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Case report

Cryptogenic stroke in the setting of intravaginal prostaglandin therapy for elective abortion

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Abstract

Vaginal prostaglandin pessaries are considered safe and effective method of abortion within the first two trimesters of pregnancy. We present a case of a young woman, with no known risk factors for cerebrovascular events, who developed a cryptogenic stroke following administration of intravaginal Misoprostol.

Case report and review of the relevant literature.

A 30-year-old woman presented with right hemiparesis and aphasia after having received three $600 \mu g$ tablets of intravaginal Misoprostol for an elective abortion earlier in the day. A brain MRI revealed an acute ischemic infarction in the left middle cerebral artery territory. An extensive workup for possible etiologies was negative.

Intravaginal Misoprostol may be associated with stroke in young women. Further study is required to determine if this case represents an isolated incident, or a true association.

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1. Introduction

Vaginal prostaglandin pessaries are considered safe and effective methods of abortion if they are administered during first two trimesters of pregnancy. Although adverse events are associated with their use, to our knowledge there are no reported cerebrovascular side effects [1,2]. The most commonly used vaginal pessary contains a synthetic analog of prostaglandin E1 (Misoprostol), with a reported side effect profile consisting of uterine hyperstimulation, uterine rupture, genital bleeding and amniotic fluid embolism. Other less common side effects from systemic use of Misoprostol include hypotension, arrhythmia, dizziness, thrombocytopenia and purpura [1,2]. We present the case of a young woman, with no know cerebrovascular risk factors, who developed a stroke within 13 h of the administration of intravaginal

* Corresponding author at: Department of Neurology, LAC+USC Medical Center, 1200N State St. Room 5640, Los Angeles, CA 90033, United States. Tel.: +1 323 226 7381; fax: +1 323 226 5869. Misoprostol. A search of the Medline database from 1966 to 2007 revealed only one similar case, reported by Lauren and Berentelg in a German journal [3].

2. Case report

A 30-year-old right-handed Chinese-Vietnamese woman presented to the emergency department (ED) of an outside hospital with right-sided paresis and aphasia of 7 h duration. The patient (gravida 3, para 2) had received three 600- μ g tablets of intravaginal Misoprostol for an elective abortion at 8 a.m. that morning. Gestation was 12 weeks. At approximately 9 p.m. on the same day she developed difficulty with production of speech and right-sided weakness. Her past medical history was significant for a previous elective abortion several months prior to this event. She had no family history of stroke, hypercoagulability, vasculitis, illicit drug abuse or smoking. A non-contrast head CT performed in the ER showed hypodensity in the distribution of the superior division of the left middle cerebral artery (MCA), with

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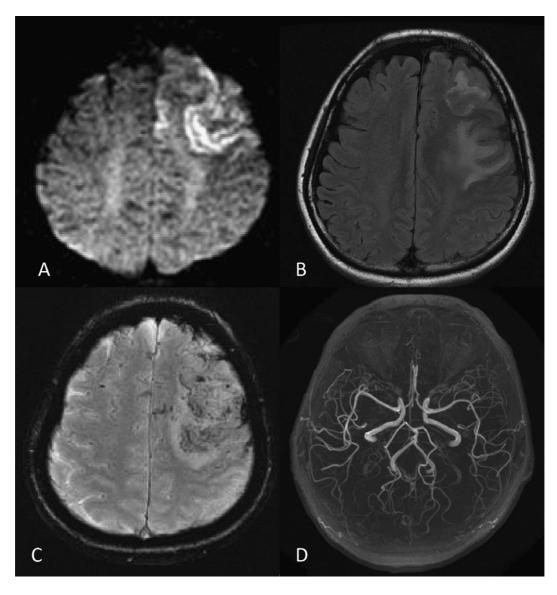


Fig. 1. MRI and MRA of the brain preformed the day after symptom onset demonstrating restricted diffusion in the left frontal lobe on diffusion weighted imaging (A), corresponding area of hyper intensity on FLAIR (B), petechial hemorrhage on gradient echo (C), and normal intracranial MR angiography (D).

sulcal effacement and loss of the gray–white junction. An electrocardiogram and cardiac catheterization were normal. A trans-esophageal echocardiogram showed mild left ventricular hypertrophy, but no evidence of thrombus, valve abnormality or foramen between the chambers of heart. She was transferred to a tertiary-care center for further workup and treatment.

