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AWAKE SURGERY FOR A PRIMARY BRAIN TUMOR: THE FIRST TIME IN CROATIA

Abstract: Awake brain surgery has been approved as a safe and effective operative procedure with the goal of maximal tumor resection and preservation of neurological function.

This case report presents the first awake primary brain tumor surgical procedure performed in Croatia.

Key words: *awake surgery, brain tumor, primary motor cortex, anesthesia, craniotomy*

INTRODUCTION

In comparison with operations under general anesthesia, operations in the eloquent areas of the brain in an awake patients provide greater security in neurological function preservation when preforming the maximum tumor resection (Chacko 2013 Perreira 2009 Peruzzi 2009 Sacko 2011). In addition, the operations in awake patients provide a more accurate localization of the eloquent brain areas and allow for a more precise determination of the safe tumor resection plane. Functional brain mapping is associated with neurological deterioration after the operation. Therefore, when performing a surgery of tumors in the eloquent areas, the use

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of functional brain mapping and continuous neurophysiological monitoring is required (Kim 2009, Shinoura 2005, Shinoura 2013).

Brain tumors in eloquent areas include tumors close to the speech and motor areas. There are many studies that describe the results of operations in awake patients with brain tumors near the speech area, but a relatively small number of papers describe the results of operations in awake patients with brain tumors near the eloquent motor areas (Bello 2007, Shinoura 2011).

The authors of this article want to share their experience of the awake brain tumor surgery. This operation, the resection of the primary brain tumor in the patient's motor area was performed for the first time in Croatia by our team of experts in neurosurgery, anesthesiology and neurophysiology.

CASE REPORT

A 47-year-old man suffered from partial motor seizures since the age of four. The seizures consisted of tonic muscle contractions of the right hand and forearm with the spreading to the neck muscles, and occasional secondary generalization. In a postictal state the patient reported loss of strength in his right hand, but he did not report any speech disturbances. Seizures persisted despite the anti-epileptic therapy. The multi-layer computed tomography (MSCT), MSCT angiography, and magnetic resonance imaging (MRI) have shown the presence of intracerebral tumor in the primary motor cortex (M 1) in the left precentral gyrus – Broadmann area 3. The dimensions of the tumor were 3 x 3 x 2,5 cm. The tumor was located subcortically: in the T 1 MRI weighted images it appeared hypointensive; in the T 2 weighted image it appeared hyper intensive. After the contrast administration the tumor enhancement was observed. (Figure 1) Radio morphological findings indicated it was a primary low grade tumor. Functional magnetic resonance imaging (fMRI) and MR tractography (MR DTI) have not been made.

The patient and the family were proposed to consider the awake brain tumor operation; they were informed about the advantages and risks of the mentioned operation, and have agreed to the procedure.

The neuropsychological assessment of the patient was conducted, and the psychologists from our medical team have confirmed that the patient is mentally prepared to undergo the awake brain surgery. The patient has passed the standard preoperative anesthetic examination with emphasis on the assessment of the airway, the degree of anxiety, pain tolerance, and present neurological deficit.

In premedication, the patient has received an antiepileptic drug (phenobarbital) and a hypnotic drug (midazolam). Upon entering the operating room he has been put under the standard surveillance and monitoring procedure: electrocardiogram (ECG), oxygen saturation (Sp 02), end expiratory C 02 (etC 02), non-invasive and invasive blood pressure, two peripheral intravenous lines, BIS (Bispectral Index) monitoring and urinary catheter. Additional equipment was prepared in the operating room (fiber optic bronchoscope, Bonfils, videolaringoscope). After setting up a standard neurophysiological monitoring equipment, the patient was monitored by our neurophysiological team.

During the preoperative preparation of the patient, he received intravenous antibiotic prophylaxis (cefazolin 1 g), antiemetic (ondansetron 4 mg and 8 mg dexamethasone), anti-ulcer prophylaxis (50 mg of ranitidine) and antidematose therapy (furosemide 10 mg of mannitol and 20% 125 mL). A combination of 20 mL of 0.5% bupivacaine and 10 mL of 2% lidocaine with the addition of epinephrine 1: 300,000 was used as a local anesthetic. When administering a local anesthetic a possible toxicity should be considered and the maximum dose calculated according to a patient's body weight. Adding epinephrine to the local anesthetic reduces the systemic absorption of the local anesthetic, extends the length of the anesthesia and reduces bleeding at the site of the surgical incision. This mixture of anesthetic and epinephrine was locally injected to the sites of Mayfield frame pin installation, and the patient was placed in the most comfortable position.

