

Possible Anaphylactic Reaction to Abciximab

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We report a patient who experienced a severe anaphylactic reaction during coronary artery stenting. Subsequent to administration of a weight-adjusted dose of abciximab, the patient developed profound hypotension and severe, acute airway obstruction. The reaction was successfully reversed with a 16-hr infusion of epinephrine, steroids, and an H1 blocker. *Cathet. Cardiovasc. Intervent.* 48:71–73, 1999. © 1999 Wiley-Liss, Inc.

Key words: platelet glycoprotein IIb/IIIa inhibitor; adverse reaction; stenting; angioplasty; integrin

INTRODUCTION

The use of a monoclonal antibody (MAb) as adjuvant therapy during coronary artery interventions has reduced the rate of death, nonfatal myocardial infarction, need for repeat revascularization, and procedural failure [1,2]. Other MAbs have also been utilized as anti-tumor agents [3]. Their use in these noncardiac indications has been limited, however, by the occurrence of hypersensitivity reactions. Chimeric human-mouse antibodies, such as abciximab (Reopro), were developed in an effort to decrease the antigenicity of MAbs. Other chimeras, such as rituximab, are in development. Although reactions to MAbs are uncommon, fatal hypersensitivity reactions to rituximab have been reported [3].

CASE REPORT

A 58-year-old woman was undergoing stenting for unstable angina. She had a past history of hypertension, hypercholesterolemia, and a cerebrovascular accident. She had also undergone a right carotid endarterectomy some years earlier. At that time she had undergone a cerebral angiogram without adverse reaction. Her medications at the time of diagnostic catheterization included amlodipine, hydrochlorothiazide, atenolol, and atorvastatin. Her only reported reaction to medications was nausea secondary to morphine use. She denied allergies to radiographic contrast, shellfish, or morphine. She had never undergone cardiac catheterization or been given abciximab or other monoclonal antibodies. Her vital signs were normal at the start of the procedure, with a systolic blood pressure (SBP) of 176 mm Hg and heart rate (HR) of 65 beats per minute. Her serum chemistries and complete blood count were normal, with a platelet count of 174,000.

Diagnostic catheterization was uneventful and coronary stenting was undertaken at the same setting. A

weight-adjusted abciximab bolus of 16.4 mg and drip of 8.5 µg/min were administered. Forty-eight minutes had elapsed since initial dye injection. During stent deployment the patient's SBP began to decrease slowly from 170 mm Hg to approximately 120 mm Hg. At the conclusion of the procedure she complained of a headache and mild chest tightness and was given 1 mg of morphine. Her ECG was unchanged and did not show ST segment elevation or depression. Her SBP continued to fall, more rapidly, to a systolic pressure of 64 mm Hg. Approximately 19 min had elapsed since the initial abciximab bolus, and 5 min since the morphine. The abciximab was discontinued. The hypotension was unresponsive to the intravenous administration of 2.5 liters of normal saline and 0.5 mg of atropine. The abciximab was discontinued. She then developed acute airway obstruction, and attempts to ventilate her by mask were difficult. A bolus of epinephrine (0.5 mg intravenous) was administered with dramatic immediate resolution of her airway obstruction. Additional boluses of epinephrine, as well as Solumedrol (150 mg intravenous), Benedryl (25 mg intravenous), and eventually an epinephrine infusion (12.5 µg/min intravenous) were required to maintain her SBP at 100 mm Hg (Fig. 1). She was stabilized and transferred to the coronary care unit (CCU) where she remained dependent on the epinephrine drip to maintain her SBP for approximately 16 hr postprocedure. Her platelet count fell to a low of 68,000 the morning following the procedure. The epinephrine was eventually

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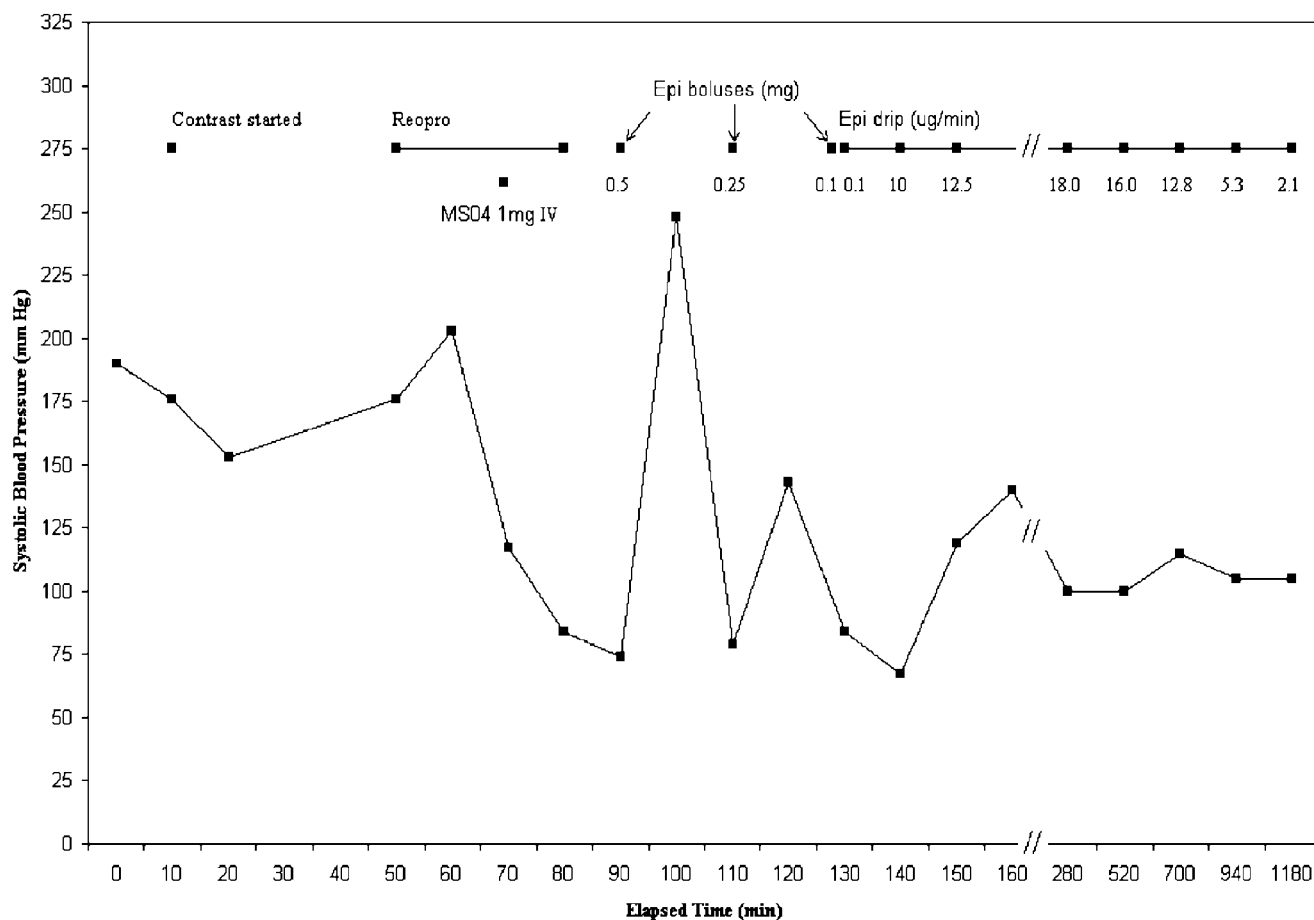


