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Anesthetic management of a pediatric patient undergoing clival tumor resection via the expanded endonasal approach

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Keypoints

Meticulous case preparation is necessary for the effective management of the pediatric patient presenting for clival tumor resection via EEA. Anesthesia providers should anticipate the use of intra-operative neuromonitoring and/or iMRI and therefore expect to use a balanced TIVA technique using MRI-safe equipment.

Abstract

The clivus is bone of the skull base located between the sella and the foramen magnum. It consists of both the sphenoid bone rostrally and the occipital bone caudally. Because of its deep central location near the brainstem, basilar artery, internal carotid arteries, cranial nerve VI (abducens), and cranial nerve XII (hypoglossal), treating clival lesions presents significant surgical challenges. Successful treatment often requires a multidisciplinary approach including otolaryngology, neurosurgery, radiology, oncology, pathology, palliative care, and anesthesiology. We report a 15 year-old female with a clival chordoma who underwent tumor resection via the expanded endoscopic endonasal approach (EEA). Given the proximity of the lesion to the abducens nerve, lower cranial nerves, and brainstem, intraoperative neuromonitoring (IONM) consisting of electromyography (EMG), motor-evoked potential (MEP) and somatosensory-evoked potential (SSEP) monitoring were utilized. As such, a propofol-remifentanil total intravenous anesthetic (TIVA) was used. To our knowledge, this is the first report detailing the anesthetic management of a pediatric patient undergoing a clival tumor resection via EEA.

Keywords: total intravenous anesthesia, remifentanil, propofol, desflurane, clival tumor, anesthesia, pediatric, neurosurgery, chordoma, expanded endonasal approach, transnasal-transsphenoidal resection.

Introduction

The clivus (Latin for "gradient" or "slope") is bone of the skull base located between the sella and the foramen magnum. It consists of both the sphenoid bone rostrally and the occipital bone caudally. Because of its deep

central location near the brainstem, basilar artery, internal carotid arteries, cranial nerve VI (abducens), and cranial nerve XII (hypoglossal), treating clival lesions presents significant surgical challenges.[1,2] Successful treatment often requires a multidisciplinary approach including otolaryngology, neurosurgery, radiology, oncology, pathology, palliative care, and anesthesiology.[3,4] We report a 15-year-old female with a clival tumor, suspicious for chordoma, scheduled for expanded endoscopic endonasal approach and resection. The surgical team requested intraoperative neuromonitoring (IONM), consisting of electromyography (EMG), motor-evoked potential (MEP) and somatosensory-evoked potential (SSEPS) monitoring. We, therefore, chose to use a total intravenous anesthetic technique consisting of propofol and remifentanil. Details of the case are discussed and potential perioperative concerns reviewed.

Case report

An otherwise healthy 15-year-old, 92 kg female with a clival mass suspicious for chordoma presented for endonasal endoscopic transsphenoidal resection. She had a one-month history of drooling, dysarthria and dysphagia. On exam, she had bilateral hypoglossal nerve palsy with markedly diminished tongue movement. CT and MR (Figure 1) imaging demonstrated a large, ill-defined, low-attenuation mass lesion in the retropharyngeal/prevertebral spaces with minimum rim enhancement. The lesion eroded the inferior clivus as well as portions of the occipital condyles and caused posterior bowing of the tectorial membrane. Initial differential diagnosis included: chordoma, chondrosarcoma, nasopharyngeal rhabdomyosarcoma and nasopharyngeal carcinoma. There was no evidence of intradural involvement.

Because the tumor was adjacent to the abducens and hypoglossal nerves as well as the brainstem, EMG, MEP and SSEP monitoring was required. We therefore chose to use a total intravenous anesthetic technique consisting of propofol and remifentanil to allow for improved neuromonitoring capabilities. The surgery was scheduled for 8 hours and was performed in our facility's intraoperative magnetic resonance imaging (iMRI) suite.

