PULMONARY ARTERY THROMBOSIS WITH POSITIVE TROponin: DO WE NEED MORE DIAGNOSIS? CASE REPORT

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Abstract: The utility of troponine for detecting the myocitary necrosis is now well known. There are also cases of false positive results, but a good clinical judgment, together with complementary evaluation, will orientate the diagnosis. We present the case of a 54 years old patient which was admitted for dyspnea, thoracic pain and severe asthenia. An increase of the troponine at a level of three times over the limit which is considered to be normal, at a patient with electrocardiograph changes suggestive for acute myocardial infarction made the differential diagnosis very hard to establish. We underline the importance of a correct interpretation of the increasing of the troponine levels, fact which will bring to an accurate diagnosis and an adequate therapeutic attitude.

Rezumat: Utilizarea troponinei pentru a detecta necroza miocitară este de acum bine cunoscută. Dar există și cazuri de rezultate fals positive, în care judecata clinică și investigațiile paraclinice orienteză diagnosticul. Prezentăm cazul unui pacient în vârstă de 54 ani care se prezintă pentru dispnee severă, durere toracică anterioară, astenie majoră. O creștere a nivelului troponinei la valori de trei ori mai mari decât limita superioară admisă normală la un pacient care a prezentat durere toracică anterioară, cu modificări electrocardiografice specifice pentru un infarct miocardic acut a pus mari probleme de diagnostic diferențial. Subliniem prin acest caz importanța interpretării corecte a creșterii nivelului troponinei, fapt care duce la acuratețea diagnosticului și la o atitudine terapeutică adecvată.

CASE REPORT

We present the case of a 54 years old patient, hospitalized in the Intensive Care Unit of the Cardiology Department of the Emergency Clinical County Hospital from Sibiu, for the next reasons: dyspnea with orthopnea, anterior thoracic pain and major asthenia.

From the pathological personal records of the patients, we mention: gastric ulcer with surgical treatment, 20 years ago, internal hemorrhoids with elastic bands ligation, severe anemia after hemorrhoid bleeding, with blood transfusion, 2 years ago. The patient is a smoker and drinks alcohol occasionally.

Physical exam at admission revealed the followings: a restless patient, cyanotic, sweating, overweight, oxygen saturation (SaO2) 80%, physiological vesicular murmur, polipnea, sibilant bilateral basal disseminated rales, BP 100/60 mmHg, pulse 100/min, rhythmic heart sounds, tachycardia, turgid jugular veins, elastic, painless abdomen. In order to clarify the diagnosis and determining the subsequent behavior, we considered necessary the following complementary explorations:

Laboratory examinations: Leucocytes 6900/mm3, erythrocytes 4.33 mil/mm3, Hemoglobin 13.2 g / dl, Ht 41.9%, MCV 96.7 fl, MCH 30.6 pg, platelets 249000/mm3, blood sugar 96 mg / dl, urea 26mg/dl, creatinine 0.82 mg / dl, uric acid 8.3 mg / dl, cholesterol 147mg/dl, triglycerides 214mg/dl, TGP 14u / l, TGO 13u / l, BT 1.48 mg / dl, BD 0.43 mg / dl, Na 142.8 mEq / L, K 4.65 mEq / L, TQ 15.7 sec (61.1%), INR 1.03, APTT 27.9 sec, cardiac markers: myoglobin 9.69 ng / ml (VN <23 ng / ml), NTproBNP 1252 pg / ml (VN <239 pg / ml), CK-MB 3.91 ng / ml (VN <4.5 ng / ml), D - dimers 0.646 ug / ml (VN <0.024 ug / ml), cTnI 0.210 ng / ml (VN <0.09 ng / ml).

Pulmonary radiography: minimum left basal interstitial process.

Figure no. 1. Appearance on admission ECG

Electrocardiogram (ECG): ECG on admission: synusal rhythm 120/min, QRS axis at 110 grades, Q waves and ST elevation of 1 mm and T negative waves in DIII and aVF, aspect of RR’ in V1, S waves till V6, ST elevation of 1 mm with T negative waves from V1 to V5. ECG performed after one day of hospitalization: Q waves and negative T waves in DIII and aVF, amputated R till V6, S wave till V6, T negative waves V1-
V4, ST elevation in V3R-V4R.

**Diagnosis of this moment:** Acute coronary syndrome without ST elevation (with positive troponin level); in observation – inferior and left ventricular acute myocardial infarction. Acute respiratory failure. Smoke dependence.

There are at least two question marks regarding the followings:
1. The substrate of the respiratory failure, in the conditions in which the size of infarct, the clinical aspects and the radiological lung aspect are not in accordance with the advanced Killip class.
2. The discrepancy between the severity of dyspnea (according to the low oxygen saturation) and the lack of major ST-T changes (under the conditions described, the coronary pathology could not be classified as acute coronary syndrome with ST elevation).

