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From: **MUHAMAD THOHAR ARIFIN** thohar@fk.undip.ac.id
Subject: Bali Med J Submission
Date: 02 July 2020 . 6 .43
To: Editor Bali Medical Journal editorbalimedicaljournal@gmail.com

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Dear Chief Editor BMJ,

Enclosed is our manuscript entitled "Awake craniotomy procedure for near eloquent cortical area for brain tumour case series: initial experience and the anaesthetic challenges"

We believe that this report and the published data we reviewed would be of interest to readers of Bali Medical Journal and hope that our manuscript will receive favorable consideration for publication.

Thank You
Muhamad Thohar Arifin

Awake Craniot...al.docx

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Bali Med J Submission ID-1916

2 pesan

Editor Bali Medical Journal <editorbalimedicaljournal@gmail.com> 24 Juli 2020 19.49
Kepada: thohar@fk.undip.ac.id

Dear M Thohar Arifin

Thank you for submitting your precious work entitled "**Awake craniotomy procedure for near eloquent cortical area for brain tumour case series: initial experience and the anaesthetic challenges"**

As per our reviewer suggestion, we have spot some point for manuscript improvement.

1. Please fill the conflict of interest form that we sent in the attachment below
2. Mention any limitation of the study, since current study only a case series.
3. Regarding the figure 3, there are some untranslated word and unknown abbreviation (lesi, S, M, please add figure complete abbreviation).
4. Please try to use grammar check software for vocabulary (e.g smokey, ginger, grammarly) enhancement and reduce any kind of mistyping.

Looking forward to hear form you soon

Best and regards

Managing editor Bali Medical Journal

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MUHAMAD THOHAR ARIFIN <thohar@fk.undip.ac.id> 27 Juli 2020 13.43
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Awake Craniotomy Procedure for Near Eloquent Cortical Area for Brain Tumour case series: Initial Experience and the Anaesthetic Challenges

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Abstract

Introduction

The main objective of the surgical procedure is to achieve maximum resections with minimal functional neurological deficits for the patient with intrinsic tumours near the eloquent cortical area. The awake craniotomy procedure is currently the key option for achieving optimum safe resection. We report our two years of experience in establishing an awake craniotomy in the Kariadi General Hospital, evaluating the adoption of the technique and the outcome of the surgery.

Methods

This is retrospective study analyzed data from all patients medical record, who were performed an awake craniotomy from January 2018 to January 2020 at the Dr Kariadi General Hospital/Diponegoro University. The specific anaesthesia technique designated for this procedure was adopted. Sonography was introduced to determine the border of the tumour before and after surgery. Phase reversal using cortical grid was used to recognize the central sulcus, motor and sensory cortex. Cortical stimulation using a monopolar stimulator was used to recognize the eloquent region surrounding the tumour. Enbloc resection was done with a fully conscious patient as well as with careful neurological testing during surgery.

Result

The pre-operative Karnofsky Performance Status (KPS) mean was 63, with remarkable improvement to 70. The length of surgery was varying from 120 to 420 minutes with mean was 270 min. Our procedure was done for tumours situated in the Broca area in 3 cases, motor gyrus in 7 cases and premotor gyrus in 3 cases. None of the patient needed intensive post-operative care. Pathological findings show glioma in 9 patients, metastases in 3 patients and tuberculoma in 1 patient.

Conclusion

Based on our experience, Awake craniotomy is a technique designed to preserve eloquent cortex and improving our knowledge of the functional structure of brain centres. Together with the neurosurgeon, neurophysiologist, neuroanaesthesia and OR nurse team, these advanced neurosurgery procedures can be performed without hesitation in developing countries.

Key Word : awake craniotomy, eloquent cortex, functional brain centres

Introduction

Surgical procedure for intrinsic tumours near the eloquent cortical area aims to obtain maximum resection with minimal functional neurological deficits for the patient. To obtain maximal safe resection in the eloquent area of the brain, the awake craniotomy procedure is currently the main choice.[1] Awake craniotomy has become more commonly used worldwide, but it is still new in our country. This approach is one of entity of safe neurosurgical procedure for the lesion on the eloquent area. As a considered advance neurosurgical procedure, it requires rather complicated pre-operative as well as intra-operative preparation.[2]

Intraoperative cortical stimulation has been used by Foerster since 1930 and then later by Penfield and colleagues.[3] Recently intraoperative cortical stimulation has been adopted to the identified eloquent cortical area in the brain. Cortex area of the brain will evoke a certain response during stimulation.[3] Currently, awake craniotomy and intraoperative monitoring were used as standard procedure for the near eloquent cortical area to achieve maximal safe resection.[1,2,5] Many neurosurgical centres with limited resource have been practising this complex neurosurgical procedure.

