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CLINICAL INFORMATION

Intraoperative ''Kounis syndrome'' that improved electrocardiography changes and hemodynamic situation after administering nitroglycerine

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KEYWORDS
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Abstract
A 58-year-old female without cardiovascular risk factors, was going to be operated to repair the rotator cuff. Induction and interscalene brachial plexus block were uneventful, but after her placement for surgery the patient started with severe bronchospasm, hypotension, cutaneous allergic reaction and ST elevation on the electrocardiogram. An anaphylactic shock was suspected and treated but until the perfusion of nitroglycerina was started no electrocardiographic changes resolved. After necessary diagnostic test the final diagnosis was variant I of Kounis syndrome due to cefazolin and rocuronium. Ephinephrine is the cornerstone of treatment for anaphylaxis but should we use it if the anaphylactic reaction is also accompanied by myocardial ischemia? The answer is that we should not use it because myocardial ischemia in this syndrome is caused by vasospasm, so it would be more useful drugs such as nitroglycerin. But what if we do not know if it is a Kounis syndrome or not? In this article we report our experience that maybe could help you in a similar situation.

PALAVRAS-CHAVE
Síndrome de Kounis;
Cefazolina;
Rocurônio

Síndrome de Kounis intraoperatória com melhoria das alterações eletrocardiográficas e da situação hemodinâmica após a administração de nitroglicerina

Resumo
Paciente do sexo feminino, 58 anos, sem fator de risco cardiovascular, submetida a cirurgia para reparação do manguito rotador. A indução do bloqueio do plexo braquial interescalênico foi feita sem intercorrência, mas, após seu posicionamento para a cirurgia, a paciente apresentou broncoespasmo grave, hipotensão, reação alérgica cutânea e elevação do segmento ST ao eletrocardiograma. Houve suspeita de choque anafilático que foi tratado, mas até que a perfusão de nitroglicerina fosse iniciada não houve resolução das alterações eletrocardiográficas. Após teste diagnóstico necessário, o diagnóstico final foi de variante tipo I

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da síndrome de Kounis por causa de cefazolina e rocurônio. Epinefrina é a base sólida do tratamento para anafilaxia, mas devemos usá-la se a reação anafilática também for acompanhada de isquemia miocárdica? A resposta é que não devemos usá-la, porque a isquemia miocárdica nessa síndrome é causada por vasoespasmo; portanto, drogas como a nitroglicerina seriam mais úteis. Porém, e quando não sabemos se é ou não uma síndrome de Kounis? Neste artigo relatamos nossa experiência que, talvez, possa ajudar em uma situação similar.

Introduction

Kounis syndrome was first described in 1991 by Nicholas Kounis and Zavras in the study: ''Histamine-induced coronary artery spasm: the concept of allergic angina''.[1]

Kounis syndrome is characterized by the simultaneous appearance of an allergic reaction and an acute coronary syndrome. It is also known as allergic angina or allergic myocardial infarction.[2] Kounis syndrome is classified into two groups:

Group I: patients without cardiovascular risk factors and nor known coronary artery disease.
Group II: patients with cardiovascular risk factors with or without associated coronary artery disease.

Recently a Group III[2-4] has been proposed which would belong to patients with drug-eluting stents that are complicated by thrombosis and in which the histology observed infiltrates of mast cells and eosinophils.

This unique syndrome is under-diagnosed because it requires an electrocardiography recording during the allergic reaction, normally prioritizing the treatment of anaphylaxis, and when we finally do the electrocardiogram it is no longer altered. Moreover, many of these reactions occur on the street and when patients reach the health center their electrocardiograms are normal, because the electrical changes tend to disappear in a brief period of time.

The question arises at the moment of using epinephrine. Epinephrine is the cornerstone of treatment for anaphylactic shock, but we should think twice before using it in Kounis syndrome because it could aggravate cardiac ischemia produced by vasospasm.

This doubt also occurs with other drugs like aspirin, indicated in the treatment of acute coronary syndrome but which in turn may cause anaphylactic reactions, or in the case of nitro-glycerine that is also used in acute coronary syndrome, but could worsen the hypotension and tachycardia caused by anaphylaxis.[5]

We report a case of intraoperative Kounis syndrome that was resolved mainly due to the administration of nitroglycerine.

