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Case Report

Grade 4 anaphylactic reaction caused by atracurium (Tracrium®) during anesthetic induction: Anesthetic and allergologic management.

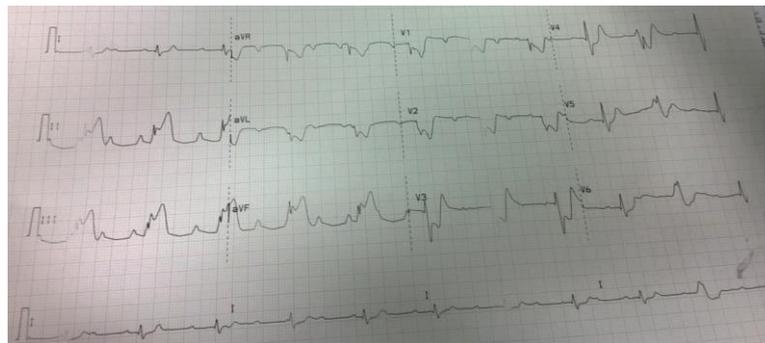
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Observation

A 54-years old man with a history of alcoholic-related chronic pancreatitis was scheduled to benefit from a jejuno-pancretic anastomosis as a consequence of the medical treatment failure. This medical treatment had consisted of a pancreatic prosthesis placement that required multiple endoscopic retrograde cholangio-pancreatographies under general anesthesia with the use of atracurium, rocuronium, mivacurium and succinylcholine. The patient weighted 60 kg, had been free of alcohol intake for two months, and was smoking 20 cigarettes a day. He did not mention any allergies during the preoperative anesthetic visit. His preoperative treatment consisted in an amylase, lipase and protease association (Creon®), tramadol (Tradonal®), colecalciferol (D-Cure®), pantoprazole (Pantomed®), gliquinone (Glurenorm®), and diazepam (Valium®). Insofar as entire preoperative evaluation was good, it was decided to proceed to surgery.

Upon arrival in the operating room, the patient was installed on the surgical tray and monitoring was started using three lead electrocardiography (ECG), non-invasive blood pressure (NiBP), and pulse oxymetry. An 18 G peripheral intravenous catheter was inserted. Anesthetic induction started with a 3 minutes pre-oxygenation. Fifty mg of lidocaine, 30 mg of ketamine, 10 μ g of sufentanil, 200 mg of propofol and 0,625 mg of dehydrobenzperidol were than administered. Ease of manual mask ventilation was checked before administering 50 mg of atracurium for muscle relaxation. The trachea was easily intubated using a size 8 cuffed tube. With the patient anesthetized, a urinary catheter was placed by the nurse, and an arterial catheter was inserted to monitor arterial blood pressure invasively during the intervention.

During arterial catheter placement in the left radial artery, tachycardia occurred, getting from 60 bpm to 140 bpm. Severe bradycardia immediately followed, in addition to very low systolic arterial blood pressure ranging between 35 and 45 mmHg. Expired CO₂ rapidly fell down from 35 mmHg to approximatively 20 mmHg, and a red cutaneous eruption appeared all over the chest. The aspect of the ECG on the monitor changed, and Pardee waves appeared. An external cardiac massage was started. The patient received 0.5 mg of atropine, 50 mg of ephedrine, and up to 1000 μ g of epinephrine. Maintaining a correct arterial blood pressure was uneasy, which prompted installation of a norepinephrine continuous infusion through a central venous catheter that was settled at that moment. The patient received a dose of 0.57 μ g/kg/min of norepinephrine. A 12 lead ECG was performed in the operating room (Picture 1), confirming the acute coronary syndrome with Pardee waves in the inferior territory.



Picture 1: Pardee waves covering the inferior territory (VII, VIII and aVF)

Initial and most probable diagnosis at that time was an anaphylactic shock caused by atracurium. Blood samples were immediately collected for further confirmation of the diagnosis.

The patient was kept mechanically ventilated for transfer to the intensive care unit, and surgery was postponed. A cardiologic check-up showed a normalized ECG, no heart failure, good left-ventricle function with a 60 % ejection fraction. Serum troponins raised to a maximum of 0.99 ng/ml. The patient stayed 24 hours at the ICU, and was then transferred to the cardiologic ward. The cardiologist decided to perform a coronarographic examination. It

highlighted a small lesion on the right coronary artery, not functionally significant. It was concluded that the patient suffered from a coronary spasm.

The serum tryptase was positive (79,1 µg/ml, normal 1-14 µg/ml), which allowed us concluding to a type 1 anaphylactic reaction. Total IgE were normal, with a measured concentration of 68 kU/l (normal 2-100 kU/l).