We are retrospectively reporting our two years' experience of establishing awake craniotomy procedure in Kariadi General Hospital evaluating the adopting technique and surgery outcome.

Method

Patient selection

This study involved an analysis of data from all patients medical record, who were performed awake craniotomy from January 2018 to January 2020 at the Department of Neurosurgery Dr Kariadi General Hospital / Diponegoro University. Starting in 2018, Dr Kariadi General Hospital Medical Centre launched its first intraoperative monitoring unit to develop more advanced and safe neurosurgery procedures. Patients who performed the procedure were patients with tumours near the eloquent area of the brain based on pre-operative MRI. We define the eloquent cortex is speech area on the dominant hemisphere and motor area on both hemispheres.

The speech function in patients which the tumour nearby the Broca area was analyzed by neurophysiologists by examining the names of objects, remembering, counting, fluency in the language, reading and writing before and intraoperatively. Currently, awake craniotomy procedure is accompanied by brain mapping of the eloquent cortex become the gold standard procedure to increase the maximal functional of resection.

Our surgery procedure was performed to achieve maximal brain tumour removal with minimal risk of permanent post operative neurological deficits.[5] In advanced neurosurgery centres, intraoperative MRI is complementary to this procedure. Intraoperative sonography was routinely used in our centre due to lack of intraoperative MRI. Intraoperative sonography (General Electric) was used routinely to achieve the maximally resection.[6]

Cortical and Subcortical Stimulation

Before tumour resection is performed, the patient is woken up, and then the neurophysiologist and neurosurgeon will communicate with the patient. Patients are asked to perform tasks verbally and visually to analyze the ability to speak during stimulation. The existence of dysnomia interrupted speech or difficult speech will be noted.

Continuous Monitoring of Transcortical MEPs by Direct Cortical Stimulation

Transcortical monitoring was performed to detect compound muscle action potentials (CMAPs), several muscles on the contralateral side of the lesion was monitored using 27-gauge bipolar subdermal needle electrodes. We monitor abductor pollicis brevis muscle and deltoid muscle for upper extremity, quadriceps femoris muscle, anterior tibialis muscle and gastrocnemius or lower extremity. Cortical stimulation was performed every 8-10 mm with repetitive biphasic square-wave alternating polarity currents (pulse width, 0.2 msec; frequency, 50 Hz; duration, 1–2 seconds). To detect seizure and after-discharge, we monitored with continuous digital electrocorticogram.[4,7] Cortical stimulus starts from 2 mA and steadily increased 1mA until electrocorticogram abnormality was noted (maximum stimulus intensity was six mA (biphasic current; 12 mA). The duration of the stimulus on the brain surface is 2 seconds each time. Generally, 4-6 mA was the maximal stimulus for speech area and ten mA for the motor area.

In patients with identified speech areas, a safe resection limit is 1-2 cm from the talking area. In the motoric area, the resection limit that has been identified is closer to 0.5 cm. Resection is stopped when there is total speech disturbance but can be continued if within 5 minutes language skills improve.

Anesthesia Procedure

All patients were then treated with 0.25% Bupivakain and 5 µg / ml of adrenaline in a scalp block mixture. Subcutaneous administration was performed at six sites on either side of the scalp. The participating nerves included the super-orbital nerve, the supratrochlear nerve, the auriculo-temporal nerve, the zygomaticotemporal nerve, the occipital nerve (larger) and the occipital nerve (lesser). [8,9]

All patients were subject to blockage at all six sites of scalp nerves. Oxygen at 3 l / min was initially supplied by nasal prongs, Dexmedetomidine infusion as initiated sedation started before the scalp block procedure at a dose of 1.0 µg / kg for 20 minutes (loading dose) followed by 0.2-0.7 µg / kg / h (maintenance dose). Fentanyl in small dose (25 µgr – 50 µgr) bolus, was prepared when the patient response to pain stimuli. Target Controlled Infusion (TCI) propofol was prepared as backup sedation in all cases where the patient was restless and agitated.[8]

The goal of the sedation was to obtain an OAAS of 2 (response only after moderate prodding or shaking) of 3 (responds only after a name is spoken loudly, or repeatedly, or both) for scalp blocks. Throughout the block, blood pressure (BP), heart rate (HR) and oxygen saturation were stable. Dexmedetomidine was maintained during cortical mapping and stimulation at the lowest dose (0.2-0,4 μg / kg / h). Speech, sensory and motor cortical areas have been mapped by cortical electrical stimulation and evaluated by EMG and clinical response. Communication with the patient was maintained throughout the assessment. All patients were comfortable during surgery without any worsening of their neurological deficits. All tumours were successfully removed while patients were in an arousable and cooperative state. All haemodynamics parameters were stable throughout the operation. During the closing stage, the sedation deepened again.[9]