Case report

A 58-year-old women and 65 kg with hypercholesterolemia in dietary treatment and operated of fibro adenoma breast and tonsils. She had no personal or family history of allergy.

The patient was going to be operated to arthroscopically repair the rotator cuff. In the operating room she was monitored by pulse oximetry, non-invasive blood pressure and electrocardiogram. She was hemodynamically stable with a blood pressure of 190/90 mmHg and was anxious.

As premedication she received 2 g cefazolin, 50 mg ranitidine, and 4 mg of ondasentron. In the operating room she was administered midazolam 2 mg, propofol 10 mg and dexamethasone 4 mg.

She was performed an interscalene brachial plexus block with ropivacaine 0.5% 20 mL without complications. It was proceeded to induct fentanyl 300 μg; propofol 100 mg; atropine 0.5 mg and 50 mg rocuronium. She was intubated by orotracheal via and maintained with inhalation anesthesia with sevoflurane. She was administered preemptive analgesia with paracetamol 1 g and dexketoprofen 50 mg and placed in the lateral decubitus position for surgery.

Traumatologists made cutaneous incision use to infiltrate lidocaine 4 mg with epinephrine 25 μg. Suddenly we observed an increase in heart rate of 140 bpm, followed by severe bronchospasm with difficulty in mechanical ventilation, with pressures up to 40 cmH_2O in the airway. Cardiopulmonary auscultation was tachycardia and hypoventilation with decrease in vesicular murmur. Subsequently, end tidal carbon dioxide descended to 9 mmHg, and oxygen saturation to 75%. Finally we observed the ST elevation in leads II and III on the monitor. Until that moment measurement of blood pressure was programmed every 5 min so, in this instant marked 120/70 mmHg.

Surgery was interrupted immediately, the patient was placed in decubitus supine, we started manual ventilation with FiO^2 of 1. Then the measurement of blood pressure revealed a hypotension of 63/39 mmHg, and we stopped the administration of sevoflurane and started with intensive fluid therapy. When we removed the cloth from the surgical field we observed generalized skin rash. It was made a twelve-lead electrocardiogram in which we could see ST segment elevation in the front and bottom of the heart (Fig. 1).

An emergent consultation to cardiologist recommended implementing the hospital protocol of acute coronary syndrome, with perfusion of nitroglycerine at titrated doses, depending on the patient's hemodynamic situation, clopidogrel 300 mg and acetylsalicylic acid 100 mg by nasogastric tube.

Suspecting an anaphylactic reaction, we administered methylprednisolone 80 mg IV, dexchlorpheniramine maleate 5 mg IV and ranitidine 50 mg IV. At first we were not sure whether to use adrenaline or not, but finally it was decided not to administer it given the possibility of the patient

