Lesson S23: Preanesthetic Assessment of the Patient for Asleep-Awake-Asleep Craniotomy

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Read this article, reflect on the information presented, then go online and complete the lesson post-test and course evaluation before the termination date below. (CME credit is not valid past this date.) You must achieve a score of 80% or better to earn CME credit.

TIME TO COMPLETE ACTIVITY: 2 hours
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Professional Gaps

Asleep-awake-asleep anesthetic technique is increasing in use in craniotomy and other neurosurgical procedures. Most anesthesiologists trained in general anesthesia for neurosurgery are not aware of the flexibility and advantages gained from this technique.

Learning Objectives

At the end of this activity, the participant should be able to:

1. Identify cases that are suited for awake-asleep-awake craniotomy
2. Prepare a patient for this technique
3. Order appropriate preoperative tests
4. Anticipate complications
5. Devise a plan for intraoperative sedation
6. Identify drugs that allow rapid response
7. List appropriate monitors
8. Draw up a fluid replacement scheme
9. Appreciate the flexibility required for asleep-awake-asleep craniotomy
10. Recognize when alternative anesthetic techniques should be used
Case History

A 35-year old woman presented to the emergency room after experiencing a grand mal seizure. She had been in good health apart from some recent headaches. Her husband noted that, over the past few months, she appeared to have difficulty in finding words. He attributed this change to stress at work. All laboratory studies were within normal limits as were her vital signs. A CT scan of her head showed a ring-enhancing lesion in the temporal area, most likely a glioblastoma.

Introduction

Neurosurgical techniques aimed at excision of glioblastomas, once considered inoperable lesions, receive much attention. These tumors are often located in close proximity to eloquent areas and injury to viable brain would severely compromise cerebral function. To better identify these areas, the neurosurgical team requires the ability to communicate directly with the patient intraoperatively.

Glioblastoma multiforme (GBM)

Glioblastoma multiforme is the most common and most aggressive malignant primary brain tumor in humans. It involves glial cells and accounts for 52% of all functional tissue brain tumor cases and 20% of intracranial tumors. Despite being the most prevalent form of primary brain tumor, GBMs occur in only 2–3 cases per 100,000 people in Europe and North America. Glioblastoma presents as two variants: giant cell glioblastoma and gliosarcoma. This pathology is also an important brain tumor in canines, and research continues to use dogs as a model for developing treatments in humans.

Pathophysiology

Glioblastoma multiforme tumors are characterized by the presence of small areas of necrotizing tissue, surrounded by anaplastic cells. This characteristic, as well as the presence of hyperplastic blood vessels, differentiates the tumor from Grade 3 astrocytomas. GBMs usually form in the cerebral white matter, grow quickly, and become very large before producing symptoms. Less than 10% form more slowly following degeneration of low-grade astrocytoma or anaplastic astrocytoma (secondary GBMs) and are more common in younger patients (mean age 45 versus 62 years). The tumor may extend into the meninges or ventricular wall, leading to high protein content in the cerebrospinal fluid (CSF) (> 100 mg/dL), as well as an occasional pleocytosis of 10 to 100 cells, mostly lymphocytes. Malignant cells carried in the CSF may rarely spread to the spinal cord or cause meningeal gliomatosis. However, metastasis of GBM beyond the central nervous system is extremely unusual. About 50% of GBMs occupy more than one lobe of a hemisphere or are bilateral.

No correlation has been found between glioblastoma and smoking, consumption of cured meat, or electromagnetic fields (i.e., cell phones). Alcohol consumption may be a possible risk factor. Recently, evidence for a viral cause has been discovered, possibly SV407 or cytomegalovirus. There may be a small link between ionizing radiation and glioblastoma. Some also believe that there may be a link between polyvinyl chloride (commonly used in construction) and glioblastoma. A 2006 analysis links brain cancer to lead exposure in the workplace. There is an association of brain tumor incidence and malaria, suggesting that the anopheles mosquito, the carrier of malaria, might transmit a virus or other
agent that could cause glioblastoma.\textsuperscript{12}

Although common symptoms of the disease include seizure, nausea and vomiting, headache, and hemiparesis, the single most prevalent symptom is a progressive memory, personality, or neurological deficit due to temporal and frontal lobe involvement, emphasizing the occurrence in eloquent areas of the brain.

