MÚLTIPLOS EPISÓDIOS DE INFARTO AGUDO DO MIOCÁRDIO APÓS USO DE ANTICOAGULANTE - RELATO DE CASO

MULTIPLE ACUTE MYOCARDIAL INFARCTION EPISODES AFTER ANTICOAGULANT USE - CASE REPORT

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RESUMO

OBJETIVO: Descrever um caso de paciente com trombocitopenia induzida por heparina (TIH) tipo II, que se manifestou através de consecutivos quadros de infartos agudos do miocárdio. RELATO DE CASO: Trata-se de uma paciente do sexo feminino, 70 anos, admitida no HC-UFPR por quadro de infarto agudo do miocárdio (IAM), duas semanas após internamento hospitalar por pneumonia e insuficiência cardíaca descompensada, manejadas com antibioticoterapia, heparina e diuréticos. Evoluiu com quadro de plaquetopenia a esclarecer e dois episódios subsequentes de IAM. Após a retirada da heparina, evoluiu com estabilização clínica - aumento do número de plaquetas, sem novos eventos trombótico e regularização dos testes laboratoriais. Recebeu alta hospitalar e, no retorno ambulatorial, apresentou anticorpos anti-plaquetas positivos e uma revisão de prontuário com história de múltiplas exposições a heparinas não fracionada e de baixo peso molecular. CONCLUSÃO: Diante do grande número de pacientes expostos à heparina, seus principais efeitos colaterais, dentre os quais a TIH, precisam ser conhecidos. Deve-se atentar para a possibilidade de a heparina possuir associação causal com IAM, quando associado à trombocitopenia, visto que a tendência nessas situações é de se manter a medicação a fim de evitar quadros trombóticos futuros.

Descritores: heparina; infarto do miocárdio; trombocitopenia.

ABSTRACT

OBJECTIVE: Report a case of patient with heparin induced thrombocytopenia (HIT) type II, which was expressed through consecutive episodes of acute myocardial infarction. CASE REPORT: A 70-year-old woman was admitted to hospital care due to an episode of acute myocardial infarction two weeks after hospitalization for pneumonia and decompensated heart failure, when she was managed with antibiotics, heparin and diuretics. She evolved with thrombocytopenia and two subsequent episodes of acute myocardial infarction. After discontinuing heparin, she progressed with clinical stabilization - an increase of platelets, without new thrombotic frames and regularization of laboratory tests. Patient was then discharged and during outpatient follow showed positive anti-platelet antibodies and a retrospective analysis of multiple exposures to unfractionated and low molecular weight heparins. CONCLUSION: Considering the large number of patients exposed to heparin, its major side effects must be known. Care must be taken to the possibly of heparin be a trigger to procoagulant state, resulting in acute myocardial infarction, for example, since a trend in these situations is to maintain the drug to prevent future thrombotic episodes.

Keywords: heparin; myocardial infarction; thrombocytopenia.

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INTRODUCTION

Heparin induced thrombocytopenia (HIT) is a major adverse drug reaction of heparin, which occurs in about 5% of patients exposed to the drug. It is a result of antibodies production against a complex of heparin and platelet factor 4 (PF4), that activates platelet, leading to formation of arterial and venous thrombi.

HIT can be classified in two distinct forms: type I and type II. HIT type I presents a mild and transient decrease in platelet count, that occurs within 48-72 hours of heparin treatment, without clinical implications, returning to normal spontaneously. HIT type II has a clinical presentation of thrombosis and thrombocytopenia, and this risk of thrombus formation exists until heparin is metabolized, excreted and another anticoagulant is set up.

The aim of this case report is describe an event of heparin induced thrombocytopenia type II in a patient manifesting consecutive frames of acute myocardial infarction, and perform literature review to emphasize diagnosis and initial treatment of this affection.

CASE REPORT

A 70-year-old female with hypertension was complaining of chest pain at pre-hospital care. An electrocardiogram was performed, showing acute myocardial infarction with ST-segment elevation (Figure 1). She received acetylsalicylic acid (ASA) 200mg, unfractionated heparin 5000 IU subcutaneously, simvastatin 40 mg, isosorbide dinitrate 5 mg sublingual tablet, oxygen therapy 100% 2L/min. The patient was referred to coronary care unit to manage this clinical condition.

