inhalation anesthetic techniques will make the intracranial pressure higher, thereby reducing Cerebral Perfusion Pressure (CPP), increasing the risk of cerebral ischemia, which can cause brain damage. Therefore, surgical removal of CPA tumors is a difficult procedure and can cause fatal complications. This case report will discuss the neuroanesthetic management of CPA tumor removal surgery. This case is interesting because it is full of challenges for neurosurgeons and anesthesiologists. The operation is carried out by maintaining hemodynamic stability by maintaining adequate CPP, reducing CBF, maintaining normal autoregulation, reducing CMRO2, maintaining adequate Cerebral Delivery Oxygen (CDO2), and making slack brain relaxing tumors (Suryadi et al., 2021)

RESEARCH METHODS

RESULTS AND DISCUSSION

CASE ILUSTRATION

A 46 years old woman (60 kg, 158 cm) complained of difficulty moving her lower limbs after CPA excision and tracheostomy about 1 month ago. In October 2022, the patient underwent a VP shunt procedure to treat excess fluid in the brain. On December 19, 2022, the patient underwent CPA tumor excision surgery. Before surgery the patient complained of tingling in all extremities, numbness in the left side of the body, and diplopia in the left eye since a year ago. After surgery the patient experienced excessive secretion production so a tracheotomy was performed on December 21, 2022. He denied any other medical history. There is no history of the same disease in the family.

On preoperative physical examination, the patient's general condition was adekuat. The patient's vital signs: blood pressure 100/80 mmHg, pulse 77 x/minute, respiratory rate 20 x/minute, oxygen saturation (SpO2) 99% with 5 lpm oxygenation via tracheotomy, and temperature 36.50 C. GCS awareness E4VxM6, 2mm/3mm anisochore round pupils and RC +/+. Lung examination found symmetrical chest movements, auscultation of vesicular breath sounds on the right and left sides,

wheezing and rhonchi were not found. Cardiac examination revealed a single S1-S2 heart sound, no murmurs or gallops were found. Soepl abdomen, no tenderness, bowel sounds within normal limits. Warm acral in all extremities, no edema and cyanosis found. Motor impairment was found in the lower extremities (L2-S1) 2/2. Physiological reflexes BPR +3/+3, TPR +3/+3, KPR +2/+1, and APR +2/+1. Pathological reflexes Hoffman +/-, Tromner +/-, Babinski -/-, and Chaddock -/-.

Preoperative investigations consist of complete blood count, blood gas analysis, AP chest photo, CT scan and MRI of the head. On complete blood examination (Table 1), high levels of leukocytes, platelets, SGOT, and SGPT were found. Albumin and potassium levels in the patient are low. Blood gas analysis (Table 2) showed a respiratory alkalosis characterized by high pH, pO2, HCO3 and low pCO2 in the blood. On the chest X-ray, cardiomegaly was seen, while the pulmonary showed no abnormalities (Figure 1). On CT-scan and MRI of the head, a well-defined hypodense lesion was found in the right and left frontal lobes and meningioma on the left petrous tentorial tubercullum sellae with perifocal edema on the pons and left cerebellum measuring 5 cm x 5.1 cm x 5.9 cm (Figure 2 and Figure 3).

Tabel 1. Preoperative Complete Blood Count Results

Examination	**25/01/2023**	**Normal Score**
Complete Blood Count		
Hemoglobin	14,4	12.0-16.0 gr/dL
Leukosit	11,1 (H)	4.5-11.0 10^9/L
Hematokrit	43,6	41-53 %
Trombosit	493 (H)	150-450 x 10^9/L
PPT		
Pasient PPT	10,5	Difference with control <2 sec
Control PPT	10,0	
APPT		
Pasient APPT	24,8	Difference with control <7 sec
Control APPT	26,0	
Blood Glucose		
Random Blood Glucose	88	<200 mg/dL
Liver Function		
SGOT	38 (H)	10-35
SGPT	75 (H)	9-43
Albumin	3,0 (L)	3,4-4,8 g/dL
Renal Function		
Serum Kreatinin	0,6	0,5-1,1
Urea	21	
BUN	10	6-20
Electrolyte		
Natrium	135,1	135-155 mmol/L
Kalium	3,24 (L)	3,5-5,0 mmol/L
Klorida	100,6	90-110 mmol/L