Patients most likely to be affected are males, over age 50, Caucasians or Asians or patients with low grade astrocytoma.\textsuperscript{13} GBM\textsuperscript{s} appear to be sporadic, without genetic predisposition. Some genetic disorders have been linked including neurofibromatosis, tuberous sclerosis, von Hippel-Lindau disease and Turcot syndrome.

**Treatment**

GBM cells are resistant to conventional therapy and, in contrast, healthy brain cells are very susceptible to the effects of drugs. Many drugs do not cross the blood brain barrier and thus cannot specifically attack the tumor cells. Furthermore, the brain has only limited ability to self-repair.

Treatment for GBM can involve chemotherapy, radiation, radiosurgery, corticosteroids, antiangiogenic therapy, surgery\textsuperscript{14} and experimental approaches such as gene transfer.\textsuperscript{15} With the exception of brainstem gliomas, glioblastoma has the worst prognosis of any central nervous system (CNS) malignancy, despite multimodality treatment consisting of open craniotomy with surgical resection of as much of the tumor as possible, followed by concurrent or sequential chemoradiotherapy, antiangiogenic therapy with bevacizumab, gamma knife radiosurgery, and symptomatic management with corticosteroids. Moreover, even with successful surgery, the possibility of major damage to otherwise healthy surrounding neural tissue is a real concern. Prognosis is poor, with a median survival time of approximately 14 months.\textsuperscript{16}

Supportive treatment focuses on relieving symptoms and improving the patient’s neurologic function. The primary supportive agents are anticonvulsants and corticosteroids. Historically, around 90% of patients with glioblastoma undergo anticonvulsant treatment, although it has been estimated that only approximately 40% of patients require this treatment. Recently, it has been recommended that neurosurgeons refrain from administering prophylactic anticonvulsants unless a seizure occurs.\textsuperscript{17} Those receiving phenytoin concurrent with radiation are prone to serious skin reactions such as erythema multiforme and Stevens–Johnson syndrome. Corticosteroids, usually dexamethasone given 4 to 8 mg every 4 to 6 h, can reduce peritumoral edema (through rearrangement of the blood-brain barrier), diminishing mass effect and lowering intracranial pressure, with a decrease in headache or drowsiness.

**Surgery**

Surgery is the first approach to treatment of glioblastoma. A GBM tumor averages 1011 cells, which is reduced to approximately 109 cells after surgery (a reduction of 99%). Surgical excision prolongs survival and allows for histologic diagnosis, debulking of a mass and removal of disease before secondary resistance to radiotherapy and chemotherapy develops.

The goal of surgery is to remove as much tumor as possible. Removal of 98% or more of the tumor has been associated with a significantly longer healthier time than if less than 98% of the tumor is
removed. The chances of near-complete initial removal of the tumor can be greatly increased if the surgery is guided by a fluorescent dye known as 5-aminolevulinic acid. GBM cells are widely infiltrative through the brain at diagnosis, and so despite a "total resection" of all obvious tumor, most people with GBM later develop recurrent tumors either near the original site or at more distant "satellite lesions" within the brain. Other modalities, including radiation, are used after surgery in an effort to suppress and slow recurrent disease.

**Anesthetic Considerations**

While time honored anesthetic management has focused on general endotracheal anesthesia, the advent of faster acting agents make it possible to move safely and rapidly between consciousness and unconsciousness.

One of the first neurosurgeons to advocate awake craniotomy using local anesthesia was Harvey Cushing. Around 1927, Cushing removed a tumor from the brain of a Pittsburgh business executive in a 4-½ hour operation. The patient wrote that “one of the secrets of Dr. Cushing’s success is that he uses nothing except a local anesthetic which permits the normal functioning of the heart and other organs during the operation”.

Prior to then, 19th century neurosurgeons including Sir William Macewen and Sir Victor Horsley recognized that there was no sensation of pain in brain tissue and after opening the skull, little anesthesia was needed.

