Case Report

Anaphylaxis to artesunate?

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Abstract

Artesunate, an artemissin derivative is a highly efficacious and relatively safe antimalarial agent. Common adverse reactions to artemissin derivatives are nausea, vomiting, anorexia and dizziness. More serious but less-frequent toxic effects of artesunate use are neutropenia, anemia, hemolysis, elevated liver enzymes and severe allergic reactions. However, anaphylactic reaction to artesunate is a rare entity. Here, we report a case of anaphylaxis to parenteral artesunate and its successful management in a female patient to whom intravenous artesunate was administered during surgery under general anesthesia.

Keywords: Anaphylaxis, artesunate, intraoperative

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Introduction

Artesunate, an artemisinin derivative is a highly efficacious and relatively safe antimalarial agent. Nausea, vomiting, anorexia and dizziness are the most commonly reported adverse reactions to artemissin derivatives. More serious toxic effects like neutropenia, anemia, hemolysis, elevated levels of liver enzymes and severe allergic reactions have also been reported with artesunate use.[1] Anaphylaxis to artesunate is extremely rare. Here we report a case of anaphylaxis to parenteral artesunate under general anesthesia (GA) and its successful management in a female patient.

Case Report

A 30-year-old 54 kg female presented to us with severe pain in the right elbow and forearm following trauma to the right elbow. Signs of neurovascular compression distal to the site of injury were evident in the injured limb. She had a history of intermittent high-grade fever with chill and rigor and generalized weakness for 3 days. There was no history of any cardio-respiratory abnormality or anaphylaxis to any drug. On presentation, her Glasgow Coma Scale was 15/15 and she was found to have heart rate, blood pressure and respiratory rate of 118/min, 124/72 mmHg and 15breaths/min respectively. She was febrile and appeared anemic, and cardiovascular and respiratory system examinations were normal. Hepatosplenomegaly was evident on per abdominal examination. Her airway examination was normal. Hemogram of the patient showed hemoglobin of 6.3g/dL and total leukocyte count of 14600/cmm. Her serum electrolytes, liver function test, renal function test and random blood sugar were within normal limits. We decided to send the patient's blood sample for parasitological examination as per the clinical presentation (other than those due to trauma). In view of suspected neurovascular compression in the right upper limb a decision to explore the fracture was taken. In the operation theater routine monitors were connected followed by premedication with intravenous (IV) fentanyl (2µg/kg). The patient's trachea was intubated with a 7.5-mm poly vinyl chloride (PVC) cuffed tracheal tube following a rapid sequence induction with standard dosage of thiopentone and rocuronium. Correct placement of the tracheal tube was confirmed and GA was maintained with isoflurane, inj vecuronium and fentanyl.

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The patient had a stable intraoperative course for 1 hour. Mean while, the patient was reported to have Plasmodium falciparum infection(with asexual forms of Plasmodium falciparum in the blood and a parasite count of 6300/cmm). After that we administered IV artesunate (2.4mg/kg) to the patient intraoperatively. Immediately following artesunate administration, hypotension and increased airway pressures was noticed. We suspected an anaphylactic reaction and all the anesthetic gases were discontinued. The patient's lung was ventilated with 100% oxygen followed by administration of IV epinephrine (0.2µg/kg), hydrocortisone (5mg/kg) and 2L of normal saline solution. In view of the persistent hypotension, epinephrine infusion was administered for a short duration. After 30 min, the patient's blood pressure and air way pressure returned to normal. The remaining 4h of the surgery were uneventful and the patient was shifted intubated to the intensive care unit (ICU). In the ICU, IV quinine dihydrochloride (10 mg/kg) was given over a period of 4 h to the patient, and was repeated every 8 hourly. Patient's trachea was extubated after 6 h of ICU admission. She had an uneventful ICU stay and was discharged from the ICU on the 3rd day. Before discharge, a positive intradermal skin test for artesunate was observed.

Discussion

Artesunate, a hydrophilic derivative of artemisinin, is the drug of choice for the treatment of falciparum malaria.[2] Artesunate has the combined advantage of rapid action, smaller infusion volumes, lesser toxicity and mortality reduction in the treatment of Plasmodium falciparum malaria.[3,4] To achieve faster reduction in parasitemia, we decided to start treatment with artesunate and administered artesunate intraoperatively.

Muscle relaxants and natural rubber latex are the most common anesthetic drugs or substances responsible for intraoperative anaphylaxis.[5] Among the antibiotics, penicillin, cephalosporins, other ß-lactams and bacitracin are reported to cause anaphylactic reactions.[5-6] Cardiovascular symptoms (73.6%), cutaneous symptoms (69.6%) and bronchospasm (44.2%) are the most common manifestations of anaphylaxis during anesthesia.[7] Intraoperative anaphylaxis often manifests as bronchospasm and cardiovascular collapse because early cutaneous signs of anaphylaxis are usually masked by sedation, unconsciousness and poor patient exposure. Discontinuation of all the anesthetics, ventilation with 100% oxygen and early administration of epinephrine are the cornerstones of treatment of intraoperative anaphylaxis.[5]

Allergic reactions to oral artesunate has been reported,[1] but anaphylaxis to parenteral artesunate is extremely uncommon in spite of its widespread use. Our assumption of the intraoperative event to be an anaphylactic reaction to artesunate was based on the clinical presentation, which was further supported by observation of a positive intradermal skin test for artesunate. Literature search regarding this event revealed only one case report of anaphylaxis to intravenous artesunate.[8] In the case report,the authors have reported anaphylaxis to intravenous artesunate in a conscious patient. But, diagnosis of anaphylaxis under GA may be very difficult mainly because of masking of the early signs of anaphylaxis by sedation, unconsciousness and poor exposure. Therefore, the gravity of anaphylactic reaction under GA cannot be overemphasized.

Management of intraoperative anaphylaxis needs prompt diagnosis and immediate management, which can only be possible with an early anticipation. In regions where malaria is endemic, prior sensitization with artesunate can be a possibility that can lead to an anaphylactic reaction on subsequent exposure. Prevention is the most important component to decrease the incidence of anaphylaxis.[5] However, avoiding a highly effective antimalarial drug like artesunate will not be prudent. Hence, an anticipation of an anaphylactic reaction to artesunate can contribute to its successful diagnosis and timely management.

Conclusion

Intraoperative anaphylactic reaction has a high mortality rate if not diagnosed and treated early. The possibility of anaphylactic reaction to artesunate should always be kept in mind prior to its administration in regions where malaria is endemic, and pre operative preparation should be made in advance to deal with such a catastrophe.

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