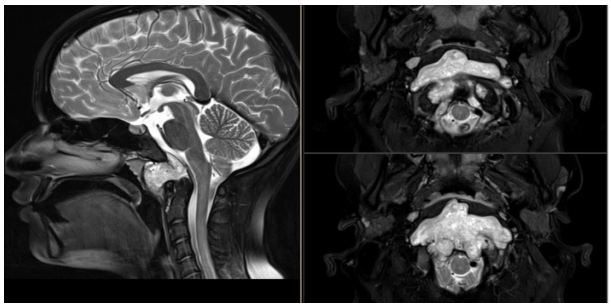

Figure 1. MRI scans of chordoma; Sagittal (left) and Axial (right) T2 MRI with fat suppression

On physical examination, the patient was noted to be moderately obese for her age, with a BMI of 31 kg/m^2. Assessment of her airway revealed a normal thyromental distance and a Mallampati score of 2. She had difficulty moving her tongue and speaking, but there was no receptive or expressive aphasia. She denied any visual disturbances and was noted to be otherwise healthy. The patient was held *nil per os* for 8 hours.

Her preoperative vital signs included a resting respiratory rate of 16 breaths/minute, a room-air oxygen saturation of 99% by pulse oximetry, a heart rate of 98 beats/minute, and a blood pressure of 119/66 mmHg. The patient had a pre-existing 20 gauge intravenous (IV) with maintenance fluids infusing. In the pre-operative area, she was given midazolam (2 mg) IV for anxiolysis and then transported to the operating room where routine American Society of Anesthesiologists (ASA) monitors were applied. After pre-oxygenation, general anesthesia was induced by the administration of intravenous fentanyl (100 mcg), lidocaine (40 mg) and propofol (140 mg). Endotracheal intubation was performed atraumatically using a Macintosh 3 blade and a cuffed, styleted 7.0 mm endotracheal tube. Following confirmation of bilateral breath sounds and sustained $ETCO_2$, the tube was secured at a depth of 20 cm. Care was taken not to manipulate the patient's cervical spine during

intubation due to significant occipital-cervical involvement of her disease process. The OR table was then positioned 180 degrees away from the anesthesia machine. This required an extended length anesthesia circuit and IV lines. To prevent accidental extubation or inadvertent tube migration during the case, the endotracheal tube was taped and secured using liquid adhesive (Mastisol ®, Eloquent Healthcare, Ferndale, MI, USA), transparent bioocclusive dressings (Tegaderm, 3M, St. Paul, MN, USA), silk tape, and pink plastic tape.

The patient tolerated anesthetic induction, endotracheal intubation and positioning without any adverse hemodynamic effects. Remifentanil infusion was started at 0.2 mcg/kg/min and propofol was started at 200 mcg/kg/min. Pressure control ventilation was initiated for the case with an $ETCO_2$ goal of 30-35 mmHg. An arterial line and second large-bore IV were then placed. After anesthetic induction and line placement, a Foley catheter was placed and the neuromonitoring team placed all required leads and electrodes.

Prior to the patient being placed in Mayfield cranial fixation pins, an IV bolus of propofol (100 mg) was given to prevent any potential coughing or movement. She tolerated pin placement well without any adverse hemodynamic response. She was prepared and draped in typical sterile fashion, and was given cefepime (2 grams) to prevent surgical site infection. A baseline arterial blood gas (ABG) and basic metabolic panel (BMP) was drawn during this time, with all results within normal limits. Her starting hemoglobin and hematocrit were 10.5 g/dL and 31%, respectively. Three units of packed red blood cells (PRBC's) were kept in the OR refrigerator on standby.

Since the surgical plan included potential need for an iMRI, considerations regarding ferro-magnetic equipment were made. If iMRI was needed, the neuromonitoring equipment would be removed prior to scanning. It is our facility's policy that a safety walkthrough be completed prior to opening the MRI bay doors. It is during this time that all non-MRI safe objects are removed. All objects that need to remain with the patient during the scan are MRI safe (anesthesia machine, infusion pumps, monitors, surgical equipment, etc.).

Overall, the anesthetic course was uneventful as evidenced by very little variation in the patient's hemodynamics. Neither anti-hypertensive or vasoactive medications were required or administered. Remifentanil and propofol were titrated accordingly throughout the case depending on the amount of surgical stimulation and the patient's hemodynamic responses. The maximum dose of remifentanil reached 0.5 mcg/kg/min but was short lived and transient. For the majority of the case, propofol infused at 200 mcg/kg/min. Hydromorphone (1 mg) was given early and often throughout the case as a transitional narcotic and to prevent the possible hyperalgesia and hypertension sometimes seen when prolonged infusions of remifentanil are discontinued. The total dose of hydromorphone administered throughout the case was 5 mg.