Tabel 2. Preoperative Bloog Gas Analysis Results

Examination	30/01/2023	Normal Score
Temperatute	36,4	37°C
FiO_2	0,33	0,21
Ca	1,19	1,15-1,35 mmol/L
pH	7,59 (H)	7,35-7,45
pCO_2	33 (L)	35-45 mmHg
pO_2	116 (H)	80-100 mmHg
BE	10,9	(-)2 – (+)2
TCO_2	33,3	
HCO_3	32,3 (H)	22-26 mmEq/L
tHb	14,3	11,7-17,4 g/dL
SO_2	99	>90%
$AaDO_2$	77	
Na	141	135-145 mmol/L
K	3,4 (L)	3,5-5 mmol/L

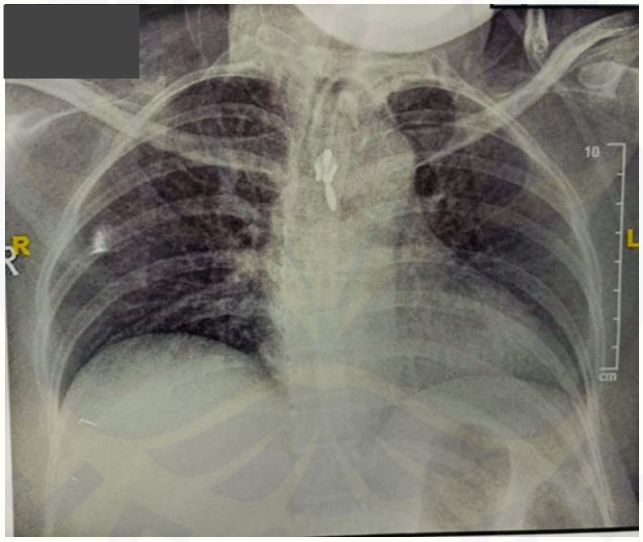

Figure 1. Preoperative Thoraks AP

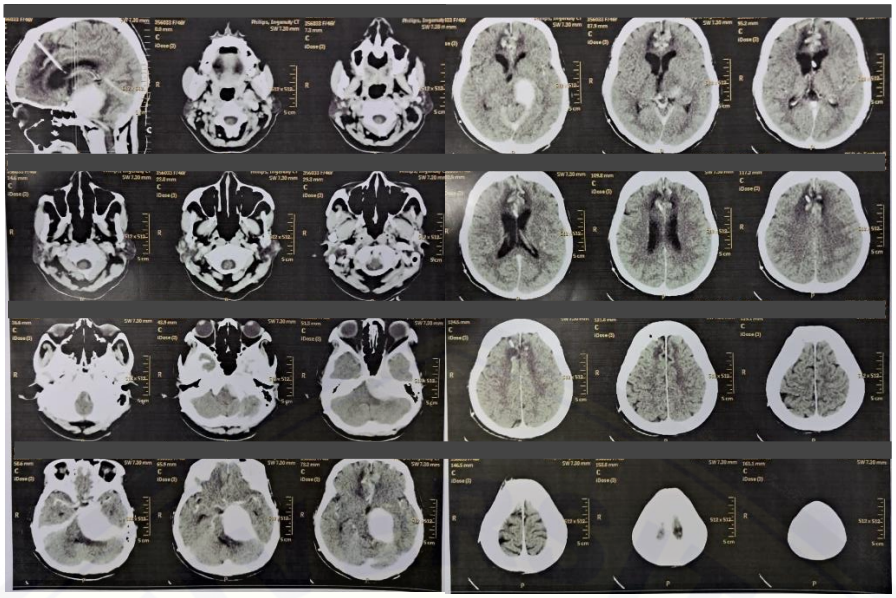

Figure 2. Preoperative Head *CT-scan* with Contrast

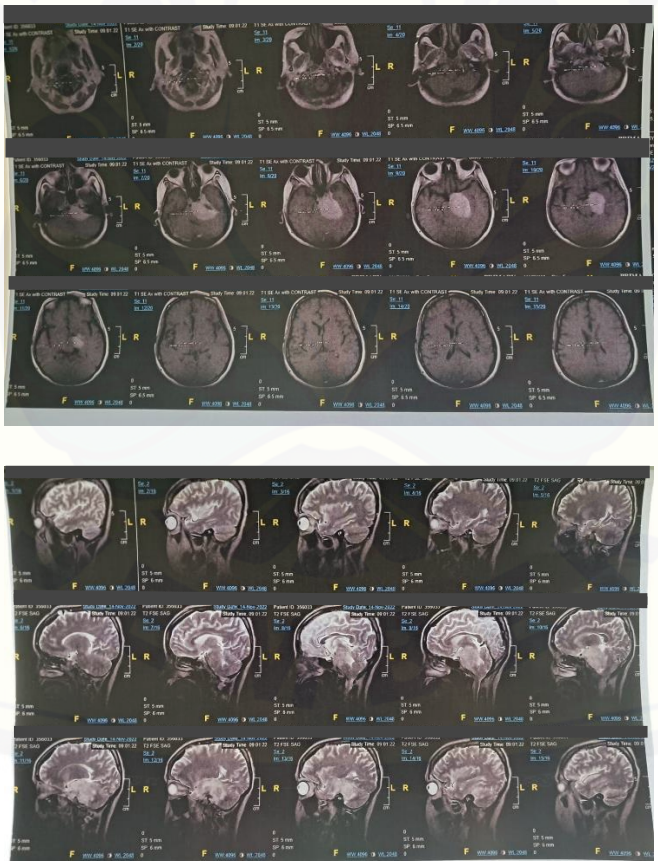

Figure 3. Preoperative Head MRI

The patient's diagnosis was a CPA tumor with (American Society of Anesthesiologist) ASA 3 physical status and complications of neurological deficits, in

the form of decreased lower limb muscle motor, tingling on the left side of the body and left diplopia. The patient was planned for tumor excision surgery. Prior to surgery, patients were given informed consent and fasted for 6 hours before surgery. The patient was positioned supine with the head tilted to the right and pre-oxygenated for 5 minutes with 100% O2 via tracheostomy. Anesthesia induction of the patient was carried out by giving a combination of propofol 150 mg iv, fentanyl 150 mcg iv, and rocuronium 50 mg iv. Maintenance of anesthesia by administering sevoflurane (MAC 2%) at a ratio of 50% oxygen:50% air, and continuous propofol, fentanyl, and rocuronium.