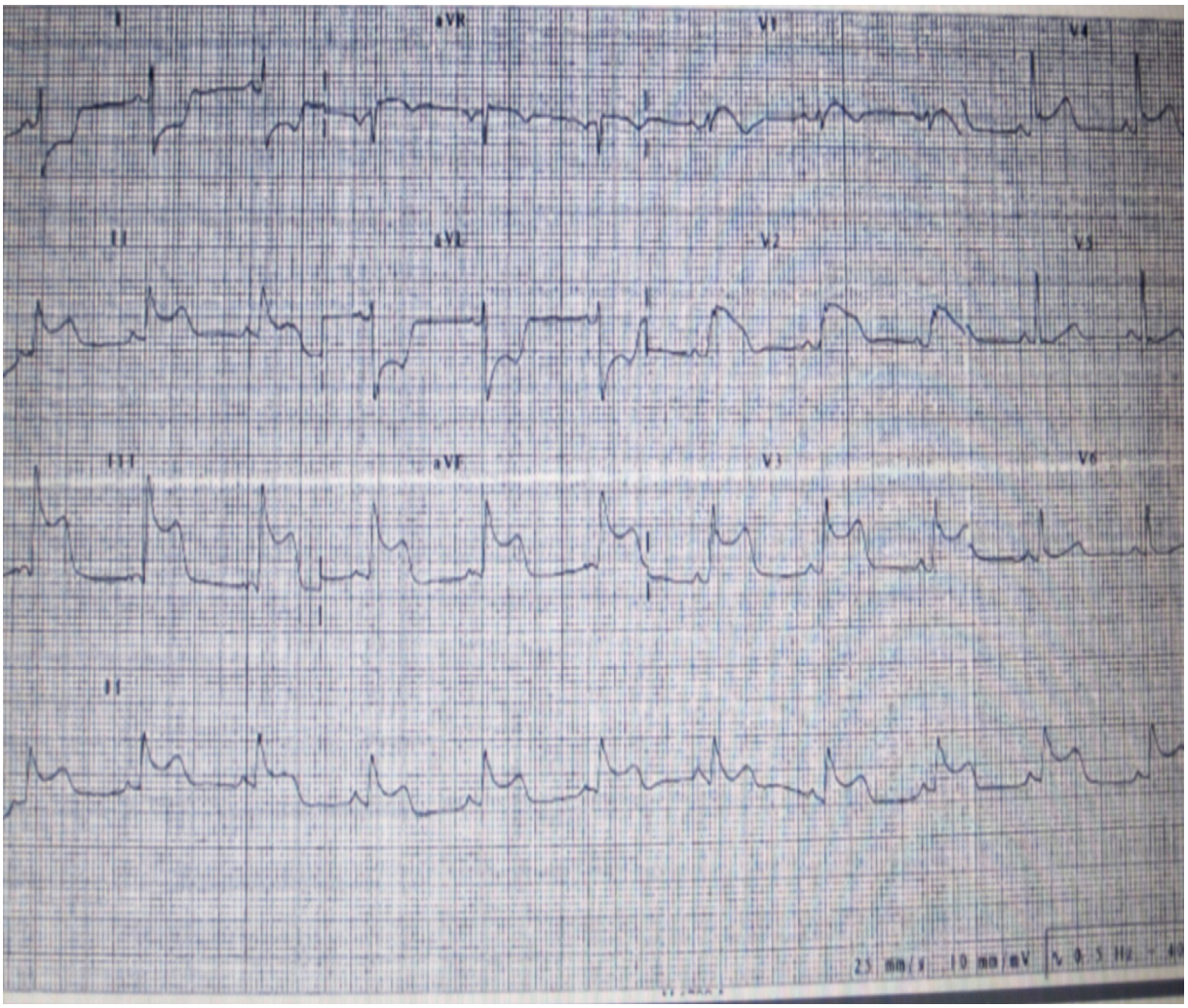

Figure 1 ST segment elevation in front and bottom of the heart.

suffering an acute coronary syndrome. She needed ephedrine boluses of 5, 10 and 20 mg to stabilize blood pressure and atropine 1 mg for bradycardia. This allowed starting acute coronary syndrome protocol.

Following our hospital allergy protocol, blood and urine samples were extracted.

After waiting during the safety period it was decided to revive the patient. She was asymptomatic, the rash had diminished and the electrocardiogram was normal (Fig. 2).

She was admitted to ICU after performing the following tests:

- Coronary angiography: normal
- General analysis: without alterations, absence of eosinophilia.
- Chest X: rise of the right hemidiaphragm (Fig. 3), probably related to interscalene brachial plexus block. Normalized in discharge.
- Electrocardiogram: unchanged.
- Serial myocardial enzymes: normal.

She was discharged from hospital and attended by the Allergy department where the study was continued with the following test:

Levels of serum tryptase 66.4 pg/L, during anaphylactic shock, 34.3 pg/L after 90 min and 27.5 pg/L after 6 h of reaction.[3] Plasma histamine > 200 nmol/L intraoperatively. Histamine levels in urine 2288 nmol/L in the operating room and 1693 nmol/L after 1 h.
Allergy skin test to latex: negative.
Protocol of general anesthetics: positive for rocuronium and doubtful for cisatracurium. The rest of the drugs tested were negative.
Skin and provocation test with lidocaine and dexamethasone: negative.
Skin prick test: positive for cefazolin.

The final diagnosis was type I Kounis syndrome secondary to rocuronium[6] and/or cefazolin.