Fig. 1. Time course of systolic blood pressure changes.

weaned and her platelets improved to 123,000 prior to discharge.

DISCUSSION

This case strongly suggests the occurrence of an anaphylactic reaction to abciximab. Reactions to radiographic contrast and morphine are also possible, but these scenarios seem less likely. The patient had received morphine in the past and did not have a history of allergic reaction; she reported only nausea. Allergic reactions to morphine are usually related to histamine release, resulting in urticaria, wheals, and local irritation [4]. The patient had none of these signs or symptoms. However, immediate anaphylactic reactions to morphine analogues have been reported and this cannot be entirely excluded as a causative agent [5]. Furthermore, a synergistic mechanism between morphine and abciximab is also possible.

The radiographic contrast is unlikely to be the inciting agent. Forty-eight minutes had elapsed from the time of initial contrast injection to adverse reaction. Additionally,

the patient had previously undergone a carotid angiogram without any adverse reactions. The hallmark of anaphylaxis is the onset of the syndrome within seconds to minutes after exposure to the inciting agent [6]. Also, case reports of allergic reactions to contrast medium describe the occurrence of the manifestation immediately following exposure [7], and studies have shown biochemical alterations due to contrast occurring immediately after exposure [8]. In this case, the timing of the reaction makes anaphylaxis to contrast unlikely.

Abciximab contains the Fab of the monoclonal antibody 7E3, which was developed to bind the IIb/IIIa receptor on human platelets, thereby inhibiting their aggregation. It is estimated that 445,000 patients have received abciximab [9]. To date, there have been no reported cases of anaphylaxis to either initial or repeated administration of abciximab. Patients have been shown to develop antibodies following treatment with abciximab, such as human antichimeric antibody (HACA) and human murine antibody (HAMA) (personal communication, Eli Lilly Research Laboratories). During phase III of the EPIC, EPILOG, and CAPTURE trials, the develop-

ment of HACA following abciximab was found in a combined total of 5.8% of patients following a single standardized administration [10].

Data regarding the readministration of abciximab to those patients who develop HACA after initial exposure is sparse. A small open-labeled trial of 41 patients with stable coronary artery disease or healthy volunteers was conducted to determine the effect of readministration of abciximab [11]. Twenty-nine of these subjects who did not develop HACA with the initial injection received a second dose of abciximab at 14 weeks. HACA developed in 24% of these patients within 12 weeks of the second injection. Thrombocytopenia occurred in two subjects; one with initial injection in a subject found to have preexisting HACA, and one with reinjection in a patient with a low-level HAMA titer at the time of readministration. There were no reported episodes of anaphylaxis, and other subjects with baseline positive HACA were not similarly afflicted. In the 3-year follow-up of the EPIC trial, those patients who were HACA positive during the initial 12-week monitoring period were studied to assess the rate and magnitude of persistent HACA positivity. Titers persisted in 15 of the 34 available patients (44%) [12]. Taken together, these data support the hypothesis that hypersensitivity reactions or anaphylaxis to abciximab could occur during initial or repeat administration.

The evidence presented implicates abciximab as the primary inciting agent leading to the anaphylactic reaction in our patient. The timing of the reaction, the patient's allergy history, and the constellation of symptoms support our hypothesis. While HACA antibodies develop in some after administration of abciximab, they have not yet been linked to anaphylaxis. The HACA status of this patient is pending. However, the assay is not commercially available and timely measurements on individual patients are not possible.

Awareness to the possibility of an anaphylactic reaction to abciximab may help the interventional cardiologist faced with a similar situation. Any time delay experienced before making the diagnosis of impending anaphylaxis and discontinuing the abciximab could be minimized, and the patient spared severe consequences. Routine measurement of HACA antibodies prior to

readministration of abciximab is currently not practiced. There is presently not enough data to make recommendations regarding routine measurement and subsequent use of alternative medications should the titer be positive. With the increased use of chimeric Mabs, anaphylaxis may increase and allow such protocols to be established.

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