At admission, the patient was normotensive, afibrile, eupneic, with a heart rate of 85 beats/min and 90% oxygen saturation on room air. A complete physical examination revealed no pertinent findings, except for fine inspiratory bibasilar crackles. Laboratory tests were performed revealing metabolic alkalosis, thrombocytopenia (30,000 platelets count, Normal Value - NV - 150-400,000/mm³), international normalized ratio of prothrombin time (INR) 1.47 (NV 0.9-1.2), creatine kinase (CK) 1,442 U/L (NV 24-200 U/L), CK-MB 350 ng/mL (NV 0-5 ng/mL) and troponin I 50,000 ng/mL (NV 0-0.5 ng/mL).

Her medical history included: essential arterial hypertension for 10 years; hyperurecemia; and cholecystectomy 12 years ago. A recent hospitalization was reported (2 weeks ago) for pneumonia and decompensated cardiac failure. She was treated with antibiotic therapy, prophylatic heparin and diuretics. The patient denied previous alcohol consumption, but she stated a 60 pack-year smoking history (quit 1 year ago).

Immediately the patient was sent to the Hemodynamics and Interventionist Cardiology Sector, where clopidogrel therapy was initiated and a coronary stent was placed at proximal third of right artery, without complications. In addition, a distal trunk lesion of 30% was diagnosed. After procedure, she was referred to the Coronary Unit and treated with aspirin 100mg/day, clopidogrel 75 mg/day and enoxaparin (prophylatic dose).

After stabilization, she was moved to cardiology ward to proceed investigation of thrombocytopenia and management of heart failure. On the sixth day of hospitalization, she developed epigastric pain, nausea and dyspnea at rest. A new electrocardiogram was performed, showing new ST segment elevation at inferior walls and V5-V6.

Patient was referred back to Hemodynamics Sector. Right coronary presented many filling holes - large thrombus sized 7-8 cm (Figure 2); circumflex with 80% residual lesions; and 30% in tronco left coronary. Because of atypic injury, it was chosen not to carry out intervention with stent. It was also detected thrombus in the left ventricular apex, inferoapical akinesia and inferior medial hypokinesia in left ventricle.

Medical management was chosen with ASA, ticagrelor and tirofiban (for 48 hours). During this period, a slight increase in platelets count was shown, reaching 40,000 platelets.

On ninth day of hospitalization, she presented fever with a diagnosis with sepsis of unknown origin, isolating Enterococcus faecium in blood culture, and she...
was treated with ampicillin. On the third day of antibiotics, she presented a new episode of chest pain, nausea and sweating. Electrocardiogram was performed, showing a new ST-segment elevation (Figure 3).

Conservative therapy was again indicated, using Tirofiban, Ticagrelor, ASA, and enoxaparin full dose. Three days later, hemoglobin decreased by 3.4 points and platelet count was 28,000. Computerized tomography was performed due to retroperitoneal hematoma suspicion, since no bleeding exteriorization was seen. It showed thrombosis involving right branch of portal vein, splenic vein, right hepatic vein and right lower lobe branch of pulmonary artery, determining perfusion defects of liver and spleen compatible with infarctions. A new catheterization three days later was carried out showing no lesions in right coronary.

After clinical stabilization, she was referred to the Internal Medicine Department, for conclusion of clinical management and investigation of thrombophilia. Warfarin was introduced and research for thrombophilia was negative. Echocardiogram showed left atrium of 42 mm, left ventricle of 40 mm, ejection fraction of 58% and normal internal dimension of left ventricle, with inferior and lateral hypokinesia and appropriate global systolic function. With prothrombin activation time on target, enoxaparin was suspended. During five days, the platelet count evolved from 74,000 to 220,000 at hospital discharge.

