Coronary artery spasm associated with blood brain barrier disruption induced by carotid sinus stimulation

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ABSTRACT

Blood brain barrier disruption (BBBD) is a novel technique for treating central nervous system lymphoma. This technique depends on the disruption of the tight junctions between endothelial cells (which represent the blood brain barrier) by intra-arterial injection of mannitol. The most common complications of blood brain barrier disruption are seizures and brain edema. Here, the authors present a rare complication of coronary artery spasm manifested by elevation of the ST segment and bradycardia due to carotid sinus stimulation in a 33 year-old-male during blood brain barrier disruption. To the authors’ knowledge, this is the first report of a coronary artery spasm complicating blood brain barrier disruption.

Key words: Blood-brain barrier - Carotid sinus - Coronary vasospasm.

Despite recent advances in the treatment of malignant brain tumors using standard tools such as surgery, radiation, and chemotherapy, patient outcome still remains discouraging. However, recent studies of targeted drug delivery show promising results. In particular, blood-brain barrier disruption (BBBD) is an established procedure that enhances chemotherapy delivery to central nervous system (CNS) tumors. Many studies have been done in the past few years to compare and optimize different techniques of BBBD, but few reports are published on its complications. Here, we report a case of EKG changes and bradycardia induced by carotid sinus stimulation during a BBBD procedure in a 33-year-old patient with primary CNS lymphoma (PCNSL).

Case description

A 33-year-old male patient with no cardiovascular disorders and a known history of cluster headaches (Figure 1) had experienced a generalized seizure, and was diagnosed with PCNSL of the left frontal lobe. A brain biopsy showed non-Hodgkin’s large B-cell lymphoma. After obtaining patient consent, the patient was started on treatment using an intra-arterial chemotherapy injection with BBBD. The treatment protocol consisted of monthly courses, with each course consisting of two sessions over two consecutive days. During these sessions the patient received 150 mL of mannitol 25% at a rate of 5 mL/sec, injected into the internal carotid artery after femoral artery cannulation in order to induce BBBD. The treatment protocol consisted of monthly courses, with each course consisting of two sessions over two consecutive days. During these sessions the patient received 150 mL of mannitol 25% at a rate of 5 mL/sec, injected into the internal carotid artery after femoral artery cannulation in order to induce BBBD.

This was followed by an intra-arterial injection of 2500 mg methotrexate. The patient completed his first course uneventfully. During the second course, the patient underwent BBBD with an intra-arterial injection of methotrexate through the left internal carotid artery. After the patient arrived at the postanesthetic care unit, the patient was found to have brady-
cardia with a heart rate of approximately 36 beats per minute. An EKG was done, revealing ST segment elevation in the lateral chest leads (Figure 2). Serum levels of cardiac enzymes were drawn and measured four times, and were found to be negative. Cardiology was consulted and serial EKGs were performed. An echocardiogram was done, which showed no regional wall motion abnormality, and eventually the EKG returned to baseline. The patient had no symptoms of shortness of breath or chest pain. Upon completion of the cardiology consultation, it was concluded that the EKG changes were related to manipulation of the central nervous system during BBBD, and no further treatment was recommended. The patient remained neurologically stable and was discharged home the next day with a normal EKG (Figure 3). Following this incident, the remainder of the BBBD treatment was carried out without further complications for the patient.

Discussion

The term “blood-brain barrier” is used to describe the barrier system that separates the systemic circulation from the brain and the cerebrospinal fluid (CSF). There are actually two physical barriers: a blood-brain barrier and a blood-CSF barrier. Although the blood-brain barrier and the blood-CSF barrier are not precisely equivalent, both barriers separate the CNS from immune responses and can affect the composition of the brain interstitial fluid and CSF. Together, this system is responsible for preventing the simple diffusion of fluids, electrolytes, and other substances from the blood to the brain and CSF.1

The blood-brain barrier has a 5000-fold greater surface area than the blood-CSF barrier and controls the content of brain interstitial fluid. The anatomic basis for the blood-brain barrier is a series of high-resistance tight junctions between the endothelial cells of capillaries found in the CNS, in addition to astrocytes with processes that terminate in an overlapping fashion on the capillary walls. Lipid-soluble small molecules with a molecular mass of less than 500-600 Daltons are transported readily through the blood-brain barrier. In contrast, many drugs and other small molecules lacking these properties do not cross this barrier system.2

The treatment of PCNSL has centered on high-dose methotrexate and fractionated radiotherapy (RT). Although the combined modality of chemotherapy and radiation has lead to a dramatic improvement in the prognosis for patients with PCNSL, over 50% of patients relapse and the risk of neurotoxicity (i.e., dementia) approaches 90% in older patients.3 Methotrexate administered intra-arterially with osmotic BBBD without RT, how-
ever, has been demonstrated to be a highly effective treatment, with a 5-year survival rate of 42% without cognitive loss.4

There are only a few complications associated with BBBD, with reported examples such as vasogenic brain edema and orbital pseudotumor. Brain edema following blood brain barrier disruption is present in many cases. According to Starling’s law,
water, ions, and plasma proteins will cross the blood-brain barrier towards the interstitium if the driving forces for the transmural bulk flow are excessive (mechanical origin) and/or if the permeability is enhanced (chemical origin). Both mechanisms coexist in most cases. However, severe brain edema is usually accompanied by increased blood pressure, convulsions, and bradycardia, not by the ST elevation as seen in our case. Also, brain edema is easily diagnosed by a computed tomography (CT) scan and all BBBD patients receive a CT scan after the procedure to evaluate the degree of disruption. In this case, excessive edema was not found.

Orbital pseudotumor is an inflammatory condition of one or more extraocular muscles that produce limitation of ocular mobility. Patients usually experience sudden diplopia associated with orbital pain, conjunctival chemosis, injection, and proptosis.

Here the authors report a case of transient EKG changes and bradycardia associated with BBBD occurring with the left internal carotid artery injection. Although the exact mechanism is unclear, the authors believe these symptoms may be related to coronary artery spasm secondary to carotid sinus stimulation as a result of rapid injection. A similar case of ST elevation was observed and reported by Choi et al., where they reported four transient episodes of marked ST elevation in a 58-year-old man, with no history of coronary artery disease, undergoing resection of a metastatic neck mass under general anesthesia, which was associated with carotid sinus compression and manipulation during surgery.

Conclusions

For the treatment of PCNSL, BBBD is a relatively novel technique that has not yet been fully explored. The authors believe further investigations of this procedure are required in order to report similar cases or other related complications.

References


Received on January 27, 2009. Accepted for publication on March 12, 2009.
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