**Doppler ultrasound** is practiced in a matter of urgency with the following conclusions:

Pulmonary hypertension with a systolic mean pulmonary artery pressure (PAP) of 65 mmHg, dilated right cavities with the sign of the letter "D", aspect of right ventricular acute solicitation with hypo/a kinetic, left cavities of normal size, without noticeable changes of kinetic, flexible and functional aortic and mitral valves, physiological gradient, normal size aorta with intact walls, pericardium with no liquid, inferior cava vein dilated, 26mm, with minimal change in inspiration. In addition, the pulmonary artery branch appears dilated: 28mm, with possible thrombosis before the bifurcation (relatively difficult to assess in these particular technical conditions).

**Figure no. 2. Echocardiographic aspects suggestive pulmonary thrombosis**

The chest CT examination reveals: MDCT chest exams, native and with contrast substrate intravenous, contiguous sections, extended to the upper abdominal region highlights: image of thrombosis in the pulmonary arteries bilaterally partially obstructive, which is extended to the branches in particular to the lobar lower pulmonary arteries bilaterally predominant right. Small single pulmonary nodule, with net shape located in the posterior right upper lobe, 1 cm diameter. There are no mediastinal pathological adenopathies revealed. No pleural collections. Liver and adrenal glands without pathological changes.

**Conclusion of the CT examination:** Bilateral pulmonary thrombosis. Solitary pulmonary nodule in the right upper lobe.

**Figure no. 1. CT images suggesting bilateral pulmonary thromboembolism**

Following the clinical and complementary exams, we outlined the **positive diagnosis:** Bilateral pulmonary thrombosis. Single lung nodule right upper lobe. Congestive heart failure NYHA II. Interstitial pneumonia. Operated stomach (for gastric ulcer). Hypertriglyceridaemia.

The problem of additional diagnosis of acute myocardial infarction (AMI) is now requested. The new definition of myocardial infarction states that "any amount of necrotic myocardium secondary to ischemia will be interpreted as myocardial infarction" (so there is no need for a substantial amount of necrotic myocardium). In the conditions in which the increases of troponin are patognomonic for mioctary necrosis, results that any isolated increase and/or decrease of troponin is sufficient to define myocardial infarction, recent or ongoing. At the end of the definition, it is specified that this dynamic
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biomarkers will be accompanied by at least one of the following criteria: symptoms, ECG changes, imaging criteria. Therefore, this definition is questionable: to what extent a transient increase of biomarkers means or does not mean a myocardial infarction? At this patient, type 2 myocardial infarction (due to decreasing supply of oxygen secondary to hypoxemia and hypotension) remains a possible diagnosis. But given the fact that the patient has coronary risk factors and that the coronarography has not yet been performed, the inclusion in the type 1 of myocardial infarction may not be totally abandoned. Finally, it is even possible that both can occur at the same time, under stress conditions and procoagulant status which are present in this situation at a patient with severe pathology, leading to acute progression of the coronary lesions (type 1 myocardial infarction) concomitantly with cell damage caused by hypoxia or hypoperfusion of noncoronarian etiology (type 2 myocardial infarction).

As a first step therapeutic regimen the thrombolysis with alteplase was initiated; the patient tolerated it well without bleeding or other adverse effects. Then, it was started the anticoagulation with heparin 5000 U in bolus, then heparin administered by injectomat, 1000 U/ hour for 7 days. After 5 days of heparin therapy, the therapy with oral anticoagulation (acenocoumarol orally 2mg/day) was initiated. At this scheme of anticoagulation scheme, there were also associated platelet antiagregants, gastric protective drugs, antibiotics, bronchodilators and oxygenotherapy.

The patients’ evolution, under this treatment was favorable, with net improvement of respiratory and haemodynamic status (the patient being discharged with SaO2 of 98%, BP 120/80 mmHg, HR 80/min, partial repermeabilisation of the pulmonary artery trunk and branches, the systolic PAP 35mmHg, with the persistence on the ECG of q waves and terminal phase changes. The long-term prognosis is relatively good, given the favorable evolution during hospitalization. Recurrence of the thromboembolism is still possible. Also, we consider appropriate some further investigations for defining the coronary status (like coronarography, angioCT or myocardial scintigraphy) as well as the hematological status (further consideration towards a possible thrombophelia).

The patient is discharged after 8 days of hospitalization, with the following recommendations: avoidance of smoking and strenuous efforts, combating venous stasis by avoiding prolonged immobilizations, dietary sodium restriction, treatment with: Clopidogrel 75 mg daily, Theophylline 200 mg/day, gastric protection. Because of his bleeding history (hemorrhoidal bleeding and secondary anemia with the need of transfusion 2 years ago, stomach operation for gastric ulcer), the recommendation for oral anticoagulant therapy at home is not without risks, but we consider it appropriate at this moment. The patient is discharged with the recommendation of a control thoracic tomography over 6 months, in order to follow the dynamics of the solitary pulmonary nodule from the right upper lobe which was found (which had all the characteristics of a benign tumor).