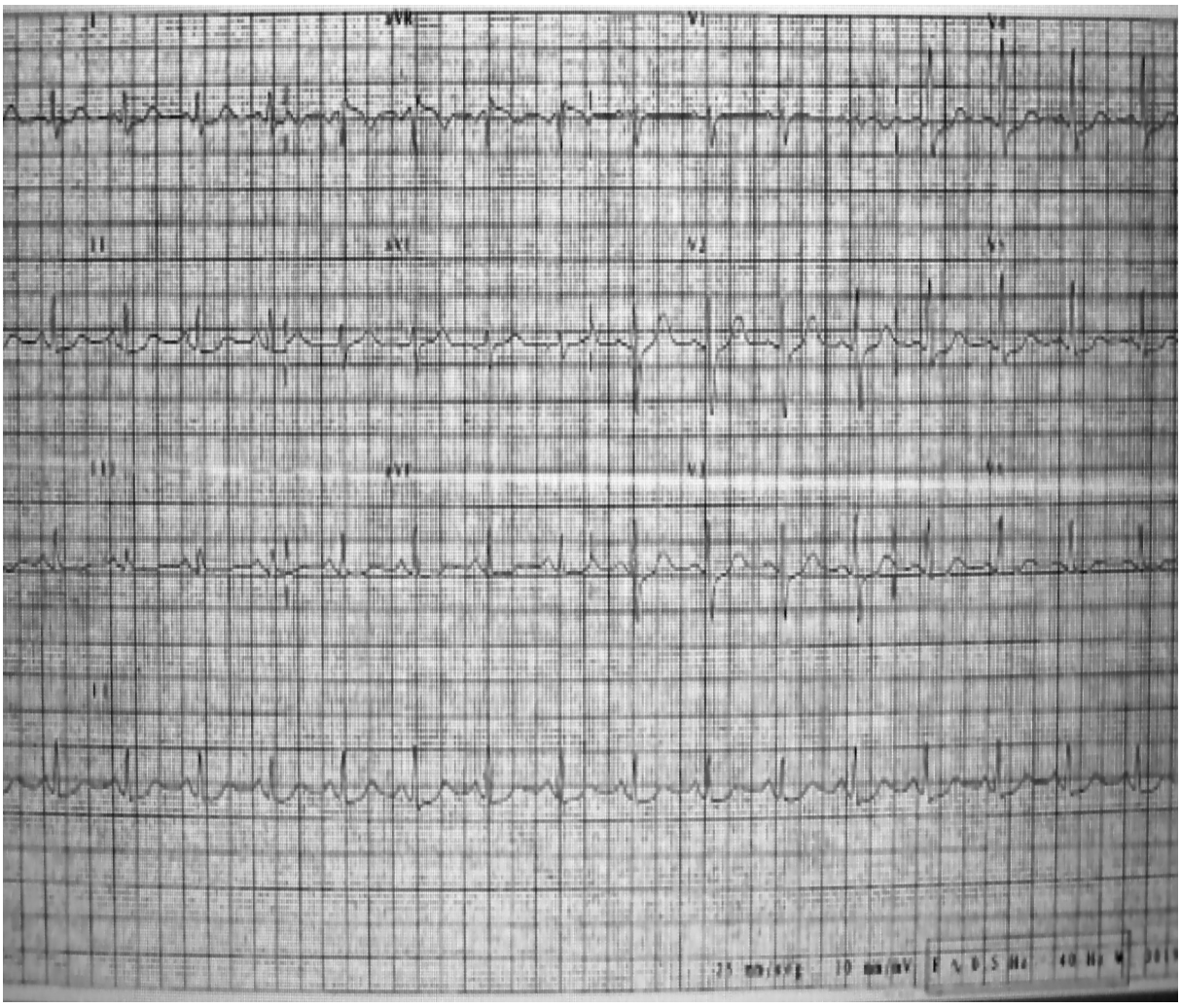

Figure 2 Normal electrocardiogram.