The case was originally scheduled for 8 hours, but gaining surgical access to the clivus, debulking this large tumor at the occipito-cervical junction, and the subsequent reconstruction that followed, ultimately required 16 hours. At approximately the midpoint of surgery, the anesthesia team became concerned about the possible risk of propofol infusion syndrome (PRIS) and/or a delayed emergence from anesthesia, making it difficult if not impossible to extubate the patient in a timely manner. This was discussed with the surgeons. Both the otolaryngologist and neurosurgeon stated they were satisfied with the results of the neuromonitoring up to this point and that an inhaled agent would be acceptable to use. Propofol was discontinued and a 0.5 minimum alveolar concentration (MAC) of desflurane was added. Remifentanil continued at 0.2 mcg/kg/min. Exhaled concentrations of desflurane ranged from 2.8-3.0%. The neuromonitoring team saw no change in their measurements with the addition of desflurane. During this time

it was noted that the patient was producing large amounts of dilute urine (approximately 11.5 ml/kg). This phenomenon only occurred for one hour. The surgeons were notified and a urine specific gravity was measured. The result of 1.005 was slightly lower than the norm of 1.007-1.030. A sodium level was also checked and the result was 144 mEq/dl. Urine output and labs continued to be monitored hourly. Ultimately, the patient did not develop diabetes insipidus consistent with a tumor location separate from the pituitary gland and stalk.

Throughout the case the patient remained hemodynamically stable, but due to continuous oozing at the surgical site and a drifting hematocrit, the patient was eventually transfused with one unit of PRBC's near the end of the case. The patient showed an appropriate response as evidenced by an increase in her arterial blood pressure and a hemoglobin concentration >8 g/dL.

Considering the length of surgery and that it lasted until early the next morning, the anesthesia team decided to postpone extubation until later in the day. The patient was safely transported to the pediatric intensive care unit (PICU) where she was successfully extubated after one hour.

Discussion and conclusion

Chordomas were first observed microscopically in 1856 by Luschka and in 1857 by Virchow, although at the time the histopathology was not completely understood. It would take another 30 years for Ribbert to introduce the term *chordoma*, believing that these lesions arose from notochord remnants instead of cartilage.[5] As of late, the notochord remnant theory has been supported by Yang and colleagues recent discovery of a gene duplication in the transcription factor T gene (brachyury) in familial chordomas.[4,6] Current estimates place the annual incidence at 0.08 to 0.1 per 100,000 individuals, with the average age at time of diagnosis being 60 years.[3,4] Skull base chordomas are even more rare with an incidence of 1 case per 2,000,000 individuals per year.[7] According to the Surveillance, Epidemiology and End Results (SEER) database overall prognosis remains poor, with a median survival time of 6.29 years and a 5-year-survival rate of just 67.6%.[8]

Because chordomas arise from notochord remnants they are found along the axial skeleton, developing at the sacrum (50%), skull base (30%) or spine (20%).[3] They tend to be slow growing, locally aggressive, invasive of nearby structures and are often radioresistant.[9] Although surgery with the goal of gross-total excision is the treatment of choice, other options include partial or radical resection with or without radiotherapy.[4,9,10] Until recently it was thought that no effective medical treatment existed, but a multicenter phase II clinical trial involving imatinib mesylate, a tyrosine kinase inhibitor, has shown promise. In a small percentage of patients imatinib was successful in shrinking tumor size, stabilizing tumor growth, decreasing pain and increasing life expectancy.[11,12,13]

When surgery is indicated, the chosen surgical approach is not absolute, but rather is based on tumor location and surgeon experience.[10] When cranial, their deep central location near important vascular and neurological structures complicates surgical access. For this reason, the expanded endoscopic endonasal approach (EEA) is often used.[9]

The resection of a clival tumor has multiple anesthetic considerations (Figure 2). The patient is routinely positioned 180 degrees away from the anesthesia provider, draped and in pins. This by itself can cause serious but preventable problems if not anticipated. Care must be taken to secure the airway in a manner that prevents any accidental extubation or tube migration, as this would be catastrophic during the case. In addition, an anesthesia circuit of adequate length should be used. Most standard circuits are not long enough to reach a patient that is 180 degrees away from the anesthesia machine. All venous, arterial and monitoring lines should have extensions on them to allow smooth turning of the OR table

and to prevent tugging or pulling, possibly leading to accidental line removal.

