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Case of recurrent pulmonary thromboembolism due to therapeutic non-compliance

Mihaela Anghele[1*], Liliana Dragomir[2], Virginia MARINA[3]

[1]MD. Mihaela ANGHELE: CLINICAL-MEDICAL Department, «Dunarea de jos» University of Galati, Faculty of Medicine and Pharmacy, Galati, Romania.

[2]MD. Liliana DRAGOMIR: CLINICAL-MEDICAL Department, «Dunarea de jos» University of Galati, Faculty of Medicine and Pharmacy, Galati, Romania.

[3]PH.D. Virginia MARINA: MEDICAL Department of Occupational Health, «Dunarea de jos» University of Galati, Faculty of Medicine and Pharmacy, Galati, Romania.

ABSTRACT

Pulmonary embolism occurs when thrombi enter the pulmonary arterial circulation. Most pulmonary embolisms are the result of deep venous thrombosis of the pelvic limbs, chest or pelvis, and, less commonly, the jugular veins or inferior vena cava.

Venous thromboembolism includes deep vein thrombosis and pulmonary embolism. It is the third most common cardiovascular disease, with a total annual incidence of 100-200 per 100 000 population.

INTRODUCTION:

Acute pulmonary embolism is the most serious clinical presentation of venous thromboembolism. Overall, pulmonary embolism is a major cause of mortality, morbidity and hospitalization. Mortality in pulmonary embolism depends on haemodynamic impairment, age and co morbidities.

The prognosis of patients with pulmonary embolism depends on two factors : underlying disease state plus diagnosis, and appropriate treatment. Approximately 10% of patients who develop pulmonary embolism die within the first hour, and 30% subsequently die of recurrent embolism.

CASE PRESENTATION:

In this presentation we present the case of a 49-year-old male patient without co morbidities, presented repeatedly to the Emergency Room for symptoms suggestive of pulmonary

***Correspondence to Author:**
Mihaela Anghele
MD. Mihaela ANGHELE: CLINICAL-MEDICAL Department, « Dunarea de jos » University of Galati, Faculty of Medicine and Pharmacy, Galati, Romania.

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thromboembolism, who benefited from life-saving therapies due to timely diagnosis and appropriate treatment, with subsequent favorable outcome.

CONCLUSIONS:

The particularity of the case is that, on the one hand, the thromboembolic event recurred in a short time, on the other hand, the evolution was favorable in both cases, with complete recovery of right ventricular function and disappearance of pulmonary hypertension, despite the fact that the patient was non-compliant with initial anticoagulation therapy. This was due to both early diagnosis and timely administration of appropriate treatment.

Keywords: Pulmonary thromboembolism, recurrent venous thromboembolism, non-compliance, treatment

1. Background

Pulmonary embolism (PE) occurs when thrombi enter the pulmonary arterial circulation. Most pulmonary embolisms are the result of deep vein thrombosis of the pelvic, thoracic or pelvic limbs, and less commonly in the jugular veins or inferior vena cava. Venous thromboembolism includes deep vein thrombosis and pulmonary embolism. It is the third most common cardiovascular disease, with a total annual incidence of 100-200 per 100,000 population [10,11].

Acute pulmonary embolism is the most serious clinical presentation of venous thromboembolism. Because PE is in most cases the consequence of deep vein thrombosis, most of the existing data on its epidemiology, risk factors and natural history are derived from studies that have examined venous thromboembolism as a whole. The incidence of PE can differ substantially from country to country, with variations likely due to differences in diagnostic accuracy rather than actual incidence.

Estimates based on an epidemiological model showed that in 2004, in six European Union countries (with a total population of 454400000), over 317,000 deaths were related to venous thromboembolism [11]. Of these cases, 34% presented with sudden fatal PE, and 59% were deaths resulting from PE that remained undiagnosed during life; only 7% of patients who died early were correctly diagnosed with PE before death. Since patients over 40 years of age have an increased risk compared to younger patients, and the risk roughly doubles every decade thereafter, an increasing number of patients are expected to be diagnosed with (and probably die from) PE in the future. [12]

In the United States, approximately 200,000 people will be diagnosed with new or recurrent PE each year, and twice as many will have a deep vein thrombosis without a confirmed PE. [13]

Venous thromboembolism affects approximately 1 to 500 people per year in North America, and approximately 1 to 300 people presented in DU will be diagnosed with the condition. Based on autopsy data, PE is the second leading cause of sudden, non-traumatic death in non-hospitalized patients. [14]

Overall, PE is a major cause of mortality, morbidity and hospitalization.

Mortality from PE depends on haemodynamic impairment, age, co-morbidities; it is 45% for PE with circulatory shock, but only about 4-5% of PE patients develop shock. In patients with hemodynamically stable PE, who are less than 50 years old, without other co-morbidities, the mortality is 1% [15].

Because the risk of recurrence is unknown in pa-

tients with pulmonary embolism, the decision about the duration of anticoagulant treatment is subject to individual preferences rather than objective recommendations.