Monitoring during surgery consist of evaluating blood pressure (systolic/diastolic), pulse, respiratory rate, and oxygen saturation which are presented in Figure 4. The operation lasted 7 hours 15 minutes. Patients received fluid intake of 2500 mL crystalloid, 500 mL colloid, 200 mL mannitol, 5 mg dexamethasone, 8 mg ondansetron, and 0.5 mg atropine sulfate. Fluid output during surgery was 2100 mL of urine and 700 mL of bleeding.

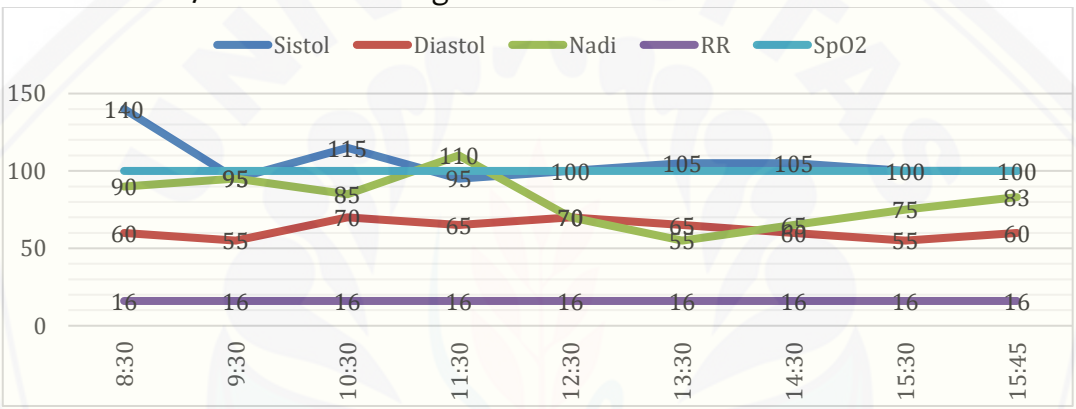

Figure 4. Vital Sign Intraoperative

Postoperative, the patient was taken to the ICU (Intensive Care Unit). Postoperative monitoring is carried out by re-evaluating the patient's vital signs, such as systole, diastolic, pulse, respiratory rate, and oxygen saturation which are presented in Figures 5, 6, and 7. On the first postoperative day, the patient uses a BiPAP mode ventilator with FiO_2 50%, respiratory rate 16 x/minute, Pinsp 18, ΔPsupp 13, PEEP 5, SpO_2 100%. The patient was sedated using midazolam 2 mg/hour and morphine 2 mg/hour. On the second postoperative day, the patient was still on a BiPAP mode ventilator with a FiO2 of 40%, respiratory rate of 14 x/min, Pinsp 14, ΔPsupp 12, PEEP 3, SpO2 100%. Midazolam and morphine were stopped and replaced with dobutamine 3 mcg/kg/minute. On the third postoperative day, the patient was on a BiPAP mode ventilator with FiO_2 40%, respiratory rate 14 x/min, Pinsp 9, ΔPsupp 16, PEEP 5, SpO_2 100%. Patient consciousness improves with GCS E3VxM4. During treatment in the ICU, the patient received other therapies, in the form of fosfomycin, ranitidine, dexamethasone, metamizole, phenytoin, tranexamic acid, dexketoprofen, paracetamol, salbutamol nebulizer, PRC blood transfusion, and albumin transfusion.