1.	If motor-evoked potential (MEP) or somatosensory-evoked potential (SEP) monitoring is requested, consider the use of a total intravenous anesthetic technique.
2.	If using a propofol infusion at moderate to high doses for extended periods of time, be alert for the development of propofol infusion syndrome (PRIS).
3.	Although it is more common during transsphenoidal pituitary surgery (sellar or suprasellar), monitor for large amounts of dilute urine, possibly indicating the development of diabetes insipidus (DI).
4.	If unable to use muscle relaxant, be extra vigilant that the patient does not move while in pins or during micro-dissection, which could be catastrophic.
5.	Have at least 2 to 3 units of PRBCs readily available to transfuse. Due to the proximity of surgery to large cranial arteries (such as carotids), blood loss could be sudden, massive, and difficult to control.
6.	After transsphenoidal surgery, the patient will not be a candidate for nasotracheal intubation or nasogastric tube placement, due to interruption of the bony skull base. Attempts could lead to intracranial tube placement.
7.	Depending on the tumor type and expected length of surgery, consider placing multiple large-bore IVs (for fluid and blood administration) and an arterial line (for frequent monitoring of lab values and for beat-to-beat blood pressure measurement).
8.	Due to the extended length of surgery, proper positioning and appropriate padding is important to prevent nerve damage or skin breakdown.
9.	If the OR table will be 180 degrees away from the anesthesia machine, make sure that the anesthesia circuit is adequate length and that venous, arterial and monitoring lines will reach.
10.	If oxymetazoline will be administered intranasally by the surgeon, monitor for hypertension and rebound bradycardia.

Figure 2. Anesthetic Considerations for Patients Undergoing Endoscopic Transnasal Transsphenoidal Surgery

Intravenous access should be sufficient to replace heavy blood loss if encountered. An arterial pressure line is useful in assessing beat to beat hemodynamics as well as allowing easy blood draws for frequent monitoring of hemoglobin, acid base balance and electrolytes.

Immediate availability of 1-3 units of packed red blood cells (depending on patient age and weight) should be considered. Due to the proximity of surgery to large cranial arteries, blood loss could be sudden, massive and difficult to control.

The length of surgery is also an important factor to consider. These patients are at an increased risk of developing pressure and nerve injuries related to improper positioning. Careful padding and frequent monitoring is imperative. In extremely long cases and in rare instances, proper positioning and padding may still not prevent skin or nerve injuries. The possibility of this should be discussed with the patient and surgeon beforehand.

After transsphenoidal surgery a patient will no longer be a candidate for nasotracheal intubation or nasogastric tube placement, due to surgical interruption of the bony skull base. Attempts at tube placement via this route could lead to inadvertent intracranial tube placement, causing great patient harm or even death. Paul and colleagues describe such a case.[14] A communication error between anesthesia providers led to the accidental intracranial placement of an endotracheal tube in a patient who underwent transsphenoidal surgery two weeks prior. The original anesthesia provider who had set-up and prepared for the case was called away for an emergency immediately prior to induction of the patient. The relieving anesthesia provider was not aware of the patients recent transsphenoidal surgery. During the attempted nasotracheal intubation, mild resistance was met. When the endotracheal tube was advanced using gentle pressure, pulsating bright blood was noted in the proximal end of the tube. The oropharynx subsequently filled with blood in a rapid manner. The patient was resuscitated and transported to ICU, but decompensated and died 4 days later, as a result of severe intracranial sequelae.[14]

Oxymetazoline is a potent alpha$_1$-adrenergic agonist. It is frequently used during transnasal transsphenoidal surgery because of its ability to decrease bleeding thereby creating a better visual field in which to operate. Although its efficacy is well established and it is sold as

an over-the-counter decongestant, systemic absorption remains a potential complication. This is more common in patients who have surgically disrupted nasal mucosae, allowing for increased vascular absorption of the drug. Thrush describes a case in which a two-year old was scheduled for nasal endoscopy.[15] After a smooth inhalation induction and IV placement, the surgeon sprayed 0.025% metazoline into each naris. Approximately one minute later, the patient became dangerously hypertensive and bradycardic. The patient eventually became asystolic but was successfully resuscitated. Surgery proceeded without any further untoward events.[15]

