Aspirin-induced Anaphylactoid Reactions in a Patient with Acute Coronary Syndrome Complicating Acute Lung Edema: a Case Report

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SOUHRN

Kontext: Antiagregační terapie sice představuje základní způsob léčby pacientů s akutním koronárním syndromem, avšak vzhledem k tomu, že již byl popsán případ hypersenzitivity na kyselinu acetylsalicylovou, může být léčba pacienta s akutním koronárním syndromem problematická.
Popis případu: Na oddělení urgentního příjmu byla přepravena 65letá Jávanka s dyspnoe přetrvávající po dobu tří dní a s ortopnoe. Na základě fyzikálního vyšetření a výsledků pomocných testů byla pacientce stanovena diagnóza akutní dekompenzace srdečního selhání. Třetí den léčby byla na EKG záznamu pozorována nová inverze vlny T ve svodech V_1 až V_6, I a aVL, prokazující akutní koronární syndrom bez elevace úseku ST. Byla podána nasycovací dávka antiagregancií (clopidogrelu a kyseliny acetylsalicylové). Tři dny po podání léčiv si pacientka stěžovala na náhlé zhoršení dušnosti; současně byly slyšet hvízdavé zvuky. Vzniklo tak podezření na alergickou reakci, a vzhledem k četným alergickým reakcím na nesteroidní antiflogistika v anamnéze pacientky se předpokládalo, že tentokrát reakci vyvolala kyselina acetylsalicylová.
Diskuse: Kyselina acetylsalicylová se jako inhibitor COX-1 často podílí na vyvolání hypersenzitivních reakcí. V takových případech je léčebnou strategií podání silnějšího antagonisty receptoru $P2Y_{12}$ a rychlá perorální desenzibilizace ihned po stabilizaci pacientova stavu.

Keyword:
Acute coronary syndrome
Anaphylaxis
Aspirin
Hypersensitivity

ABSTRACT

Background: Antiplatelet therapy is an essential treatment for patients with acute coronary syndrome. But a history of aspirin hypersensitivity has been reported and it might be challenging to treat a patient with this case.
Case: A 65-year-old Javanese woman came to the emergency department and presented with dyspnea for three days and with orthopnea. Based on physical and supporting examination, the patient was diagnosed with ADHF. However, on the 3rd day of treatment, ECG showed new T wave inversion at lead V_1 to V_6, I, and aVL lead to NSTEACS. Loading doses of antiplatelets (clopidogrel and aspirin) were administered. Three hours after the drug administration, the patient complained of sudden worsening shortness of breath with pronounced wheezing. Allergic reaction was suspected and due to the patient's history of multiple NSAIDs allergies, aspirin was suspected as the culprit.
Discussion: Aspirin as a COX-1 inhibitor, is often implicated with hypersensitivity reactions. Using a more potent $P2Y_{12}$ receptor antagonist and performing rapid oral desensitization once the patient has stabilized is a strategy in this kind of case.

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Background

Antiplatelet therapy is an essential treatment for patients with acute coronary syndrome. Aspirin has been regarded as the cornerstone treatment due to its potency, efficacy, wide availability, and low cost, particularly for patients in developing countries. Aspirin was long recommended for the treatment of ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation acute coronary syndrome (NSTEACS) based on its survival benefit in the ISIS-2 trial.[1] Dual antiplatelet therapy consisting of aspirin and $P2Y_{12}$ receptors antagonist becomes more important, particularly if stent implantation is considered.[2]

Treatment for acute coronary syndrome patients with a history of drug hypersensitivity might be challenging.[3] Hypersensitivity reactions force clinicians to determine whether to continue administering aspirin or halt aspirin treatment and begin alternative programs such as aspirin desensitization procedures. Here, we reported invaluable experience identifying strategies to improve clinical outcomes in a patient with acute coronary syndrome who had anaphylactoid reactions to aspirin.

Case report

A 65-year-old Javanese woman came to the emergency department and presented with dyspnea for three days and with orthopnea. Chest pain, fever, or cough are denied. The patient had a history of hypertension controlled by candesartan, diabetes mellitus treated with insulin injection, and spondyloarthropathy treated with methotrexate. The patient has an allergy to some nonsteroid anti-inflammatory drugs (NSAIDs) and antibiotics, if exposed to the drugs which she is allergic to, she starts coughing and wheezing.