This anaphylaxis reaction was attributed to atracurium six weeks later, upon an allergologic consultation, where new blood samples were analyzed. The IgE for latex and suxamethonium (NH₄) were negatives, ensuring that succinylcholine and latex were not responsible for the shock. The patient also underwent prick tests for all medications

Drug	Dilution	Result
Propofol 10 mg/ml	10 ⁻¹	-
Atracurium 10 mg/ml	10 ⁻³	+
Lidocaïne 1%	pure	-
Ketamine 10 mg/ml	10 ⁻²	-
Sufentanil 5 µg/ml	10 ⁻¹	-
Rocuronium 10 mg/ml	10 ⁻²	-

Table 1: Intradermal reaction test results

received during the anesthetic procedure. Five of them were negatives, namely for propofol 10 mg/ml, lidocaïne 1 %, ketamine 50 mg/ml, sufentanil 5 µg/ml, and succinylcholine 5 mg/ml. The only medication showing positivity on the prick test was atracurium 1 mg/ml. Intradermal reaction tests (Table 1) were performed, which were only positives for atracurium 10 mg/ml diluted to 10⁻³ mg/ml. It was concluded that the patient suffered from an anaphylactic reaction due to atracurium.

Insofar as surgery was necessary for this patient, and muscle relaxation is very helpful for this kind of procedure, a muscle relaxant tolerated by the patient had to be found. Rocuronium (Esmeron®) was chosen. Indeed, skin tests were negative for this drug. Rocuronium belongs to another class of muscle relaxant, namely aminosteroids as opposed to benzyloisoquinoline for atracurium. The ability to use sugammadex in case of a new anaphylactic shock was a supplementary reason for using rocuronium. To confirm innocuousness of rocuronium, a basophile activation test was performed. This test was unfortunately uninterpretable.

The jejuno-pancreatic anastomosis was finally performed without muscle relaxants for tracheal intubation, and induction was successful. After surgical incision, 10 mg of rocuronium were given to the patient intravenously, and no anaphylactic shock took place.

Discussion

The principal anesthetic challenge of this clinical case was the identification of hypotension, bradycardia, and tachycardia origin, as well as the cause of expired CO₂ drop. A lot of pathologies can arise with these symptoms, and the major difficulty is to find the one that affects the patient. Efficient resuscitation depends on diagnosis accuracy.

Anaphylactic shock treatment consists in (1) stopping the administration of allergenic medications and products, pure oxygen ventilation, insuring good venous access, fluid loading with 30 mL/Kg of cristalloids, and intravenous epinephrine administration. Intravenous epinephrine can be titrated, and dose will depend on the severity grade. This scheme was followed in our patient, in addition to external cardiac massage. After successful resuscitation, investigations to find out responsible allergens must be undertaken. These investigations must take place during an allergologic consultation, and consist in blood sample analyses, prick-tests, intradermal tests, and, sometimes other tests (for example: basophile activation test). Drug dilutions are evidence-based (2)

The most frequently incriminated medications in case of anaphylactic shock in the operating room are muscle relaxants (2). However, frequency of such an adverse event vary as a function of used muscle relaxant. For example, anaphylaxis is more common with succinylcholine and rocuronium than with atracurium (3). In any case, an anaphylactic shock

must be investigated to find the responsible drug, although it may sometimes be difficult. Indeed, investigation results are not always those that were expected (4). For example, total IgE were normal in our patient. This finding is probably due to the important fluid loading, which has probably diluted these immunoglobulins. This example illustrates the difficulty of interpreting testing results.

As soon as the patient is safe, accurate information must be provided for future anesthetic procedures (5). In our patient, allergologic investigations hopefully provided a solution by proving rocuronium innocuousness, although using it without performing those investigations would have been hazardous. Rocuronium has also the advantage of being trapped by sugammadex (Bridion®). This gamma-cyclodextrine encapsulates rocuronium and allows good muscle relaxation antagonization (6). Some case-reports tend to demonstrate that sugammadex lowers anaphylactic shock severity when due to rocuronium (7, 8). This potentiality is still debated, and further studies are needed to provide strong evidence of such an effect (9).

Conclusion

Every anesthesiologist can face with a muscle relaxant-induced anaphylactic shock during career time. Differential diagnosis is not always easy, this pathology mimicking coronary syndromes or other pathologies. In case of such an acute event, adequate resuscitation manoeuvres must first be started, even if we exact diagnosis is still unknown. Anaphylactic shock must always be kept in mind when enumerating the possible causes of sudden shock. Delayed investigations will provide the key, and multidisciplinary collaboration helps approaching exact diagnosis. In that respect, internists and biologists are of great value. Finding the allergen is of utmost importance, because the patient's life depends on it. Last but not least, it must be keep in mind that an anaphylactic shock can occur in patients who already received the responsible allergen in the past.

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