In another report by Latham and Jardine,[16] a 4 year-old presenting for dental restoration developed severe hypertension following the intranasal administration of oxymetazoline 0.05%. The authors postulate that systemic absorption occurred due to the patient's disrupted nasal mucosa, following a somewhat traumatic nasal intubation. The patient's diastolic blood pressure exceeded 100 mmHg for 30 minutes. Surprisingly during this time the patient never became bradycardic. There were no long-term sequelae reported and the patient was discharged home after 3.5 hours.[16] The authors further explain that when a spray bottle is used, the dose of oxymetazoline administered is dependent on the position of the bottle, with the inverted position leading to much greater volume of the drug being administered, which in turn leads to an increased potential for toxicity and its associated signs. This conclusion is further supported by a separate study which looked specifically at the amount of oxymetazoline administered in relation to bottle position. The study by Hakim and colleagues found that when oxymetazoline was administered with the bottle in the inverted position, even if the bottle was half empty, a 10-fold amount of the medication was given.[17] These publications reinforce the importance of accurate dosing and uniform administration of intranasal oxymetazoline. In a neurosurgical patient, systemic absorption of oxymetazoline leading to arterial hypertension could have profound consequences.

During surgical resection of clival tumors via EEA, intraoperative neuromonitoring (IONM) is common practice. The choice of anesthetic technique, therefore, depends not just on the experience and comfort level of the anesthesia provider, but more importantly on the needs and requests of the surgical team. All anesthetic medications, whether inhaled or intravenous, decrease signal amplitude during neuromonitoring to varying degrees, as their mechanism of action relies upon inhibition of the central nervous system. Inhaled anesthetics increase latency and decrease waveform amplitude in a dose-dependent fashion. Intravenous agents have the same effect, but to a lesser degree.[18] At comparable MAC values, inhaled agents cause more signal depression than intravenous agents.[18] For these reasons, when IONM is requested, a TIVA technique may be the preferred option. The safety and efficacy of TIVA in neurosurgical patients is also well established.[19-24]

Propofol is one of the most widely used intravenous anesthetic medications in the world. Its preeminence in the realm of TIVA is due to its favorable pharmacodynamic profile, including a rapid onset, rapid recovery time and lack of active metabolites.[25] However, the use of propofol is not without its limitations. Propofol lacks analgesic properties, necessitating the use of an opiod infusion during painful surgical stimulation. In addition, propofol infusion syndrome (PRIS), a severe and potentially life-threatening metabolic complication, remains a very real concern.[30] First described in pediatric ICU patients receiving long-term infusions, PRIS has since been described in pediatric patients undergoing short-term sedation and even brief surgeries.[26-30] A case report by Liolios et al describes PRIS in an adult undergoing a three hour neurosurgical case, illustrating the fact that this phenomenon can occur in patients of varying ages.[31]

Clinical features of PRIS include acute refractory bradycardia leading to asystole, in addition to one or more of the following findings: metabolic acidosis (base deficit > 10 mmoL), rhabdomyolysis, hyperlipidemia, and an enlarged or fatty liver.[30] Doses greater than 4 mg/kg/hr (66.6 mcg/kg/min), for greater than 48 hours, have been shown to place patients at an increased risk for developing PRIS.[30] One feature of PRIS that may aid in its early identification is the development of a right bundle branch block, with convex-curved ST elevation in leads V1 to V3.[30]

Different intracellular mechanisms have been offered as possible explanations for the development of PRIS. Current theories postulate that development of the syndrome may result from either a direct mitochondrial respiratory chain inhibition or impaired mitochondrial fatty acid metabolism.[30] Treatment for PRIS includes prompt discontinuation of the infusion and replacement with another anesthetic agent. Supportive measures, including correction of acid-base derangements, intravenous hydration if rhabdomyolysis is present, vasopressors and/or advanced cardiac life support (ACLS), and in rare cases hemodialysis may be required.[30]

In summary, care of the pediatric patient presenting for clival tumor resection via EEA requires a multidisciplinary approach and can present significant challenges to the anesthesia provider. With meticulous case preparation, open communication between the surgical and anesthesia teams and careful implementation of the aforementioned anesthetic considerations, these patients can be managed safely and effectively.

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