DISCUSSIONS

The key concept incorporated in the new definition of myocardial infarction is the interpretation of biomarkers in the clinical context. This was illustrated by presenting this case in which there is debated the common problem of the biomarkers increase interpretation in patients hospitalized for non-coronary reasons (1).

Which is the interpretation (conform to reality) of this situations?

1. Pulmonary thrombosis with false positive troponine?
2. Type 2 acute myocardial infarction?
3. Pulmonary and coronary thrombosis in the context of an eventual thrombophilia?
4. Coronary obstructive atherosclerosis, “validated” by hypoxemia?

A transient increase of the troponin level three times higher than the normal upper limit at a patient who developed chest pain prior to admission with ECG changes, has raised serious problems of differential diagnosis. Interpretation is difficult given the possibility of false positivity of troponin (even stress can cause severe isolated ascents of biomarkers). We are afraid not to miss the possibility of a severe diagnosis (like acute myocardial infarction). This case is the “happy” one because of the overlapping therapeutic indications for anticoagulants/fibrinolitics. But there are cited in the literature some false positive increases of troponin in cases of dissection of the aorta or bleeding strokes, where the establishment of the correct diagnosis is absolutely necessary in terms of therapy. Furthermore, patients hospitalized in intensive care units (with such false positive ascents of troponin), have often relative contraindication to anticoagulants, to the invasive cardiac maneuvers (or interventional procedures). Even non-invasive assessment of these patients may be limited and even when the coronarography is being practiced there is possible that it cannot be decide whether the investigated episode is one of acute coronary ischemia or is the myocardial injury in the presence of significant, but stable coronary artery disease. (3)

Finally, it is even possible that both can occur at the same time, under stress conditions and procoagulant status which are present in this patient with severe pathology, leading to acute progression of the coronary lesions (type 1 myocardial infarction) concomitantly with cell damage caused by hypoxia or hypoperfusion of noncoronarian etiology (type 2 myocardial infarction).

Beside these problems regarding the clinical and therapeutic decisions, this case illustrates the advantage of having at disposal the inclusion in type 2 myocardial infarction. It is also called into question the extension and severity of the diagnosis of myocardial infarction. Based on relatively small increases of troponin and specific changes in ECG, the size of the cardiac impact at this patient appears to be small, so that would require additional imaging techniques. But the terminology of myocardial type 2 is applicable, even if we use the adjacent details (as possibly or probably).

It is also known that troponin levels may be abnormal in the absence of symptoms, ECG changes or any evidence of myocardial dysfunction or structural damage. Indeed, transient ascent to very high troponin increases can be detected at about quarter to one third of the athletes, at the end of the race, but would not be highlighted any pathological consequence (4,5). However, excluding the healthy athletes, at patients seriously affected even small increases in biomarkers cannot be ignored. (6)

Type 2 of myocardial infarction is not equivalent with non-coronarian injury, also including coronary spasm or embolism. Even if these events are not related to atherosclerotic plaque both spasm and emboli are coronary events and have more in common with the unstable plaque than the myocardial injury induced by hypoxia, hypotension, myocarditis, etc. It seems more important to classify the acute myocardial events in coronarian and non-coronarian (especially in terms of therapeutic strategy). In this case for example, the coronary injury is also possible. Indications for anticoagulation and invasive intervention exists in this situation but would not be necessary if it will only be involved other mechanisms (hypoxia
or hypotension) (7).

The American guidelines referring to the unstable angina and non ST elevated acute coronary syndrome use the term of "secondary angina" in order to describe the enzyme increases precipitated by extrinsic coronary bed pathology. The term "secondary myocardial infarction" would have several advantages compared with that of type 2 myocardial infarction. The new myocardial dysfunction, clinically relevant often is missing, so the term "secondary damage" does not require the existence of significant lesions (as in myocardial infarction). In this way, this patient with pulmonary thrombosis will not be interpreted as myocardial infarction. It would be better to tell him that his tests indicate heart impairment due to the thrombemolism and that if further data will require, further testing will be performed. Finally it can be concluded that the myocardial injury is equivalent and will be treated as a positive stress test.

In conclusion, the increased troponin levels need further diagnosis and subsequent therapy investigations in this patient with pulmonary thrombosis. At patients who suffer myocardial infarction in the context of other diseases, the evolution and prognosis differ substantially compared with those who suffer myocardial infarction initially. U.S. guidelines for the treatment of patients with unstable angina and non ST elevated acute coronary syndrome promote an aggressive approach to these entities, without customizing the recommendations for type 2 myocardial infarction. Optimal therapeutic strategy for these patients remains somewhat uncertain. By including a new diagnosis it is possible to encourage the progress in the therapy of these patients and the accurate interpretation of troponin increases.

REFERENCES