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Case report

Critical limb ischemia after accidental subcutaneous infusion of sulprostone

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Abstract

A 34-year-old patient was treated with constant intravenous infusion of sulprostone because of postpartum hemorrhage from a hypotonic uterus. The arm in which sulprostone had been infused was painful 23 h after infusion. A day later, the arm was found to be bluish, edematous and extremely painful as a result of arterial spasm. The vasospasm was probably caused by accidental subcutaneous infusion of sulprostone as a result of a displaced intravenous catheter. A diagnosis of critical limb ischemia was made. Treatment with the prostacyclin-analogue iloprost resulted in full recovery. Critical limb ischemia as a serious complication of sulprostone has not been previously reported.

Keywords: Hemorrhage; Postpartum; Uterotonics; Ischemia; Sulprostone; Iloprost

1. Introduction

Sulprostone is a synthetic prostaglandin E2 derivative that increases muscular tone and is used for termination of pregnancy and for atomic hemorrhage. Several side-effects of sulprostone have been reported, including common ones, such as nausea, vomiting and chills, and more threatening side-effects, such as bronchial spasms in predisposed patients, uterine rupture [1], convulsions in epileptic women [2] and myocardial ischemia as a result of coronary artery spasm [3]. Critical limb ischemia has not previously been reported as a complication of sulprostone treatment.

2. Case report

A healthy 34-year-old, normotensive, non-smoking, black woman, gravida-VIII, para-II was admitted at 33 weeks gestation because of vaginal blood loss. In the past she had two uncomplicated term deliveries, one ectopic pregnancy treated with salpingotomy and four artificial abortions. She had recovered from hepatitis-B infection and had been treated for syphilis. In this pregnancy gestational diabetes was treated with a diet. At 29 weeks, a diagnosis of polyhydramnios was made, with amniotic fluid pockets of 14 cm in diameter on ultrasound examination and a normal fetus. At 33 weeks, 2 days after admission for vaginal blood loss, the membranes ruptured spontaneously and threatened preterm labor was treated with fenoterol in a dose of 1.0 μg·min⁻¹ until 34 weeks gestation. Three days later, at a gestational age of 34 3/7 weeks she developed signs of
an intra-uterine infection with fever, a painful uterus, fetal tachycardia and foul-smelling amniotic fluid and she went into spontaneous labor. Antibiotic therapy (amoxycilline and cefotaxime) was initiated and 2 h later she delivered vaginally of a healthy female infant, 2450 g, with Apgar scores of 8 and 7 after 1 and 5 min, respectively, and an umbilical artery pH of 7.22. The newborn infant was immunized with hepatitis-B vaccine, was treated with antibiotics for several days and did well. Following intramuscular injection of 5 units of oxytocin and controlled cord traction, the placenta was delivered 40 min after the infant and found complete. Blood loss at that time measured 700 ml and 0.2 mg methylergometrine i.m. was given prophylactically. The uterus was normally contracted. Forty minutes later, after a sudden hemorrhage of 800 ml blood, the patient went into shock (blood pressure 70/40 mmHg, heart rate 112 beats • min⁻¹). Volume depletion was treated with 1.0 l colloid solution and uterine atony was treated with uterine stimulants (oxytocin 10 units and methylergometrine 0.2 mg intravenously). The bladder was empty. Under general anesthesia, the uterine cavity was manually checked for retained placental fragments and the vagina was inspected for lacerations and both were found absent. Curettage was performed because the anterior wall of the uterus was slightly irregular, but virtually no material was obtained. Because the atomic hemorrhage persisted, 500 µg sulprostone was given by intracervical injection, followed by intravenous infusion of sulprostone in a dose of 125 µg • h⁻¹ into the cephalic vein of the left arm, and the uterus was packed with gauzes. After a transfusion with six units of packed cells to substitute for a total blood loss of 2.5 l, the patient was hemodynamically stable. The packing was removed after a few hours and sulprostone infusion was discontinued after 23 h. At that time the patient complained of pain and edema of the left hand and the infusion line was removed. The next day the patient complained of an increasingly painful left arm and hand. On inspection the hand and forearm were found to be blueish, edematous and very painful on palpation. Movements of the wrist and fingers were virtually impossible because of the pain. The forearm was cold, pulsations of the radial, ulnar and brachial arteries could not be felt and capillary refill was poor. Doppler examination showed virtual absence of blood flow in the radial and ulnar arteries. Selective angiography of the subclavian artery showed a normal axillary artery. The brachial artery showed marked narrowing and the distal parts of the ulnar and radial artery could not be visualized because of strong vasospasms. The hand was poorly supplied predominantly by the median artery (Fig. 1). A thrombotic mass was not seen. A presumptive diagnosis of arterial spasm, resulting from subcutaneous rather than intravenous infusion of sulprostone, was made. The patient was treated intravenously with the vasodilating prostacyclin analogue iloprost in a dose of 6 µg • h⁻¹ for 6 h per day for 4 days. During this treatment the heart rate and blood pressure were monitored. Apart from mild hypotension and a slight headache, the patient experienced no side-effects from iloprost treatment. About 12 h after the initiation of iloprost treatment the color of the skin of the left arm returned to normal, indicating that the circulation had recovered. Two days after the initiation of treatment the pain had virtually disappeared. With physiotherapy, the arm and hand regained complete normal function and on the twelfth day after delivery the patient was discharged in good condition.

3. Discussion

Sulprostone, a synthetic prostaglandin-E2 derivative, has a range of side effects which include bronchial spasms, uterine rupture and convulsions. Serious cardiovascular side-effects, including acute myocardial infarction attributed to coronary artery spasm, are rare [3]. Adverse vascular sequellae in the form of critical limb ischemia have not been previously reported. Critical limb ischemia is defined as continuous ischemia in a limb, with pain at rest and the imminent prospect of amputation. This serious condition is usually caused by atherosclerosis or rare diseases such as Raynaud's and Buerger's disease [4]. Ischemia as a side-effect of medication is a rare event. In our department at the time of treatment, sulprostone was routinely given in a dose twice of which is currently recommended for termination of pregnancy [5]. Although one cannot exclude a toxic effect of the high dose of sulprostone or of the methylergometrine, or a direct trauma to the artery by the displaced intravenous catheter, we feel that in the

Fig. 1. The angiograms of upper arm (A) and hand (B) show vasospasm of the brachial (1) and ulnar (2) artery, indicated by the arrows. The hand is poorly perfused, predominantly by the median artery (3).
present case critical limb ischemia developed probably as a result of arterial vasospasm caused simply by accidental subcutaneous infusion of sulprostone. The relatively high dose, the prolonged duration of infusion, the measuring of blood pressure on the infusion arm, the relative long biologic half-life of sulprostone (30–45 min according to the manufacturer) and the use of an infusion pump, which can build up a high infusion pressure, may all have contributed to the damage.

Vasospasm can be treated with a vasodilating agent. The prostacyclin (PGI2) analogue iloprost is an important, relatively new, drug. Iloprost dilates the arterioles and venules, increases the capillary density, reduces increased vascular permeability of the microcirculation, inhibits platelet aggregation and promotes fibrinolysis [6]. Although spontaneous recovery from vasospasm may occur without medical treatment, persistent vasospasm in critical limb ischemia may end in amputation. In the present case, the use of iloprost seems to have been beneficial, with rapid improvement of signs and symptoms to complete recovery from critical limb ischemia. However, prevention is better than treatment. Critical limb ischemia can be prevented by taking great care when sulprostone is administered intravenously.

References