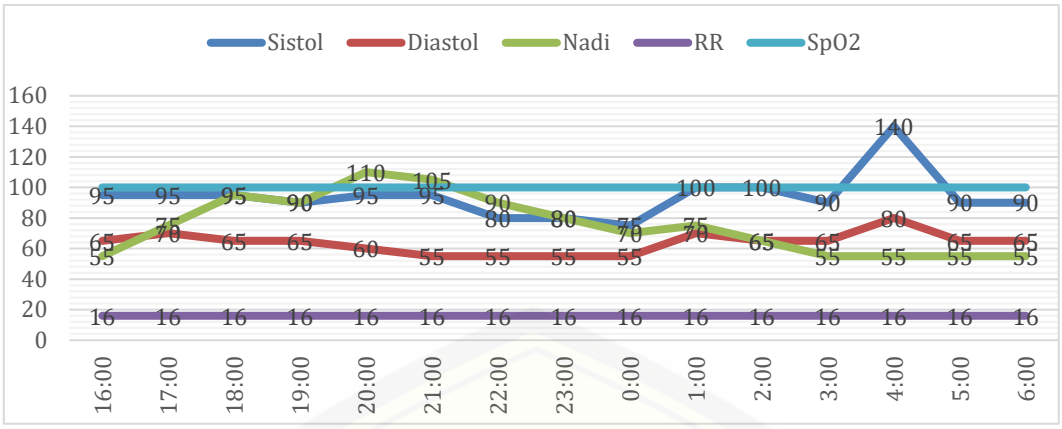

Figure 5. Vital Sign Day 1 Postoperative

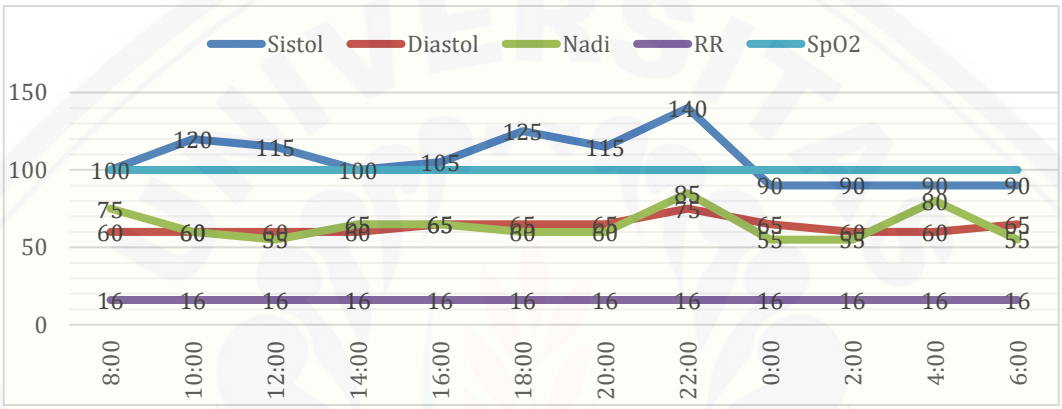

Figure 6. Vital Sign Day 2 Postoperative

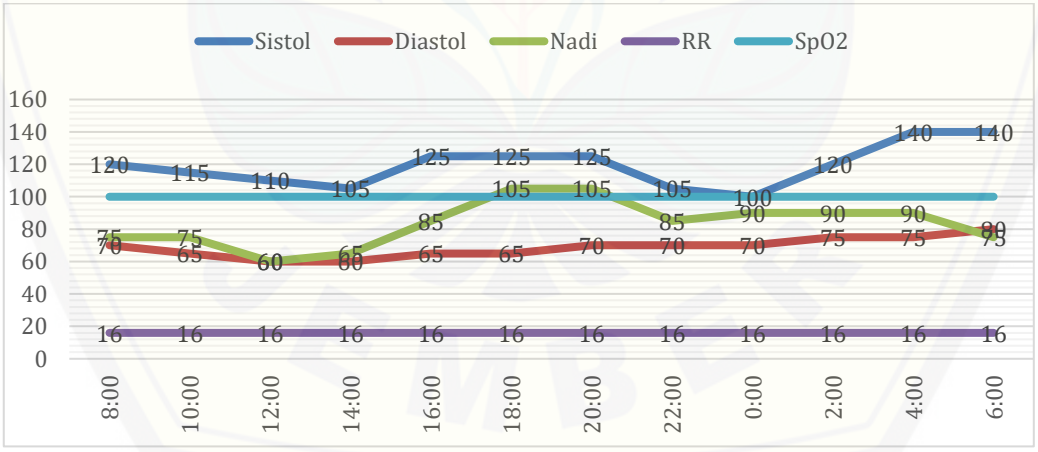

Figure 7. Vital Sign Day 3 Postoperative

On the 5th postoperative day, the patient's general condition improved. The patient was able to breathe with a 10 lpm tracheostomy mask with an average RR of 14-16 x/minute, BP 102/61 mmHg, HR 59 x/minute, GCS E3 Vx M3, and SpO2 100%. No wheezing was found, pupils were rounded isorkor +3/+3, with a head up position of 300. The patient was transferred to the usual treatment room. The patient was transferred to the usual room with Inf therapy. NaCl 0.9% 1500 cc/24 hours, per oral

cefixime 2 x 100 mg, mefenamic acid 3 x 500 mg, phenytoin 3 x 100 mg, dexamethasone 3 x 1 mg, salbutamol nebulizer 3 x 3 mg, diet milk 6 x 200 cc, periodic suction cannulas.

On the 6th day of treatment the patient's condition improved with GCS E4 Vx M5, spontaneous breathing with a tracheostomy mask 20x/minute, SpO2 99%, BP 102/67 mmHg, HR 80 x/minute, To 36.5°C, CRT <2 s, MAP 78.6, DC 900 cc/12 hours, sonde 6x200 cc, EWS 1, normal nutritional status. The patient's general condition tends to be stable and improving until the 12th day, which is the day when the patient is planned to go home. The therapy given in the room does not change much. On the 8th day of treatment, the patient's diet was changed to T5M6 extra egg white and 1 fruit juice. On the 10th day of treatment, there was a change in infusion to inf. RD5 500 cc/24 hours and there is an additional 6 x 100 cc filter team diet.

On the 12th day of treatment the patient's condition improved, the general condition was adequate, and the patient appeared stable. Spontaneous breathing with tracheostomy 20x/minute, SpO_2 99%, BP 100/60 mmHg, HR 77 x/minute, To 360C, CRT <2 s, DC 750 cc/12 hours, sonde 6x200 cc, EWS 6, GCS E4 Vx M5 , normal nutritional status. Patients are advised to go home and control 1 week later. The patient was given home medicine, namely cefixime 2 x 100 mg, mefenamic acid 3 x 500 mg, phenytoin 3 x 100 mg, and dexamethasone 3 x 0.5 mg.