Surgery procedure

The patient's head was positioned using a Mayfield headframe with a suitable position, mainly supine with a slight bending. (Figure 1) Skin incisions are made in a number of ways determined by the location of the tumour followed by craniotomy and dural opening, and we identify the Rolandic portion then a 6-contact titanium electrode strip is placed. (Figure 2). The median nerve then stimulated, identifying the central sulcus and precentral gyrus with somatosensory evoked potential (SSEP) phase reversal. The functional mapping of the motor cortex is then performed using the Caldwell© stimulator. Identification of eloquent cortical area was made, then strip electrode and the margin of the tumour were placed. We adjust the strip electrode to achieve maximal CMAPs of the target muscles with a threshold of 30 mA or less.

A strip electrode is used to track the continuous MEP (stimulation train, 5; frequency, 500 Hz; pulse length, 0.5 msec) during tumour removal using a neurophysiological monitoring system (Caldwell). During tumour removal, we monitor the motor trajectory through the resection cavity with subcortical stimulation.6 Each eloquent cortical area was stimulated at least two times.

Our surgical procedures are carried out to achieve maximum removal of brain tumours with a minimum risk of permanent neurological deficits after surgery. Intraoperative sonography (General Electric) is used routinely to get the maximal resection. Maximum brain removal was defined by visualization of T1-weighted contrast-enhanced MRI for tumours with a ring enhancement suspected to be grade IV gliomas and elimination of the region identified by signal hyperintensity of T2-weighted MRI for non- or partially contrast-enhanced tumours suspected to be grade I, II or III gliomas. Histopathological diagnosis of tumours was based on the previous criteria of WHO in 2007.10

Intraoperative electrostimulation technique

By the time of electrostimulation of the brain aimed at direct identification of cortical speech centres, the patient must be awakened out of anaesthetic sleep. Further, stable verbal and psycho-emotional contact should be established with the patient.11 Cortical area remote from tentative Broca's and Wernicke's area should be selected to adjust electrostimulation current. After current adjustment, the mapping itself should be carried out. The entire opened surface of the cerebral cortex should be consistently studied starting from the supposedly "silent" regions to the functional areas. When detecting errors in test execution during intraoperative neuropsychological testing, the procedure should be paused, and then stimulation should be repeated 1—2 times in the area identified as a cortical speech centre. Cortical speech areas identified using direct electrical stimulation should be marked with sterile paper (cellulose) labels with numbers. Seizure activity of the cerebral cortex should be monitored during the entire electrical stimulation procedure. In the case of readiness for convulsions, electrical stimulation of the brain is stopped, and surgical wound is irrigated with prefabricated cooled saline solution, and intravenous anticonvulsants are administered, if necessary: sodium valproate or levetiracetam. Electrical stimulation of motor areas of the cortex is carried out either during the search for cortical speech areas, or, additionally, cortical motor centres in the case of anatomical spread of space-occupying lesions in the direction of the motor cerebral convolutions.12 The areas of the motor cortex are also labelled with numbered cellulose piece. (Figure 3.)

Ethical clearance

This research was approved by the institution review board of Kariadi General Hospital, in accordance with the Helsinki declaration. Prior written informed consent was obtained from all patients. For patients under the age of 18 years, informed consent obtained from a parent and/or legal guardian.

Result

We already performed awake craniotomy in 13 patients from January 2018 to January 2020 at Kariadi General Hospital Semarang. In our centre included ten male patient and three females, with a range of age between 29 - 60 years old. In all cases, diagnosis pre operative was done based on multimodal 1,5 Tesla MRI, which included pre- and post contrast T1-weighted, T2-weighted and fluid-attenuated inversion recovery images (FLAIR). Pre-surgical consideration was made on eloquent brain area.

Awake craniotomy procedure was performed on the left side in 911 cases and on the right side in 2 cases. The awake craniotomy procedure in this study was 50 per cent for the eloquent motor cortex (7 cases), 3 cases for the Broca area and 3 cases for the premotor gyrus. The median length of surgery for the waking craniotomy procedure was 270 minutes, with a range between 120 and 420 minutes. (Table 1.)

Awake craniotomy improved the Karnofsky Performance Score, the mean pre-operative KPS was 63 ± 5, and the post-operative KPS was 70 ± 6. The findings of the histopathological analysis included 3 cases of high-grade glioma, 6 cases of low-grade glioma, three patients with metastatic tumour and one patient with tuberculoma. In this study, one patient who died five days after surgery was reported according to the above data. (Table1.)