Awake craniotomy is a well-established neurosurgical technique for lesions involving eloquent cortex and other areas. The technique is also applied to procedures that involve deep brain stimulation to improve conditions such as intractable epilepsy, cephalgias, restless legs syndrome, multiple sclerosis, pantothenate kinase-associated neurodegeneration, Tourette syndrome, major depressive disorders, obsessive compulsive derangements, movement disorders such as essential tremor, post traumatic tremor and intractable pain disorders.

**Preanesthetic Assessment**

Patient cooperation is essential and it is important to explain to the patient that they will be awake during part (if not all) of the procedure to assure that the healthy part of the brain is identified and not injured. The patient should be familiarized with what will be required of them such as the questions that may be asked to assess the speech center and tasks that must be performed, such as “move your toes”. The patient may be asked to read from a paper. In such circumstances, the anesthesiologist should ensure that the patient can read without glasses or that the print is large enough that enhanced vision is not necessary. The anesthesiologist must ascertain the language and competency of the patient. The patient must be reassured that the anesthesiologist will be close by to monitor and to give pain medications if necessary. The anesthesiologist should also be aware of any aura that the patient may experience prior to a seizure so that appropriate medications may be promptly given to avert a major attack. Although urinary catheters are not usually placed in awake patients, especially males, the patient should be told that if there were a need to urinate, a bottle would be made available. The procedure usually requires 2-4 hours. If arthritis prevents the patient from lying comfortably, pillows and appropriate padding must be available.
Routine evaluation includes complete blood count, electrolyte screening panel including blood sugar level (which should be controlled at or below 120mg/dl), urinalysis to exclude urinary tract infection, and assessment of renal and liver function. Most of these patients have few other co-morbidities and baseline screening usually indicates no abnormalities. A chest X-ray will help to exclude evidence of aspiration, a common occurrence in patients who have seized. An electrocardiogram should also be available. Dysrhythmias may be due to increased intracranial pressure. Blood pressure should be controlled at or below 150 systolic to minimize the risk of hemorrhage. A blood specimen for type and screening of blood prior to surgery should be obtained. Blood transfusion is rarely necessary. Antiseizure medications such as carbamazepine or valproate may cause thrombocytopenia even though leukopenia is more common. Therefore, the type of anti-seizure drugs used and any history of bleeding should be carefully evaluated preoperatively; and platelet and white blood cell counts measured.

Use of premedication depends on the procedure and the needs of the patient. If the patient is to undergo a procedure unlikely to provoke a seizure, a benzodiazepine is a suitable agent. Also, intravenous diazepam given prior to contrast injection may reduce the incidence of contrast-associated seizures. The exception is the amytal test, which is preceded by cerebral angiography (amobarbital 30mg is injected into an artery supplying eloquent cerebral areas to determine neurologic function prior to devascularization). Under these circumstances, no sedative drugs are given. Antiemetics and antacids can also be indicated. Anticonvulsants are usually given preoperatively but in reduced doses at the discretion of the neurosurgeon. Hemodynamic stability may be increased during pin head holder insertion if clonidine is given orally 90 minutes before placement. Neurosurgeons often have protocols in place for sedation and hemodynamic control. The anesthesiologist should be conversant with these documents and discuss their content with the other members of the team preoperatively.

Of particular importance in the preanesthetic assessment of these patients is the airway evaluation. Patients who have been receiving dilantin may have gum hypertrophy and loosening of teeth that may hamper placement of an airway. The head may be held in a pin head holder that is attached to the table, limiting neck extension. Sedation may be increased if the procedure is lengthy or intraoperative complications develop. Should aspiration, vomiting or respiratory depression occur, a means to support ventilation must be immediately available. Thus, as well as careful preoperative assessment of the airway, the difficult airway cart should be available, including at a minimum different blades and tube sizes and even means for fiberoptic intubation. Availability of a Glidescope® is desirable. Supraglottic airways are particularly valuable as they can be placed with little or no head movement and minimal opening of the mouth. A tracheostomy kit should also be available.

**Anesthetic Management**

Several techniques have been described. Of particular importance is the need to maintain close communication with the neurosurgeon. Positioning is usually in a lateral position with as much padding as necessary to keep the patient comfortable. Monitors include standard ASA monitors, with special emphasis on capnography (usually side stream) and warming techniques to increase patient comfort. Arterial cannulation is not usually necessary. If a Mayfield head holder is indicated, then a scalp block or local infiltration may be used after induction. Accessibility to the face must be maintained.

