Case Studies

Continuous Monitoring of Spreading Depolarization and Cerebrovascular Autoregulation after Aneurysmal Subarachnoid Hemorrhage

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Delayed cerebral ischemia (DCI) is a prominent complication after aneurysmal subarachnoid hemorrhage (aSAH). Although vasospasm of proximal cerebral arteries has been regarded as the main cause of DCI, vasospasm of distal arteries, microthrombosis, impaired autoregulation, cortical spreading depolarization (CSD), and spreading ischemia are thought to be involved in DCI after aSAH. Here, we describe a patient with aSAH in whom CSD and cerebrovascular autoregulation were evaluated using simultaneous electrocorticography and monitoring of the pressure reactivity index (PRx) after surgical clipping of a ruptured posterior communicating artery aneurysm. In this patient, a prolonged duration of CSD and elevation of PRx preceded delayed neurological deficit. Based on this observation, we propose a relationship between these factors and DCI. Assessment of cerebrovascular autoregulation may permit detection of the inverse hemodynamic response to cortical depolarization. Detection of DCI may be achieved through simultaneous monitoring of CSD and PRx in patients with aSAH. **Key Words:** Subarachnoid hemorrhage—cortical spreading depolarization—delayed cerebral ischemia—spreading ischemia—vasospasm—cerebrovascular autoregulation.

Introduction

Delayed cerebral ischemia (DCI) and early brain injury induced by initial hemorrhage are major lethal complications in patients with subarachnoid hemorrhage (SAH).[1,2] The risk for DCI correlates with the amount of blood in the subarachnoid space and DCI is presumably caused by erythrocyte products in the subarachnoid space, but the pathophysiology is complex.[3] Delayed vasospasm of major cerebral arteries has been regarded as the main cause of DCI, but chronic vasospasm of distal arteries, microthrombosis, impaired autoregulation, spreading

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depolarization, and spreading ischemia are possible complementary factors in the pathogenesis of DCI.[2,4-9]

Cortical spreading depolarization (CSD) is characterized by near-complete breakdown of ion gradients, near-complete sustained depolarization in individual recordings of neurons, extreme shunt of neuronal membrane resistance, loss of electrical activity, and neuron swelling and distortion of dendritic spines.[5] CSD is observed as a prominent negative slow potential change (SPC) measured in the low-frequency or direct current (DC) range in electrocorticography (ECoG).[10] CSD causes brain electrical silence, which is referred to as spreading depression of brain electrical activity[11] and is observed as a silencing of spontaneous activity measured in the high frequency or alternating current (AC) range in ECoG. CSD is induced by various noxious conditions but can also occur in healthy naive tissue.[5] Resistance vessels respond to CSD by transient hyperperfusion, which is a physiological hemodynamic response (spreading hyperemia) in healthy tissue, but severe hypoperfusion (spreading ischemia, inverse response) due to changes in vascular reactivity in tissue at the risk of cell death from various noxious conditions leads to DCI in patients with SAH.[5,12-14]

The pressure reactivity index (PRx) is a moving correlation coefficient between the mean arterial blood pressure (ABP) and intracranial pressure (ICP) that reflects cerebrovascular autoregulation.[15,16] PRx has recently been reported to be useful for clinical monitoring of patients with severe SAH and traumatic brain injury.[17,18]

We describe a patient with aneurysmal subarachnoid hemorrhage (aSAH) in whom CSD and cerebrovascular autoregulation were evaluated using simultaneous ECoG and PRx monitoring after surgical clipping of a ruptured posterior communicating artery aneurysm.

Protocol of CSD and PRx Monitoring

The present study was approved by Yamaguchi University Hospital, Ube, Yamaguchi, Japan. The research protocol was approved by the Center for Clinical Research, Yamaguchi University Hospital. Informed consent for the study was obtained after a clinical decision had been made to perform clipping surgery.

Placement of Electrode and Microsensor

Clipping surgery allowed placement of a single, linear, 6-pole (platinum) subdural electrode (SD-6P; Ad-Tech Medical Instrument Corp., Racine, WI) on the ipsilateral frontal lobe through craniotomy or via a burr-hole.[13] An intraparenchymal ICP sensor (Codman MicroSensor Basic Kit; Codmann & Shurtleff, Raynham, MA) was placed in the same manner.[19]

ECoG

ECoG was performed continuously in 5 active channels from the 6-pole (linear array) subdural electrode. Electrode 6 served as ground, whereas electrodes 1-5 (sealed brain contacts, 1.0-cm spacing) were connected in a sequential unipolar fashion to a NicoletOne (.016-45.0 Hz) system (CareFusion, Yorba Linda, CA), each referenced to an ipsilateral subgaleal electrode (Disposable Subdermal Needle Electrode; Nihon Koden, Tokyo, Japan). The DC-ECoG of electrodes 1 and 3 was also recorded using a MT-BA-B3S-R2 (0-45 Hz) system (Melon Technos, Kanagawa, Japan). DC-ECoG was sampled at 200 Hz and recorded and reviewed using a PowerLab 16/SP analog/digital converter, Chart-7 software (ADInstruments, Bella Vista, New South Wales, Australia). ECoG (.016-45.0 Hz) was also reviewed using Chart-7 software (ADInstruments).

PRx Monitoring

Continuous ICP monitoring was achieved using an intraparenchymal ICP sensor connected to an ICP transducer (Codman ICP Express, Codmann & Shurtleff).[19] ABP was continuously monitored from the radial artery using a standard monitoring kit (TruWave; Edwards Lifesciences, Irvine, CA). The ABP sensor was placed at the cardiac level and signals were viewed on a bedside monitor (Life Scope, Nihon Koden). The continuous ICP and ABP signals were sampled at 200 Hz and recorded and reviewed using a PowerLab 16/SP analog/digital converter and Chart-7 software (ADInstruments).

Data Analysis

CSD was defined by sequential onset in adjacent channels of a propagating SPC. SPC is expressed as a negative DC potential change (TrueDC) and can be detected using AC amplifiers (higher frequency limit: .05 Hz, near DC).[20,21] Criteria for SPC detected using AC amplifiers are a bi- or triphasic change in potential with a duration of 2-5 minutes and an amplitude of .06-3.0 mV.[12] CSDs were classified as single or clusters (CSDs with an interval <2 hours).[13,22,23] Simultaneous high-frequency ECoG depression was a priori defined by a rapidly developing reduction of the power of the ECoG amplitude by at least 50%.[21] The duration of the depression period of the high-frequency ECoG activity was measured as the interval between onset of depression and restoration of activity using the integral of the power of the bandpass-filtered activity (bandpass: .5-45 Hz; time constant decay, 60 seconds).[13,20]

PRx was calculated every 5 minutes using a 5-second moving window as a Pearson correlation coefficient between the mean ABP and mean ICP averaged over 5-second periods.[18] The mean PRx for 24 hours was calculated. ECoG and PRx monitoring were started as soon as possible after surgery. We show the association between