Upon transfer her physical examination was notable for an expressive aphasia and complete right-sided hemiplegia with intact comprehension. A brain magnetic resonance image (MRI) showed acute ischemic infarction in the middle cerebral artery territory (Fig. 1A–C). Intracranial magnetic resonance angiography (MRA) (Fig. 1D), and MRA of the neck and carotid duplex scan were unremarkable. Multiple additional studies were performed to identify stroke and thromboembolic risk factors, including cardiac monitoring, trans-esophageal echocardiogram, and serum tests of hypercoaguability, and vasculitis (including D-dimers, fibrinogen, protein C, protein S, antithrombin III, activated protein C resistance, antineutrophilic antibody, antineutrophilic cytoplasmic antibodies (ANCA), factor V deficiency, lupus anticoagulant, anticardiolipin antibodies, homocysteine, alpha-galactosidase mutation and rheumatoid factor). All were negative.

The patient was in the intensive care unit for 48 h. During this time, continuous cardiac monitoring was conducted. No arrhythmias were noted. She was treated with a standard dose of aspirin during her hospitalization. Over a period of 5 days, there was gradual improvement in her expressive aphasia and arm strength until her discharge to acute rehabilitation. Upon a follow-up visit 2 months later, she demonstrated significant improvement of strength and language.

3. Discussion

Prostaglandins are 20-carbon derivatives of unsaturated fatty acids that are found in almost all organs and tissues and function as hormones in a wide variety of physiological contexts. The prostaglandin family of molecules are designated A-K, with numerical or Greek subscripts further defining key structural features of individual PG family members. Misoprostol is a synthetic analog of PGE1, and is available as oral and intravaginal preparations [1]. Intravaginal preparations are considered safe and effective methods of abortion if administered within the first two trimesters of pregnancy, often prescribed in a regimen of 400 μ g every 3 h to a maximum of five doses [2]. The duration of the biological actions of Misoprostol is 2–6 h.

Prostaglandins are potent vasodilators; increasing peak cardiac output and cerebral blood flow. They also inhibit platelet aggregation [4,5]. These properties are considered potentially beneficial in the setting of ischemic stroke [5]. However, some studies in animals have revealed a biphasic, dose dependent action of PGs, especially PGE1, in which low doses cause vasoconstriction and high doses induce vaso-relaxation [6,7]. This has also been demonstrated upon intracarotid injection and topical application of PGE1 in humans [8].

Prostaglandins also have direct effects in the brain. PGE binds to a family of G protein-coupled receptors, the EP receptors, which are expressed in brain tissue. Stimulation of the EP3 receptor subtype results in enhanced release of intracellular calcium reserves, which activates enzymes such as phospholipase C, phospholipase A2 and neuronal nitric oxide synthase [9]. Activation of these enzymes may lead to cerebral ischemia [9].

It should be noted that the dose of Misoprostol administered in this case was 1800 µg as a one-time dose. Misoprostol is often given in doses up to 2000 µg, in 400 µg increments. The reason this patient received a higher initial dose was not clear, but we suggest that it may have triggered or contributed to her stroke. This possibility is supported by the lack of evidence for any known risk factor, such as reversible cerebral vasoconstrictive syndrome (RCVS), eclampsia, vasculitis or thromboembolic phenomena. Reversible cerebral vasoconstrictive syndrome typically presents with thunderclap headache, seizures, focal neurological deficits and segmental narrowing of cerebral arteries [10]. The absence of these symptoms and the normal MRA argues against RCVS. In addition, the patient showed no evidence of high blood pressure, proteinuria or seizures in her history or during her hospitalization, ruling out pre-eclampsia. Serum markers and clinical signs of vasculitis were also negative.

The only published report of a stroke following PG treatment indicated that prostaglandins can cause ischemic stroke due to their dose dependant vasoconstrictive effects [3]. It is also important to note that myocardial infarctions have been reported to occur upon PGs administration [11–15]. Although a formal diagnosis of cryptogenic stroke was made in the current case, we hypothesize that intravaginal Misoprostol may have provided a trigger for the event. In order to determine whether this case represents an isolated incident, or reflects an increased risk for stroke associated with Misoprostol treatment, requires more extensive studies.

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