The “asleep” phase is the first part of the anesthetic process during which the skull is opened and the
flap turned. This phase is accomplished generally with intravenous anesthesia and the placement of a supraglottic airway.

At the request of the surgeon, the infusions are stopped and the patient awakened. The airway is withdrawn, spontaneous ventilation returns, and adequate oxygen saturation can be maintained. Supplemental humidified oxygen should be provided with side stream capnography. A jaw thrust maneuver by the anesthesiologist, while improving oxygenation, might well alter the position and distort the surgical field and testing. Thus sedation must be extremely well balanced to ensure that the patient continues to breathe nasally, can cooperate with the surgeon and does not experience pain. In the event of ventilatory compromise, a supraglottic airway and nasal and oral airways of all sizes must be immediately available. A patient that is awake should be able to maintain their airway. Should circumstances change, the anesthesiologist must be able to secure the airway rapidly by fiberoptic means or through an intubating laryngeal mask. In some instances, it suffices to pass a laryngeal mask airway and allow continued spontaneous ventilation. Controlled ventilation may also be possible if there is no leak. Communication with the surgeon is essential.

Neurologic tests can be performed even after administration of small doses of narcotics and/or anxiolytics during the cortical and subcortical mapping as well as during the tumor resection. The resection is stopped when neurophysiologic testing identifies the eloquent areas. The second sleep phase is then commenced, either following intubation or by reinsertion of the supraglottic airway. The lateral decubitus position is maintained.

Several anesthetic techniques have been described in the literature. Lobo et al in 2007 described a propofol (25-50ug.kg/min) and remifentanil (0.1-0.2 ugm/kg/min) combination with effect-site concentrations estimated by pharmacokinetic simulation and bispectral monitoring with intraoperative awakening for brain tumor resection.29 Another study of 23 patients was reported using a similar technique by Glostrup in 2008.30 Gadhinglajkar et al also used the same combination of drugs using a supraglottic airway in place of intubation for the asleep phase, a substitution that has gained popularity in recent years, as placement is easier, ventilation can be controlled and there is less laryngeal stimulation.31,32

In many centers, dexmedetomidine has replaced propofol because it is less likely to depress respirations and has a faster wake up time.33,34 Dexmedetomidine is a potent and highly selective α2-adrenoceptor agonist that provides dose dependent sedation, analgesia, sympatholysis and anxiolysis without respiratory depression. Dose is about 0.1 - 0.2ug/kg/min without the need for bolus injection. At this level, the patient is sedated and comfortable. When the dexmedetomidine infusion is stopped, the patient can wake up and respond in less than 5 min. Adding dexmedetomidine to propofol can reduce the amounts required for both drugs.

Solutions with sugar should be avoided in all situations where there is risk of cerebral damage. Some practitioners prefer to limit fluid intake if a urinary catheter has not been placed. Others place a condom catheter preoperatively. Patients with chronic hypertension may by hypovolemic and become hypotensive after administration of sedatives. Appropriate care requires replacement of fluids.

Hemodynamic stability can best be achieved with small doses of narcotics such as fentanyl, remifentanil or alfentanil. Labetalol, 5-10 mg may be used in a patient with a history of hypertension. Hydralazine is another choice in low dose. Scalp infiltration with bupivacaine can reduce the chance of
alteration in blood pressure on incision. Hypertension has been associated with an increased risk of intracerebral hemorrhages. Dexmedetomidine offers better control and less need for antihypertensive medications.

**Complications**

A recent study described a low rate of serious complications but reported bradycardia (10%), leaking laryngeal mask airway (55%), nausea (10%), vomiting (5%), focal seizures (28%), generalized seizures (10%), hypoxia (2%), hypotension (5%) and hypertension (2%). The authors concluded that the procedure was safe and well tolerated. Another review also found a similar complication rate and noted that careful patient selection and communication within the team are essential.