DISCUSSION

CPA is the most common location for neoplasms in the posterior fossa. CPA is a cisternal space in the posterior fossa bounded by the petrous temporal bone from the lateral side, the cerebellum and brainstem from the medial side, and cranial nerves IX, X, and XI from the inferior side (Connolly, Ali, & Keil, 2020). Approximately 5% -10% of intracranial tumors are CPA tumors. The most common CPA tumor types are vestibular schwannoma (80%), meningioma (10%), and epidermoid cysts (1-3%) (Khalsa et al., 2018). In this case, CPA tumor occurred in a 46-year-old woman. Research by (Jenny Mbaye & Dinardi, 2019) reported that the prevalence of CPA tumors in women is higher than men. The ratio of women to men is 2-3:1 with an average age ranging from 40-50 years (Mame Ndew Mbaye et al., 2019)a

Clinically, CPA is characterized by symptoms of increased ICP including headache, nausea, vomiting and papilledema. Other signs and symptoms are cranial nerve dysfunction, such as tinnitus, vertigo, motor weakness, gait disturbance or ataxia, facial muscle pain and weakness (Connolly et al., 2020). In this case, the patient had clinical manifestations of headache, vertigo, difficulty walking, tingling in all extremities, numbness on the left side of the body, and diplopia in the left eye for one year. In line with research by (Khan et al., 2018) reported that the average duration of symptoms in CPA tumor patients ranges from 8 days – 12 years. Signs of acute hydrocephalus were also found in this case, so a preoperative VP-Shunt was

performed. This is due to obstruction of the Cerebrospinal Fluid (CSF) pathway which causes an increase in CSF and ICP. (Ali et al., 2021) and Mbaye et al., (2019) reported that hydrocephalus was found in 72.7% of CPA tumor patients with a tumor size of more than 4 cm. The VP-Shunt preoperative procedure was also performed in 25% of CPA tumor patients and showed clinical improvement (Ali et al., 2020).