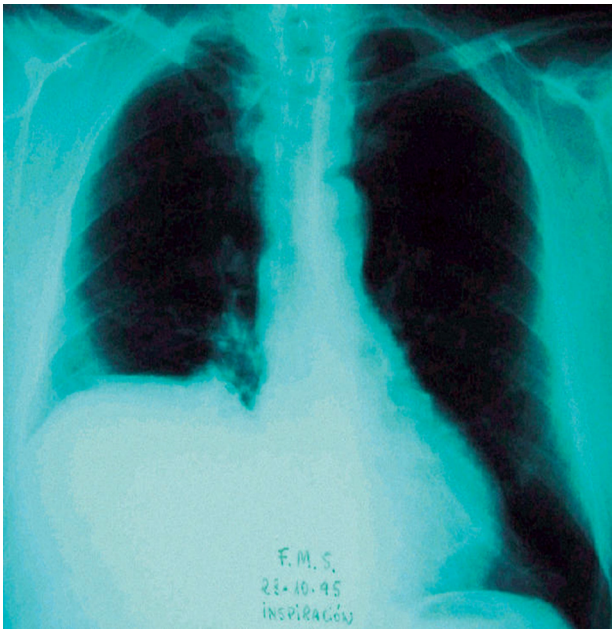

Figure 3 Rise of the right hemidiaphragm.

Discussion

This is a real case of Kounis syndrome type I, in which electrocardiography abnormalities were resolved with the help of nitro-glycerine; so how was severe hypotension improved by using nitro-glycerine? This could be explained because in this syndrome, heart failure is mainly produced by coronary vasospasm produced in turn by massive activation mast cell[7] of cardiac tissue and liberation of histamine, prostaglandin, thromboxane, leukotrienes[8] and platelet activating factor.

Other clinical manifestations may be tachycardia, ventricular contraction dysfunction and atrioventricular blocks.[9]

Boluses of ephedrine helped to stabilize blood pressure and heart rate, respectively but segment ST did not normalize until nitroglycerine infusion started.

The great doubt that we had was the use of adrenaline. In any clinical guideline, adrenaline is the ''gold standard'' treatment for anaphylactic shock, but its use in a Kounis syndrome could have serious consequences.

As we have said previously, many of these Kounis syndromes are undetectable due to the absence of monitoring in the acute phase and treatment with adrenaline is

unquestionable in anaphylactic shock and cannot be delayed. This can aggravate vasospasm and cardiac ischemia. Furthermore, in the case we had monitored the patient, the use of adrenaline would have masked the diagnosis of Kounis syndrome, because you could not have known whether the electrocardiography changes were due to adrenaline or Kounis syndrome.[10]

Therefore, if we diagnose a Kounis syndrome, adrenaline would not be indicated, or it would have to be used with caution given that it could aggravate vasospasm and myocardial ischemia, besides the possibility to produce lethal cardiac arrhythmias.

On the other hand, if we are faced with an anaphylactic shock that we do not know if it is a Kounis syndrome or not, what happens most of the time, we would not delay the use of adrenaline[6] if we need it, as long as we make a 1:1000 dilution in the case of intramuscular route or 1:10,000 to 1:100,000 if intravenous route is used.[10]

To sum up, we agree with using epinephrine to treat anaphylactic shock, what we offer is an alternative in case of failure to improve patient homodynamic after its administration: ''the use of nitroclycerine carefully, as long as patient's hemodynamic status permits it, might help if the cause of this situation was a vasospasm by a possible Kounis syndrome''.

To end, with the clinical manifestations and alterations in the results of diagnostic tests described, we should bear in mind in differential diagnosis other ischemic heart diseases like myocardial infarction, stable and unstable angina, Prinzmetal Angina and, of course Tako-Tsubo syndrome. The skin reaction and elevated serum tryptase levels will give us the clue to diagnose Kounis syndrome.

Conclusions

If we diagnose an anaphylactic shock, first treat it, and if it is possible do an electrocardiogram and extraction of samples for making the diagnosis of Kounis syndrome.

If a monitored patient presents during an anaphylactic shock electrocardiography changes of acute coronary syndrome, a probable cause could be a Kounis syndrome and we will have to value the use of nitroglycerine, if the patient's hemodynamic situation permits it.

If we face an anaphylactic shock that we are not sure if it is a Kounis syndrome, the use of adrenaline is unquestioned, but if we dilute it (1:1000 intramuscularly or 1:10,000 to 1:100,000 intravenously), we will minimize the chances of aggravating vasospasm, ischemia and arrhythmias that may cause this syndrome.

Conflicts of interest

The authors declare no conflicts of interest.

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