Reviewing patient’s medical history and previous hospital admission in another institution, we found out unfractionated heparin use as prophylaxis of deep vein thrombosis. At follow-up, she showed positive anti-platelet antibodies and normal platelet count using warfarin. Patient remained clinically stable, with no further new thrombotic events.

DISCUSSÃO

Defined as an adverse drug reaction, HIT is characterized by thrombocytopenia and high risk of arterial or venous thrombosis\(^3\). It can lead to high morbidity, with 10% of disability and it is fatal in 5-10% of cases\(^4\). About 8% of patients produces antibodies of HIT when treated with heparin. (4) However, less than 10% of these patients will develop HIT and lower proportions symptomatic thrombosis\(^5\).

Risk factors include: (a) unfractionated heparin (UFH), (b) bovine UFH, (c) therapeutic doses, (d) long term use (over 5 days), (e) female (2:1), (f) elderly, (g) postoperative\(^7\).

HIT type II occurs in approximately 1% to 3% of patients exposed to heparin\(^8\). It is an immune disorder which leads to an increased risk of 20 to 40 times of arterial and venous thromboses\(^9\). Originally, heparin and platelet factor 4 (PF4) (a cytokine stored in alpha granules of platelets) are avoid of immunogenicity. However, when both are bound result to an antigenic macromolecule that bind on activated platelets surface. Thus, there is a conformational change that stimulates production of immunoglobulin G (IgG)\(^10\). The binding of IgG to the neo-antigen heparin-PF4 surface leads to a process of self-amplification inducing...
high specificity and sensitivity for HIT. The gold standard test, Serotonin release assay (SRA), has sensitive for detecting clinically relevant PF4/polyanion enzyme immunoassays (EIAs), both washed platelet activation assays and commercial To confirm diagnosis, laboratory testing may be performed:

- Scoring can be performed with the Warkentin score, which is composed by thrombocytopenia, time, thrombosis and other causes for thrombocytopenia (table 1). Scoring can lead to three estimate probability: low (score of 0-5), intermediate (score of 6-9) and high risk (score of 10-14).
- To confirm diagnosis, laboratory testing may be performed: washed platelet activation assays and commercial PF4/polyanion enzyme immunoassays (EIAs), both sensitive for detecting clinically relevant HIT antibodies. The gold standard test, Serotonin release assay (SRA), has high specificity and sensitivity for HIT.

### Table 1: “4 T score”

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>30-50% fall in platelet count or a trough of 10-15\times10^9/L</td>
</tr>
<tr>
<td>0</td>
<td>&lt;30% fall in platelet or a thought of &lt;10\times10^9/L</td>
</tr>
<tr>
<td>2</td>
<td>&gt;50% fall in platelet count or a trough of 20-100\times10^9/L</td>
</tr>
<tr>
<td>1</td>
<td>Unclear or platelet count falls after 10 days</td>
</tr>
<tr>
<td>0</td>
<td>Platelet count falls before 5 days of exposure and without recent exposure to heparin</td>
</tr>
<tr>
<td>2</td>
<td>New thrombosis; skin necrosis at heparin injection sites</td>
</tr>
<tr>
<td>1</td>
<td>Progressive or recurrent thrombosis; skin lesion e.g. erythema</td>
</tr>
<tr>
<td>0</td>
<td>Possible other cause</td>
</tr>
<tr>
<td>2</td>
<td>No other cause identified</td>
</tr>
<tr>
<td>1</td>
<td>Other cause clearly identifiable</td>
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### Treatment

Treatment is mandatory when high suspicion or confirmation of HIT. The principles are: (a) stop use and avoid any form of heparin; (b) start any anticoagulant non-heparin; (c) add warfarin after substantial platelet recovery (if warfarin has already begun, vitamin K must be used); (d) search for HIT antibodies; (e) investigate thrombosis of lower extremities and deep vein thrombosis; (f) avoid prophylactic platelet transfusion.

### Conclusion

Considering the large number of patients exposed to heparin, its major side effects must be known. HIT type II should be considered as differential diagnosis in patients with myocardial infarction and thrombocytopenia, since heparin use must be avoided and a specific therapeutic promptly applied.

### References