The main goals of anesthesia in this case are to control ICP and brain volume, prevent secondary brain injury, and reduce the occurrence of bleeding during surgery. Factors to avoid include hypoxemia, hypercapnia, anemia, and hypotension. Brain autoregulation and response to CO_2 must be maintained to prevent this from happening. The three intracranial components include brain tissue, blood, and CSF. The volume composition of these three components can change according to Monroe Kellie's law, but the total volume is always constant because the intracranial volume is always the same (Steensma et al., 2019). A decrease in the volume of one component will follow an increase in the volume of the other component. Autoregulation of blood flow to the brain under normal conditions ranges from 50 cc/100 g/minute with basal brain oxygen consumption reaching 3.3 cc/100 g/minute and glucose consumption of 4.5 mg/100 g/minute. This condition can occur if the Mean Arterial Pressure (MAP) is maintained between 50-150 mmHg. MAP below 50 mmHg can cause ischemia in brain tissue, while MAP above 150 mmHg will cause damage to the blood-brain barrier resulting in brain edema or severe bleeding. In the case of CPA tumor removal, the target PaO_2 is expected to be 100–200 mmHg. Administration of high oxygen levels with PaO_2 >200 mmHg should be avoided because cerebral vasoconstriction can occur and cause brain tissue ischemia. Changes in the partial pressure of CO_2 in the arteries ($PaCO_2$) will result in changes in cerebral blood flow because CO_2 is a potent vasodilator in the blood vessels of the brain. Each mm Hg change in $PaCO_2$ between 25 and 80 mm Hg will change cerebral blood flow by about 4% (Suryadi et al., 2021).

Proper patient positioning during CPA tumor surgery is one of the important factors in the success or failure of the procedure. The greatest challenge for the anesthesiologist is to choose the most appropriate surgical position that provides the best surgical exposure while posing the minimum position-related risks to the patient. The most common positions for CPA tumor surgery are supine, lateral, park bench (semiprone), prone, and semisitting. In this case, the patient is positioned supine with the head turned to the right. Supine or supine position with the head directed to the opposite side and placement of a pillow under the ipsilateral shoulder to minimize stretching of the brachial plexus (Jagannathan & Krovvidi, 2014) Induction of anesthesia using a combination of propofol, fentanyl, and rocuronium. Propofol is widely used in induction of anesthesia and sedation in neuro-intensive care. Several studies have shown that propofol has a protective effect on the brain. Propofol reduced CBF by 30%, $CMRO_2$ (30%), and ICP. CPP is also decreased because

propofol has a strong hypotensive effect. The mechanism of action of propofol is to facilitate inhibition of neurotransmission mediated by Gamma-Aminobutyric Acid (GABA). In this case, propofol 150 mg was given to a patient weighing 60 kg. The effect of propofol administration on the cardiovascular system can cause hypotension and bradycardia (Desai et al., 2019; Kulsum & Suryadi, 2021). This can be seen in Figure 4, the patient's blood pressure and pulse tend to decrease after induction of anesthesia.

Fentanyl is an opioid analgesic drug that is often used as an anesthetic agent. Fentanyl acts as an opioid agonist that binds to μ-opioid receptors in the central nervous system (Aiola et al., 2020). Research conducted by (Quispe Pérez, 2019) and (Palomares et al., 2020) demonstrated that fentanyl can increase ICP, but at the same time decrease MAP and CPP in patients with traumatic brain injury. This is because fentanyl can have a cerebral vasodilatory effect which causes an increase in ICP and a decrease in CPP.

The muscle relaxants that have the least effect on increasing CBF are vecuronium and rocuronium, so they are the drugs of choice for intracranial surgery. In this case, 50 mg of rocuronium was administered to the patient. Rocuronium was chosen because it is a competitive muscle relaxant that has the fastest onset of action, which reacts within 2 minutes with an intermediate duration of action. (Kulsum & Suryadi, 2021). Research by (Kosciuczuk et al., 2021) reported that rocuronium has minimal cardiovascular effects and has a mild vagolytic effect. This is because rocuronium is a non-depolarizing type of neuromuscular blocking agent. The effects of non-depolarizing muscle relaxants on the cardiovascular system are related to antagonistic effects on the muscarinic receptors of the vagus nerve in the heart (vagolytic effect), activation of post-ganglionic adrenergic fibers, release of catecholamines and their inhibition, as well as uptake by adrenergic nerve endings.