On admission, blood pressure was 160/100 mmHg with a heart rate of 112 beats per minute, respiratory rate of 30 times per minute, and oxygen saturation of 91% in room air. From physical examination, we found grade II/IV systolic heart murmur at the apex, crackles at the base of both lungs with no wheezing, and no edema at all limbs. Chest X-ray showed cardiomegaly with prominent pulmonary vasculature (Fig. 1). The initial electrocardiogram showed sinus tachycardia without any other abnormality (Fig. 2, day 1). From echocardiography, we found restrictive motion of posterior mitral leaflet with moderate mitral regurgitation and normal left ventricle ejection fraction. Based on this examination, the patient was diagnosed with acute decompensated heart failure (ADHF) and got loop diuretic and intravenous nitrates as treatment. The patient felt relieved, and no more orthopnea was found with this treatment but crackles still present minimally.

Laboratory findings showed impaired renal function with serum creatinine 1.8 mg/dL and blood urea nitrogen 27 mg/dL, other laboratory parameters are within normal limit.

On Day 3 admission, ECG showed new T wave inversion at lead V_1 to V_6, I, and aVL which was not present at the initial ECG (Fig. 2, day 3). We followed it up by checking troponin I level and the result was 42.34 ng/mL (normal range < 35). We assessed the patient with non-ST-segment elevation acute coronary syndrome (NSTEACS) and categorize it to very high risk with GRACE score 153. We decided to give a loading dose of antiplatelets using 300 mg aspirin and 300 mg clopidogrel orally for the patient, and started giving fondaparinux subcutaneous injection.

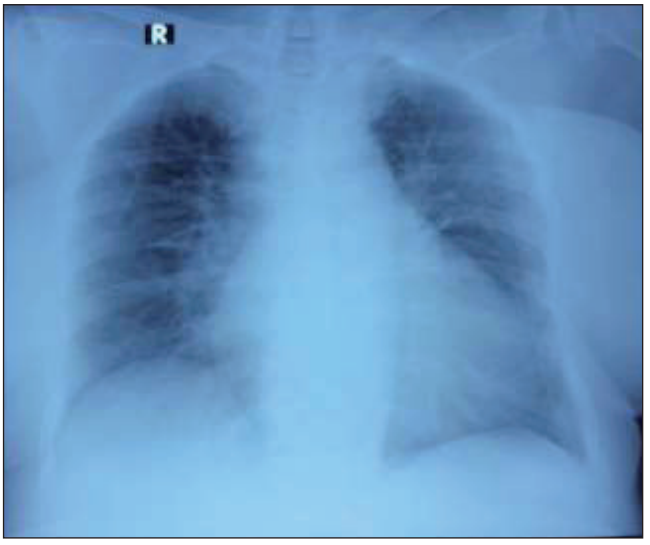

Fig. 1 – The patient's initial chest X-ray results.

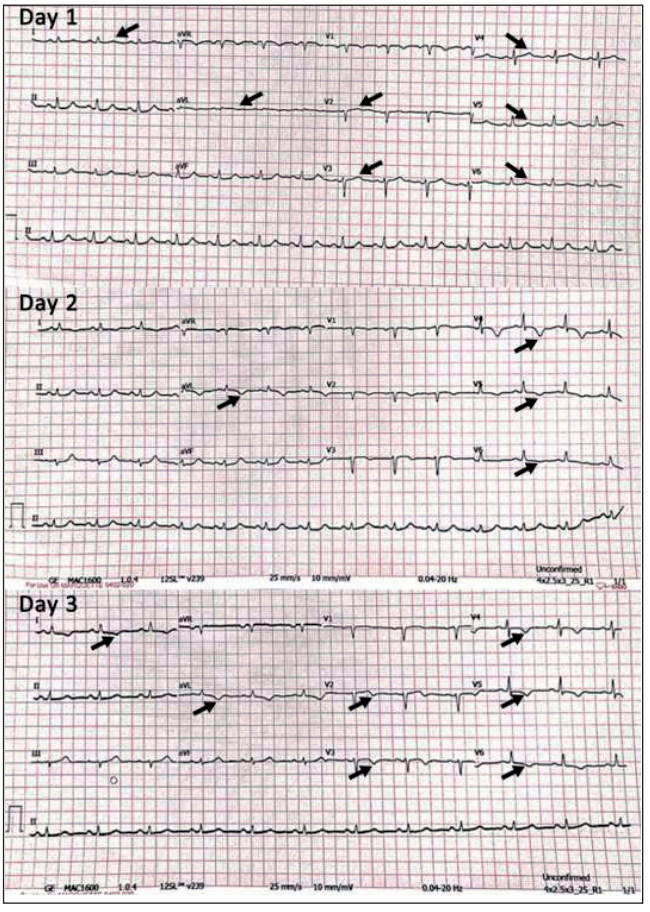

Fig. 2 – The patient's ECG evolution from day 1 to day 3. Showing new T waves inversion on day 2, indicating acute myocardial ischemia. Note the arrows pointing at the T waves which all still upright in the first day but started to be inverted in the second and third day.

