Acute allergic reaction due to the administration of fibrinolytic therapy for ST-segment elevation myocardial infarction: case report and discussion

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ABSTRACT

Although a rare phenomenon, acute allergic reactions to fibrinolytic and heparin therapy have been described in the literature. We report the case of a 63-year-old woman who experienced a severe anaphylactic reaction while undergoing fibrinolytic therapy with tissue plasminogen activator for an ST-segment elevation myocardial infarction. Overall outcome was successful, but patient morbidity was increased because of the reaction and the subsequent therapy administered.

Key words: fibrinolytic therapy, allergic, anaphylaxis, tPA, heparin.

RÉSUMÉ

Bien qu'il s'agisse d'un phénomène rare, les réactions allergiques aiguës à la thérapie fibrinolytique et à l'héparine ont été décrites dans la littérature. Nous présentons le cas d'une femme âgée de 63 ans qui a connu une réaction anaphylactique sévère au cours d'un traitement fibrinolytique à l'aide d'un activateur tissulaire du plasminogène pour un infarctus du myocarde avec élévation du segment ST. Dans son ensemble le devenir de la patiente fut un succès, mais celle-ci connut une morbidité plus importante en raison de la réaction et de la thérapie subséquente.

Introduction

Anticoagulation and fibrinolytic therapy are cornerstones in the treatment of ST-segment elevation myocardial infarction, and emergency physicians are often responsible for obtaining patient informed consent prior to initiating therapy. Informed consent includes an explanation of the possible risks associated with anticoagulation and fibrinolytic therapies — most importantly the possibility of life-threatening hemorrhage. These therapies may cause significant allergic reactions that increase patient morbidity, and this is rarely discussed with patients prior to treatment. The following case report describes an allergic reaction to anticoagulation and fibrinolytic therapy, which is less likely than bleeding but not necessarily less serious.

Case report

A 63-year-old female presented to the emergency department with the chief complaint of retrosternal chest pressure. One day prior to presentation she had returned from a 3-month trip to Asia. While abroad, she was diagnosed

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with angina pectoris and started on a beta-blocker, an oral nitrate preparation and daily entericcoated acetylsalicylic acid (ASA). Her risk factors for coronary artery disease included smoking and a positive family history. Medications included indapamide, perindopril, isosorbide dinitrate, metoprolol, ASA, and metered-dose oral nitrates. She had no known allergies.

On the morning of presentation, she developed 10/10 crushing retrosternal chest pressure that radiated to her neck, occiput and left arm. The pain was transiently relieved by oral nitrate metered-dose inhaler, but returned, lasting approximately 1 hour, prior to presentation. Emergency medical services were called and en route to hospital, administered 160 mg of ASA as well as additional doses of sublingual nitroglycerine, which decreased her pain to 5/10. No morphine or other histaminergic medications were administered in the prehospital setting. Upon arrival, the patient's vital signs included the following: blood pressure 136/68 mm Hg, heart rate 65 beats/min, respiratory rate 18 breaths/min, temperature 36.8°C and oxygen saturation 95% on room air. She was placed on 2L nasal prong oxygen, and intravenous (IV) access was established.

Her physical examination was otherwise non-contributory, and a 15-lead ECG showed marked ST-segment elevation in leads II, III, and aVF, as well as T-wave inversion in leads V4 through V6. After establishing informed consent, the patient received tissue plasminogen activator (tPA) with concurrent IV unfractionated heparin (UFH). The tPA (1 mg/mL) dose was given as a 15-mL IV bolus over 2 minutes followed by 50-mL continuous infusion over 30 minutes, followed by 35-mL continuous infusion over 60 minutes. At the same time as the tPA, intravenous UFH was given as a 5000-unit bolus followed by an infusion of 1000 units per hour (20 000 units in 500 mL D5W, running at 25mL/h). Intravenous nitroglycerine was also administered for the treatment of ongoing chest pain.

Within 20 minutes of the UFH bolus, and within 10 minutes of the tPA bolus (30 mg total tPA administered), the patient developed a pruritic rash on her upper trunk and extremities. Soon after the eruption of the rash, the patient began to complain of difficulty breathing and swallowing. At this time, oropharyngeal edema and audible respiratory stridor were noted. Intravenous diphenhydramine (50 mg), ranitidine (50 mg) and methylprednisolone (125 mg) were administered, and the tPA, heparin and nitroglycerine were stopped. The patient's blood pressure fell to 75/63 mm Hg, her heart rate was 90 beats/min and oxygen saturation was 96% on high-flow oxygen. At this time an intravenous 0.9% saline bolus was administered. Audible expiratory wheezing became apparent and was treated with nebulized salbutamol and ipratropium bromide, as well as subcutaneous epinephrine (0.3 mL of 1:1000 solution). Shortly thereafter, the patient's blood pressure and peripheral perfusion improved.

She was modestly sedated with midazolam and fentanyl, and "quick look" laryngoscopy revealed a markedly edematous glottis with Mallampati Class III visualization. Neuromuscular blockade was achieved with succinylcholine, and she was intubated with a number seven endotracheal tube. During the procedure she briefly desaturated to 81% but responded quickly to intubation and 100% oxygen. Her vital signs subsequently remained stable, with a blood pressure no less than 115/64 mm Hg and a heart rate above 80 beats/min. A chest radiograph confirmed endotracheal tube placement and clear lung fields. She was transferred to the critical care unit, and emergent coronary angiography showed 90% occlusion of her dominant right coronary artery. She subsequently underwent angioplasty and right coronary artery stenting, and was extubated within 24 hours. The initial troponin-I of 1.3 µg/L rose to a peak of 6.4 µg/L. The patient was discharged from hospital 4 days after admission.

Discussion

Although a rare occurrence, allergic reaction to the fibrinolytic agents have been described in the literature. Reactions more commonly occur following streptokinase administration[1,2] but have been described with tPA.[3–7] True anaphylactic reactions to tPA are rare, but anaphylactoid reactions occur in up to 0.02% of patients treated for acute myocardial infarction and from 1.5% to 1.9% of those being treated for acute ischemic stroke.[5,7,8]

Anaphylactic reactions have also been described after the administration of unfractionated heparin, but these are rare, with only a few reports cited in the literature.[9–13] The mechanism of heparin-induced allergic reaction is poorly understood but may be related more to preservatives rather than the heparin itself.[14]

In this case, it remains unclear whether the allergic reaction was due to unfractionated heparin or tPA; however, the patient received 4200 units of UFH during the angiography and stenting procedure with no evidence of recurrent allergic symptoms or hemodynamic instability. This heparin re-challenge without adverse sequelae strongly suggests that tPA was the causative agent. The reaction was assumed to be unrelated to ASA because the patient was on daily coated aspirin prior to admission. Although the patient did well, the anaphylactic reaction, its therapy, and

related complications, including transient hypotension, hypoxia, and epinephrine administration, may have increased myocardial workload and ischemic injury.

Conclusion

Although relatively rare, acute allergic reactions to fibrinolytic and heparin therapy do occur and may have significant consequences. These reactions and their potential consequences should be discussed when a physician obtains informed consent.

Competing interests: None declared.

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