With longer procedures, there is a greater likelihood that the patient will become restless and less cooperative. The patient may need to urinate and may complain of being cold, hungry or thirsty. It is important to take measures to maximize the patient’s comfort, including a warming blanket and moistening of the lips. Small doses of benzodiazepines may be indicated with the understanding that the effect can be reversed. If the patient’s head is secured to the table, even small movements should be avoided as the scalp may be torn. Small doses of remifentanil 0.01-0.05 mcg/kg/min for 3-5 minutes combined with propofol 15 ug/kg/min have been shown to be effective in relieving pain during conscious sedation. Onset of action of fentanyl is longer than that of remifentanil, making it less useful. Fentanyl is also cumulative but may be beneficial in doses of 25 ug. Alfentanil offers no particular advantage.

Communication with the surgeon is essential to making decisions and exercising all the options. Difficulties can include technical problems in isolating the appropriate area of the brain, as well as issues with achieving appropriate readings and movement by the patient. In the event of sudden bleeding, then the patient should be released from the pin head holder, followed by induction of general anesthesia induced and securing the airway by endotracheal intubation. Blood should be obtained and preparation made for transfusion. Open craniotomy may be required to identify and secure the bleeding point.

Patient satisfaction with the technique has been studied. Manchella et al found that, while 27% of patients had no recollection of being awake, only a minority reported more than slight pain (8%) and discomfort (12%). Ninety-two percent of patients were satisfied with the experience. Similar findings were described in a Canadian study, which also noted that the technique could allow for outpatient neurosurgery.

The technique remains an anesthetic challenge but one with which anesthesiologists have become much more comfortable as experience has increased.

**Management of the Case**

The surgeon and anesthesiologist met the patient and her husband on three separate occasions and the planned procedure was carefully explained. All agreed to proceed. The first phase was achieved with total intravenous anesthesia, using propofol, dexmedetomidine and remifentanil. A laryngeal mask airway was placed. After about 50 minutes, the surgeon requested that the patient be awakened.
The infusions were discontinued and she opened her eyes in 6 minutes. The awake and testing phase, followed by tumor resection then commenced and lasted 110 minutes. Thereafter, general anesthesia was reinstituted, this time with sevoflurane through the supraglottic airway. At the end of the procedure, the patient was awakened. She was discharged the following day.

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Post-test

1. **Glioblastoma are:**
   a. Usually genetically determined
   b. Linked to cell phone use
   c. Perhaps caused by viruses and linked to the anopheles mosquito
   d. Caused by smoking

2. **Glioblastoma:**
   a. Involves glial cells
   b. Accounts for < 5% of malignant brain tumors
   c. Represents the least prevalent form of primary brain cancers
   d. Is a single variant tumor

3. **Astrocytomas:**
   a. Are pathologically the same as GBMs
   b. May develop into GBMs
   c. Display hyperplastic blood vessels
   d. Are surrounded by anaplastic cells

4. **A true statement regarding GBMs:**
   a. Metastases are frequent
   b. Formation is in the gray matter
   c. Growth is generally slow
   d. Tumors may become large before symptoms develop

5. **Prophylactic seizure medication:**
   a. Is probably not indicated in 60% of patients
   b. May result in Stevens-Johnson syndrome when combined with radiation
   c. Is prescribed for the majority of patients
   d. All of the above
6. **Awake craniotomy:**
   a. Is a totally new concept
   b. Generally is not tolerated
   c. Requires close communication between surgeon and anesthesiologist
   d. Should not be used for mapping procedures

7. **During preanesthetic assessment prior to asleep-awake-asleep craniotomy:**
   a. Explanation to and cooperation from the patient are essential
   b. Anxiolytic agents should never be used
   c. Patients who need reading glasses should be excluded
   d. A seizure history is a contraindication to the technique

8. **Complications of awake craniotomy are most likely to include:**
   a. Seizures and a leaking supraglottic airway
   b. Nausea and vomiting
   c. Bradycardia
   d. Hypertension

9. **Techniques for asleep-awake-asleep craniotomy include:**
   a. Dexmedetomidine infusion
   b. Remifentanil infusion
   c. Propofol infusion
   d. A combination of the above

10. **Monitors during asleep-awake-asleep craniotomy are least likely to include:**
    a. Temperature
    b. Non invasive blood pressure
    c. ETCO2
    d. Arterial cannulation