About 3 hours after we administered the drugs, the patient complained of sudden worsening shortness of breath with pronounced wheezing with no progressive crackles, itchy rash almost on almost all of her body surface and edema of palpebra. Allergic reaction was suspected, methylprednisolone and diphenhidramine intravenous injection was given and the symptoms diminished. Due to the patient's history of multiple NSAIDs allergy, aspirin was suspected as the culprit and was discontinued from the patient, and after that the patient did not have any allergic reaction symptoms any more. Methylprednisolone was also administered routinely once a day afterwards. Since we decide not to use aspirin for the patient, we decide to use ticagrelor 90 mg twice daily as the antiplatelet and continue administering the fondaparinux injection. From the diagnostic coronary angiography, we found coronary artery disease with significant stenoses at left main, left anterior descending, and left circumflex coronary artery. The patient was suggested then to undergo bypass surgery.

Discussion

Platelet activation and coagulation cascade is an essential process in the initial phase and evolution of NSTE-ACS. Therefore, platelet activation inhibitors and anticoagulation are essential in managing NSTE-ACS.[1] Aspirin, as the cornerstone of treatment, and other NSAIDs, especially COX-1 inhibitors, are often implicated with hypersensitivity reactions. The prevalence of aspirin hypersensitivity is 0.5–1.9% of the general population.[4] The hypersensitivity reaction varies from respiratory and cutaneous manifestation to anaphylactic shock, and in general, the intensity is dose-dependent.[5] Aspirin-exacerbated respiratory disease (AERD) can manifest as respiratory and non-respiratory, with 64–66% of cases allergic to common allergens tested by skin test.[5] Non-respiratory manifestations develop more frequently in patients with severe respiratory manifestations and occur within a few minutes to three hours after drug exposure.[5] Aspirin desensitization is recommended, and rapid desensitization may be performed for patients who urgently need aspirin treatment. Despite its effectiveness, potential risks of reactions like urticaria, angioedema, bronchospasm, and dyspnea may arise and make it underutilized.[5,6]

Clopidogrel 75 mg daily is an appropriate alternative for patients who are intolerant or allergic to aspirin for long-term treatment. In cases of aspirin intolerance, more potent $P2Y_{12}$ inhibitors, such as prasugrel or ticagrelor, may be preferred over clopidogrel as single antiplatelet therapy for a limited duration.[2] With a history of lots of NSAID allergy from the patient, it is dilemmatic for us to differentiate between a true allergic reaction and an anaphylactoid reaction. Since there is no record of an aspirin desensitization program at our center, we decide to stop aspirin and give ticagrelor as a more potent $P2Y_{12}$ for the patient.

The patient's shortness of breath needs to be differentiated between bronchoconstriction or acute heart failure. Rales and rhonchi manifest as a result of fluid leakage from pulmonary capillaries into alveoli, while wheezing manifests as reactive bronchoconstriction. Rales caused by heart failure are usually finer, extending upwards from the base of the lungs, while those due to other causes tend to be coarser. In congested patients with advanced heart failure, rales or rhonchi may be absent due to a compensatory increase in local lymphatic drainage. The physical presence of fluid in the bronchial wall and secondary bronchospasm can lead to a condition known as cardiac asthma. Misdiagnosed and incorrect therapy with bronchodilators may be associated with an increased risk of death.[7]

Conclusion

Aspirin is essential in the treatment of acute coronary syndrome, particularly if percutaenous coronary intervention is considered. For patients with a history of hypersensitivity to aspirin, the optimal management of acute coronary syndrome is unclear. We follow a strategy for addressing this problem by using a more potent $P2Y_{12}$ receptor antagonist and performing rapid oral desensitization in the ensuing hours, once the patient has been stabilized.

Conflict of interest
The authors declare there is no conflict of interest.

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Ethical statement
Ethical consent for this case study was provided by Dr. Soetomo General Hospital.

Informed consent
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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