Discussion

The anaesthetic management objectives of awake craniotomy are to facilitate patient cooperation, maintain general homeostasis and reduce interference between anaesthetic agents and the quality of the electrophysiological recording.[12] It creates unique sedation that acts in subcortical regions similar to natural sleep without respiratory depression. This does not interfere with electrophysiological monitoring and thus enables brain imaging during awake craniotomy.[9,13]

Evoked potential technique aimed at somatosensory and motor mapping is widely used in the past decade. However, the reliability of this method with respect to the localization of Rolandic fissure is not optimal; the accuracy of this method is 91 to 94%. In addition, the phase reversal procedure makes the position of the Rolandic fissure easier to find and does not provide details on the distribution of motor functions in the surrounding areas under surgery. The total sensitivities and adverse effects are calculated at about 96% and 79% respectively.[14] Although the motor evoked potential technique has been improved, it enables evoked potential recording only in monitored muscles but does not allow detection and prevention of possible deficit in the muscles not subject to monitoring. Monitoring of motor evoked potentials does not include the assessment of complex movements and voluntary movements, which are the ultimate goal of the patient's physical activity. A further limitation of this method is that it cannot be used to monitor speech functions, memory, and other higher brain functions, which are of key importance for patient's quality of life.[15]

After bone removal, sonography was used to identify the location and the border of the tumour to determine the appropriate incision for dura mater. After dura mater opening, strip electrode for direct corticography is placed. Participation of neurophysiologist, neuroaneasthesist and neurosurgeon is key for this procedure. Direct identification of cortical speech area, motoric or sensory area was done using electrostimulation.15 Intraoperative electrostimulation mapping provides pre-operative real-time detection of the location of functional areas and facilitates the choice of the best surgical approach of tumour resection within these areas. Another important task is mapping of the subcortical structures along with an examination of the cortex prior to resection. Brain damage studies suggest that damage to the pathways is followed by the development of more severe neurological deficits than in the case of cortex injury.[15]

Enforced supporting equipment included the intraoperative monitoring unit, the headframe and the rest were the standard neurosurgery OR instruments.

Limitations of this study

Methodological rigour and the meticulous performance of the direct electrical stimulation procedure are required to avoid any false positive or false negative results, which could lead to inadequate tumour resection or cause permanent neurological deficits. If all the technical rules are not respected faithfully, inaccurate results will create a false sense of security, which could lead to undesired surgical results and permanent neurological sequelae.

Another limitation, this report is retrospective, no randomization to select the case and does not have a control arm.

Conclusion

Anatomical consideration and pre-operative data (neuroimaging, intraoperative electrophysiological and neuropsychological monitoring), as well as strategies for active surgical intervention, are presented. Awake craniotomy is a technique designed to preserve speech and motor functions and improving our knowledge of the functional structure of brain speech centres, memory, counting, writing, hearing and visual perception and other higher neurological functions.

Funding

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Glossary

Table 1. Characteristic data

Characteristic	No.
Median age in years (range)	46 (29 – 60)
Sex (%)	
Male	10 (77)
Female	3 (23)
Karnofsky Performance Scale (KPS)	
Pre op (Mean ± SD)	63 ± 5
Post op (Mean ± SD)	70 ± 6
Length of surgery	
Range (minutes)	120 - 420
Mean (minutes)	270
Relationship w/ eloquent brain areas (%)	
Broca area	3 (23)
Motor gyrus	7 (53)
Premotor gyrus	3 (23)
Pathology (%)	
Glioblastoma multiforme	1 (7,6)
High-grade glioma	2 (15,3)
Low grade glioma	6 (46)
Metastasis	3 (23)
Tuberculoma	1 (7,6)
Side of the lesion (%)	
Left	11 (84)
Right	2 (15)

Deleted: mean

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Figure 1. Positioning for surgery using headframe Mayfield®

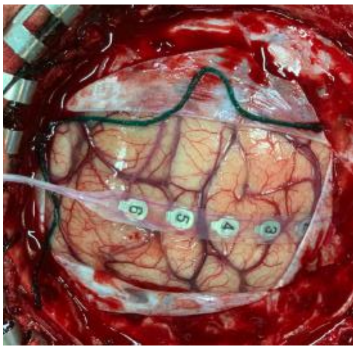

Figure 2. Cortical grid mapping

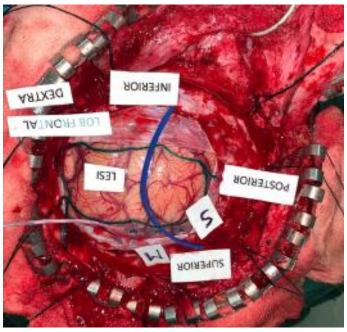

Figure 3. Surgeon view for tumour located on right frontal lobe (abbreviation S= Sensoric gyrus, M= Motoric Gyrus, Lesi = lesion)

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