2. Case presentation

In the emergency room of the Emergency Clinical Hospital of Galati, a male patient, 49- year old, without significant personal pathological history, was brought by an emergency crew of the Ambulance Service for the following reasons: altered general condition, fatigue, dyspnea of effort, with insidious onset of about 72 hours, with progressive character reaching dyspnea of rest, profuse sweating , pain in the left calf and ankle, caused, according to him, by repeated small traumas at this level.

From a clinical point of view, at the time of admission, we mention: altered general condition, pale, warm skin, no leg oedema, polypneic, no superadded rales on pulmonary auscultation, rhythmic, tachycardic heart sounds.

Vital function monitoring reveals: blood pressure -110/60mmHg, pulse- 147b/min, SpO2 88% on air, respiratory rate - 38 breaths/minute, temperature 37ºC.

Laboratory investigations include: D-dimer>5µg/ml and CK-MB 8,36ng/ml.

Electrocardiogram of 12 leads showed T wave inversion in precordial leads V1-V4 (sign of right heart overload) and classic S1-Q3-T3 appearance. At this point the suspicion of pulmonary thromboembolism is raised, which is why imaging investigations will be performed, consisting of transthoracic ultrasound (Figure 1-2-3) and chest computer tomography angiography with intravenous contrast medium (Figure 5).

Based on the clinical examination in conjunction with paraclinical and imaging investigations, the diagnosis of left massive pulmonary thromboembolism is established (Figure5).

The Pulmonary Embolism Severity Index is calculated using the score from the "European Guidelines for the Diagnosis and Treatment of Pulmonary Embolism", which in our patient's case had a value of 70 points, which means a low risk of mortality.

Analyzing a series of parameters and risk scores, we classified our patient in the intermediate-high risk of death class which is why treatment with:

Unfractionated heparin 5000 IU intravenous bolus, followed by continuous infusion at a dose of 1000 IU/h, under A control of partially activated thromboplastin time.

After 7 days, oral anticoagulation was switched to Thrombostop (Acenocoumarol) 4mg/day, with good evolution.

After 11 days, the patient was discharged cured, with normal electrocardiogram(Figure 7) and normal transthoracic cardiac ultrasound (Figure 10), without signs of pulmonary hypertension.

Recommendations at discharge include anticoagulant treatment consisting of Trombostop 2mg, ½ tb alternating with ¾ tb, under periodic INR control, maintaining calories between 2-3 and cardiological control over 3 months.

In evolution, the patient returns to the Emergency Department, after only 2 months, with the same symptoms. This time, however, he is accompanied by a team that performs a 12-lead electrocardiogram, which shows no changes specific to pulmonary thromboembolism, but only sinus tachycardia (Figure 8).

On admission to the emergency room, the general condition was serious, hemodynamically unstable, with the following vital parameters: blood pressure 90/40 mmHg, pulse 45 beats/minute, SpO2 <70% with additional O2 administration at 8l/min, respiratory rate 40 breaths/minute, Temperature 36.8ºC.

Given the pathological history, the suspicion of recurrence of pulmonary embolism is raised and administration of unfractionated Heparin 5000 IU

intravenous bolus is started, followed by continuous intravenous administration on the injectometer at a dose of 1000 IU/h.

Para clinically, we mention: NTproBNP 19.5pg/ml and cTnI 0.088ng/ml.

Due to the critical condition it was not possible to perform a thoracic CT angiography, and transthoracic ultrasound showed dilatation of the right ventricle, with a Right ventricle/Left ventricle ratio>1, flattened interventricular septum (Figure 13) and an increase in systolic pressure in the pulmonary artery - 74 mmHg. (Figure 14)

Calculating the Pulmonary Embolism Severity Index, we placed our patient in Class III, with moderate risk of mortality, because of the 100 points according the Pulmonary Embolism Severity Index, from the « European Guidelines for the Diagnosis and Treatment of Pulmonary Embolism ». Our patient's case had a value of 100 points, which means a low risk of mortality.

According to the recommendations of the « ESC Guidelines on the diagnosis management of acute pulmonary embolism », in terms of risk of death, we classified this patient as high risk.

It is decided to perform systemic fibrinolysis by administering Alteplaza 100mg intravenously during 2 hours, resume administration of unfractionated Heparin at a dose of 1000 IU/h, under APTT control. After 4 days, with a slowly favourable evolution, oral anticoagulation with Trombostop 4mg/day is started.

After fibrinolysis, changes specific to pulmonary embolism were observed on the electrocardiogram (Figure 9)and transthoracic ultrasound performed at 24 hours showed the presence of a pericardial fluid layer (Figure 15).

Twenty-four hours after fibrinolysis, the patient's condition allows chest CT angiography, which shows re-permeability of the left main pulmonary artery. (Figure 6)

The patient will be discharged after 2 months of hospitalization, healed, with complete recovery, so that, on transthoracic ultrasound, shows straight cavities of normal size, without signs of pulmonary hypertension and without pericarditis.

3. Discussion

The prognosis of patients with PE depends on two factors: the underlying disease state and appropriate diagnosis and treatment. Approximately 10% of patients who develop pulmonary embolism die within the first hour, and 30% subsequently die of recurrent embolism.