The application of the local anesthetic in the incision area followed. The incision was placed in the left frontoparietal area. The skin flap was formed and a left – frontoparietal craniotomy was performed. The operation was performed with the help of neuronavigation device. After opening the dura, the surface of the brain has been exposed. With the aid of neuronavigation we confirmed the exact position of the central sulcus, precentral gyrus (M 1) and postcentral gyrus (S 1) (Figure 2).

During the operation we conducted a multimodal intraoperative monitoring: bilateral somatosensory evoked potentials (SSEP) of the median nerve, electroencephalography (EEG) and electrocorticography (ECoG). Motor evoked potentials (MEPs) were obtained by direct cortical stimulation. Cortical stimulation mapping was conducted using a bipolar Penfield stimulation tehnique; of the duration of 1 ms with the interstimulus interval (ISI) of 20 ms (50 Hz); the intraoperative subcortical stimulation of corticospinal tract was performed by a newer „short train of stimuli" (STS) technique of stimulation, using a short series of 5–9 monopolar cathode ray pulses of the duration of 0.5 ms (ISI = 4 ms, 250 Hz).

Upon detection and confirmation of the central sulcus by the neuronavigation device and neurophysiological „phase reversal" technique, we performed the stimulation of the motor cortex area („functional cortical mapping"). Cortical tonic motor responses for the right hand, forearm, upper arm and shoulder were registered with the lower stimulation threshold of 4.5 mA. During cortical mapping the patient was performing the motor tests: flexion and extension of the fingers of his right hand, abduction and adduction of his right thumb, extension and flexion of the elbow of the right hand, and raising his right hand in the shoulder. In the mute motor cortex area the cortex incision (corticotomy) was performed. The tumor was found subcortically, at the depth of 5 mm, It had relatively clear borders to the surrounding normal brain tissue.

The tumor was removed with the ultrasonic aspirator (CUSA). During the tumor removal the patient was continuously performing the motor tests described above. Additionally, the sub-cortical stimulations were carried out to identify eloquent white matter. At a depth of 2.5 cm, while removing caudal and medial edge of the tumor, the patient reported a weakening of the strength of the right thumb abduction and adduction, but after completion of the hemostasis within the tumor lodge, the patient noted recovering of the motor strength and skills in his right thumb. After the tumor removal, neurophysiological motor and sensory potentials were preserved. Electrical stimulation, intraoperative controlled EEG and ECOG, did not cause any form of epileptic activity. The closure of the operating wound was well tolerated by the patient. Remifentanil and propofol were used as analgosedative agents. Both drugs are administered via Target Controlled Infusion (TCI) pumps, which allowed for the fine titration of the drugs. Remifentanil was included after setting up the neurophysiological monitoring; Ce 0.5 – 3 NG / ml, and it was administered throughout the entire operation. Propofol was administered prior the setting up the Mayfield 's frame, Ce 1–2 mcg / mL, and discontinued at the beginning of the incision of the dura to keep the patient completely awake for intraoperative mapping. At the beginning of the wound closure, propofol was administered again, and it lasted until the end of the procedure. Before remifentanil discontinuation, the patient has intravenously received 1 g of paracetamol and 0.05–0.1 mg / kg morphine for post-operative analgesia. After the operation the patient was placed in the intensive care unit for the period of 24 hours. Within 48 hours the patient underwent magnetic resonance imaging (MRI) with the application of the contrast. MRI showed no signs of the residual tumor. Histopathological diagnosis was diffuse astrocytoma. Follow up MRI after three and nine months, showed no evidence of the tumor process (Figure 3). The patient was free of seizures and uses reduced dose of antiepileptic therapy.