The inhalation anesthetic used was sevoflurane (1 MAC = 2%) with 50:50 oxygen and air. The use of 50% oxygen flow is carried out to prevent PaO2 pressure above 200 mmHg. Sevoflurane was used in this case because its cerebral vasodilating effect and increase in CBF is the least of all anesthetic gases. Sevoflurane also has a neuroprotective effect in the form of anti-apoptosis. The reduction in cardiac output by sevoflurane is also less than that of isoflurane or halothane, thus avoiding excessive fluid administration or the use of vasoconstrictors (Kulsum & Suryadi, 2021). Reasearch by (Maruzs, Simon-Vecsei, Kiss, Csizmadia, & Juhász, 2019) demonstrated that during the induction phase, the combination of propofol, fentanyl-rocuronium and addition of sevoflurane resulted in a decrease in MAP (mainly due to a decrease in diastolic pressure) and an increase in aortic pressure and pulse.

Postoperatively, the patient was treated intensively in the ICU. The patient used a bilevel positive airway pressure (BiPAP) mode ventilator for 4 days, then

switched to Continuous Positive Airway Pressure (CPAP) mode on the 5th day. In BIPAP mode, the patient can breathe spontaneously, but the amount has been controlled. Breathing is synchronized with the patient's efforts in both inspiration and expiration. If the patient does not have a spontaneous respiratory effort indicated by the inspiratory trigger window, the ventilator will set the patient's respiratory trigger. CPAP mode is used to maintain a patent airway. Collapsed airways can be seen in people with breathing problems such as Obstructive Sleep Apnea (OSA), in which breathing stops or pauses during sleep. If the patient is still too weak to manage complete respiratory efforts independently, volume support can be added (Deden, 2015).

While in the ICU, the fluid therapy given postoperatively was 1000 cc/24 hours of tutosol infusion. A 2 mg/hour midazolam pump and a 2 mg/hour morphine pump were given on the first postoperative day and continued with a 2 mg/hour dobutamine pump. Other therapy in the form of inj. fosfomycin 2x1 gr, inj. ranitidine 2x50 mg, inj. dexamethasone 3x5 mg, inj. metamizole 3x100 mg, inj. phenytoin 3x100 mg, inj. tranexamic acid 3x500 mg, inj. dexketoprofen 3x50 mg, inf. paracetamol 3x1 gr, salbutamol nebulizer 3x3 mg, transfusion of Packed Red Cells (PRC) 1 colf and transfusion of 25% albumin 100 cc. The patient had a good hemodynamic profile while in the ICU, so that on the fifth day the patient could be moved to the usual treatment room.

CONCLUSION

CPA is a type of neoplasm found in the cisternal space in the posterior fossa which is bounded by the petrous temporal bone from the lateral side, the cerebellum and brainstem from the medial side, and cranial nerves IX, X, and XI from the inferior side. Operative action on patients with CPA tumors is a challenge in the field of anesthesia, which is a narrow location and contains many vascular and nerve tissue fibers. The surgical management of CPA tumors can be carried out using various approaches to surgical techniques, such as determining the patient's position and selecting an anesthetic agent. Supine position in CPA tumor surgery and the use of the combination of propofol, fentanyl, and rocuronium have special concerns that must be observed during surgery. Preparation for patients undergoing CPA tumor surgery includes preoperative evaluation, premedication, induction of anesthesia, durante op position, durante op observation, and postoperative management. Postoperative management needs to be considered to prevent hypoxemia, respiratory problems, infections due to the use of mechanical ventilation, and other complications. The main principle of CPA tumor surgery is neuroprotective, namely maintaining intracranial pressure and cerebral blood flow. Therefore, it is important to know the effect of the operative management given to maintain the patient's hemodynamic condition.

BIBLIOGRAPHY

Aiola, Simone, Calabrese, Erminia, Maurin, Loïc, Naess, Sigurd, Schmitt, Benjamin L., Abitbol, Maximilian H., Addison, Graeme E., Ade, Peter A. R., Alonso, David, & Amiri, Mandana. (2020). The Atacama Cosmology Telescope: DR4 maps and cosmological parameters. *Journal of Cosmology and Astroparticle Physics*, *2020*(12), 47.

Ali, Bayad Jamal, Saleh, Pakzad Fadel, Akoi, Shwana, Abdulrahman, Aram Ahmed, Muhamed, Awezan Shamal, Noori, Halwest Nowzad, & Anwar, Govand. (2021). Impact of service quality on the customer satisfaction: Case study at online meeting platforms. *Ali, BJ, Saleh, Akoi, S., Abdulrahman, AA, Muhamed, AS, Noori, HN, Anwar, G.(2021). Impact of Service Quality on the Customer Satisfaction: Case Study at Online Meeting Platforms. International Journal of Engineering, Business and Management*, *5*(2), 65–77.

Connolly, Creighton, Ali, S. Harris, & Keil, Roger. (2020). On the relationships between COVID-19 and extended urbanization. *Dialogues in Human Geography*, *10*(2), 213–216.