DISCUSSION AND CONCLUSION

Awake brain surgery is used on patients with pharmacologically resistant epileptic seizures and in patients with tumors in eloquent areas of the brain. Awake patient operation is the standard procedure for determining the functional brain areas (Berger, 1992, Berger 1995). The development of the technology and anesthetics has enabled the development of the awake brain surgery (Sanai 2008, Danks 2000, Taylor 1999). Different combinations of sedation, analgesia and anesthesia techniques are described in the literature as possible choices for brain tumor surgery in awake patients (Costello 2004, Sarang 2003 Mannii 2006, Hans 2007, Hansen 2013). There is no consensus on the best anesthetic protocol. Anesthesia techniques for awake craniotomy are: monitored anesthesia („Monitored Anesthesia Care-Mac”) and different types of general anesthesia – asleep-awake-asleep and asleep-awake technique. Propofol and remifentanil are the most used drugs for all types of anesthesia for awake craniotomy (Hans 2000). We chose monitored anesthesia (MAC) technique for our awake craniotomies (Zorzi, 2008, Picconi 2008). As defined by the American Society of Anesthesiologists, MAC is a specific anesthetic protocol that includes the monitoring and maintenance of vital functions. During the MAC technique, the anesthesiologist uses sedatives, analgesics and hypnotics, solves all clinical problems, and provides psychological support to the patient during the operation. The main difference between MAC and other anesthetic techniques is that the patient is breathing spontaneously and that there is no airway manipulation. Good ventilation monitoring, airway access, emergency planning and the management of the difficult airway, make this technique safe and effective. The anesthesiologist is ready at all times to convert to general anesthesia if necessary.

Today, the awake brain surgery is considered a viable alternative to surgery under general anesthesia (Taylor 1999 Serletis 2007). That was confirmed by Sacko et al. in their study of 575 patients, comparing the results of tumor operations in eloquent brain areas in awake patients and in general anesthesia. They found that the neurological functional outcome and the degree of tumor resection were better in patients who were operated awake (4). Duffau et al. have shown that even the patients with low grade gliomas who were, primarily operated under general anesthesia, and in relapse/residual tumor surgery re-operated awake, had better neurological functional outcome and a higher degree of tumor resection (DeBenedictis 2010). Nevertheless, the usefulness of the information obtained from the patients undergoing functional brain mapping while awake is still a matter of discussion (Taylor 1999 Serletis 2007, Khu 2010).

This especially applies to the interpretation of the findings of the so-called negative response to stimulation of eloquent areas. The absence of response to stimuli does not necessarily mean normal neurologic outcome after surgery. Bernstein et al. in their study listed 13% of new neurological deficits after the awake brain surgery, while Duffau in his work noted that 6.5% of patients operated awake had a new neurological deficit, compared to 17% of patients operated in general anesthesia (Serletis 2007 Duffau 2005). Other adverse aspects and complications of awake brain tumor surgery include loss of co-operation in patients, intraoperative epileptic seizures, brain edema, vomiting, air embolism and so called motor neglect.

To prevent the loss of patient cooperation, a strict preoperative patient selection is required and compliance to a detailed anesthesiological protocol (Carabba 2008). Intraoperatively, the epileptic seizure can be prevented by using the preoperative antiepileptics; in the case of epileptic seizures during the operation, a seizure can be predicted by monitoring EEG and is dealt with by pouring a cold solution of ringer lactate onto the brain surface; the administration of drugs is rare. Air embolism is uncommon complication since the sitting position is avoided in awake craniotomy. Vomiting is prevented by using antiemetic drugs before surgery. In the case of the motor neglect (complete absence of patient's response to the direct stimulation of the motor cortex) an indirect motor monitoring is applied – the monitoring of motor evoked potentials. In our case, the patient underwent a successful surgical procedure without intraoperative complications.

From a psychological point of view, as reported by our patient, the procedure was not experienced as a traumatic experience. Later on, the patient stated that he did not remember the most of the operation. This is in line with other studies in which authors discuss that there are patients who are completely amnestic of the procedure (Danks 2000, Manninen, 2006, Whittle 2005). Tumor operations in eloquent areas of the brain with the indirect surveilance, using motor and sensory evoked potentials, are used routinely at the Department of Neurosurgery of The Clinical Hospital Center „Sestre Milosrdnice", Zagreb. A multidisciplinary team consisting of a neurosurgeon, anesthesiologist, neurophysiologist and psychologist facilitated the introduction of the awake brain tumor operation as a new operating procedure in the Republic of Croatia to achieve the maximum resection of brain tumors and improve neurological outcome.

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