Deden, Deden. (2015). Pengaruh Jarak Tanam dan Aplikasi Pupuk NPK terhadap Pertumbuhan dan Hasil Tanaman Kedelai (Glycine max L. Merril) Varietas Kaba. *Agrikultura*, *26*(2).

Jagannathan, Sathyanarayanan, & Krovvidi, Hari. (2014). Anaesthetic considerations for posterior fossa surgery. *Continuing Education in Anaesthesia, Critical Care & Pain*, *14*(5), 202–206.

Khalsa, Sahib S., Adolphs, Ralph, Cameron, Oliver G., Critchley, Hugo D., Davenport, Paul W., Feinstein, Justin S., Feusner, Jamie D., Garfinkel, Sarah N., Lane, Richard D., & Mehling, Wolf E. (2018). Interoception and mental health: a roadmap. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *3*(6), 501–513.

Khan, Aziz, Fornes, Oriol, Stigliani, Arnaud, Gheorghe, Marius, Castro-Mondragon, Jaime A., Van Der Lee, Robin, Bessy, Adrien, Cheneby, Jeanne, Kulkarni, Shubhada R., & Tan, Ge. (2018). JASPAR 2018: update of the open-access database of transcription factor binding profiles and its web framework. *Nucleic Acids Research*, *46*(D1), D260–D266.

Kosciuczuk, Urszula, Gluszynska, Paulina, Diemieszczyk, Inna, Lukaszewicz, Aleksander, Bauer, Krzysztof, Kokoszko, Maciej, Szarpak, Lukasz, Ladny, Jerzy Robert, & Hady, Hady Razak. (2021). Effect of rocuronium on the heart rate and arterial blood pressure during combined general anaesthesia. *Disaster and Emergency Medicine Journal*, *6*(3), 104–111.

Maruzs, Tamás, Simon-Vecsei, Zsófia, Kiss, Viktória, Csizmadia, Tamás, & Juhász, Gábor. (2019). On the fly: recent progress on autophagy and aging in Drosophila. *Frontiers in Cell and Developmental Biology*, *7*, 140.

Mbaye, Jenny, & Dinardi, Cecilia. (2019). Ins and outs of the cultural polis: Informality, culture and governance in the global South. *Urban Studies*, *56*(3), 578–593.

Mbaye, Mame Ndew, Hou, Qingzhen, Basu, Sankar, Teheux, Fabian, Pucci, Fabrizio, & Rooman, Marianne. (2019). A comprehensive computational study of amino acid interactions in membrane proteins. *Scientific Reports*, *9*(1), 12043.

Palomares, M. L. D., Froese, Rainer, Derrick, B., Meeuwig, J. J., Nöel, S. L., Tsui, G., Woroniak, J., Zeller, D., & Pauly, D. (2020). Fishery biomass trends of exploited fish populations in marine ecoregions, climatic zones and ocean basins. *Estuarine, Coastal and Shelf Science*, *243*, 106896.

Quispe Pérez, Juana Raquel. (2019). *RELACIÓN ENTRE LAS ENFERMEDADES PERIODONTALES Y EL BIOTIPO GINGIVAL EN PACIENTES ATENDIDOS EN LA CLÍNICA ODONTOLÓGICA DE LA UNIVERSIDAD PRIVADA NORBERT WIENER. LIMA 2018-2019*.

Steensma, David P., Wermke, Martin, Klimek, Virginia M., Greenberg, Peter L., Font, Patricia, Komrokji, Rami S., Yang, Jay, Brunner, Andrew M., Carraway, Hetty E., & Ades, Lionel. (2019). Results of a clinical trial of H3B-8800, a splicing modulator, in patients with myelodysplastic syndromes (MDS), acute myeloid leukemia (AML) or chronic myelomonocytic leukemia (CMML). *Blood*, *134*, 673.

Suryadi, Taufik, Zulfan, Zulfan, & Kulsum, Kulsum. (2021). The Relationship between Knowledge and Attitudes about Community Disaster Preparedness in Lambung Village, Banda Aceh. *International Journal of Disaster Management*, *4*(1), 1–10.

Yasmin, Farah, Shujauddin, Syed Muhammad, Naeem, Aisha, Jabeen, Adina, Shah, Syed Muhammad Ismail, Ochani, Rohan Kumar, Mohiuddin, Osama, Khan, Anosh Aslam, Jalees, Sumeen, & Razzack, Aminah Abdul. (2021). Exploring the impact of the COVID-19 pandemic on provision of cardiology services: a scoping review. *Reviews in Cardiovascular Medicine*, *22*(1), 83–95.