Mortality in acute pulmonary embolism differs according to the two forms of presentation: massive pulmonary embolism and non-massive pulmonary embolism.

Non-massive pulmonary embolism is defined as having a systolic blood pressure greater than or equal to 90 mm Hg. This is the most common form of pulmonary embolism presentation and accounts for 95.5-96% of patients. [16,17]

Hemodynamically stable pulmonary embolism has a much lower mortality rate due to treatment with anticoagulation therapy. In non-massive pulmonary embolism, the mortality rate is less than 5% in the first 3-6 months of anticoagulation therapy. The rate of recurrent thromboembolism is less than 5% during this time. However, recurrent thromboembolism reaches 30% after 10 years. [18]

Anticoagulation treatment decreases mortality to less than 5%. At 5 days of anticoagulation therapy, 36% of lung scan defects are resolved; at 2 weeks, 52% are resolved; and at 3 months, 73% are resolved. The majority of patients treated with anticoagulants do not develop long-term sequelae at further assessment. Mortality in patients with undiagnosed pulmonary embolism is 30%.

The risk of recurrent pulmonary embolism is due to recurrence of proximal venous thrombosis; about 17% of patients with recurrent pulmonary

embolism were found to have proximal deep vein thrombosis. In a small proportion of patients, the pulmonary embolism does not resolve; therefore, chronic thromboembolic pulmonary arterial hypertension results.

Increased plasma levels of natriuretic peptides (brain natriuretic peptide and N-terminal pro-brain natriuretic peptide) have been associated with higher mortality in patients with pulmonary embolism. [19] In one study, pro-brain N-terminal natriuretic peptide levels greater than 500 ng/L were independently associated with central pulmonary embolism and were a possible predictor of death from pulmonary embolism. [20]

4. Conclusion

To the patients with symptomatic pulmonary embolism, the risk of recurrence is unknown.

Recurrent venous thromboembolism can be prevented by treatment with oral anticoagulants. [1,2] Because these drugs can cause bleeding, [3,4,5] determining the optimal duration of anticoagulation involves balancing the risk of bleeding with the risk of recurrence. Pulmonary embolism is considered a consequence of deep vein thrombosis rather than a separate clinical entity. Most studies on the risk of recurrent venous thromboembolism have not distinguished between patients with deep vein thrombosis and PE [6,7,8,9].

But, what do we do when the patient is non-compliant to treatment? Hard to answer!

Thus, depending on the risk of mortality, in low-risk patients patient compliance and preferences will be assessed.

For this reason, in patients with pulmonary embolism, the decision on the duration of anticoagulant treatment is subject to individual circumstances rather than objective recommendations.

The particularity, of the case presented, is that: to this patient, the thromboembolic symptoms recurred shortly after the first pulmonary thromboembolic event and that the outcome was favourable in both cases, with complete recovery of right ventricular function and disappearance of pulmonary hypertension, despite the fact that the patient was non-compliant with initial anticoagulation therapy. This was due to both early diagnosis and the timely administration of appropriate personalized treatment.

The second peculiarity of the case is that the patient did not respond to standardized therapy within medical protocols.

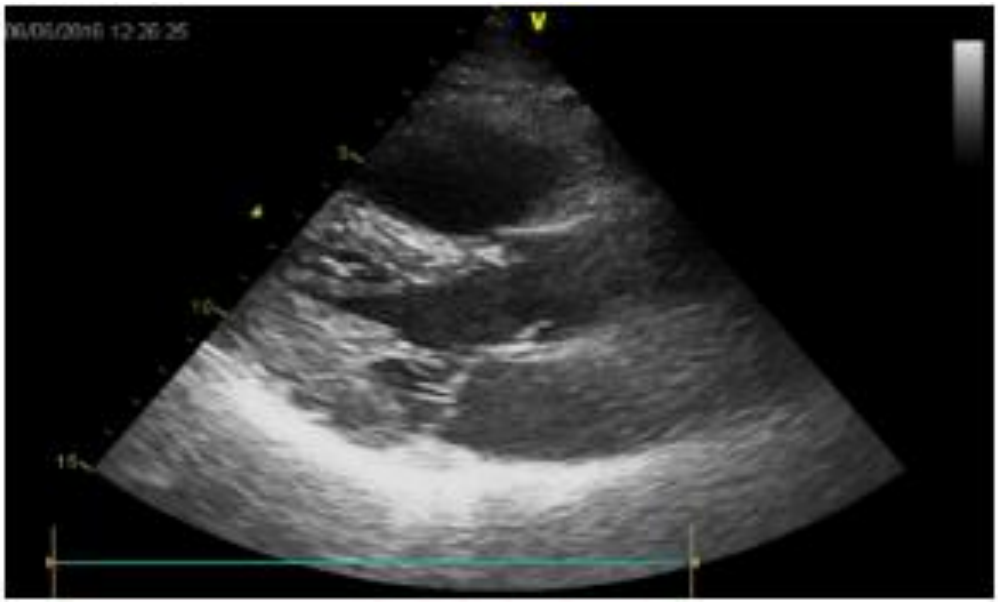

Figure 1: Transthoracic cardiac ultrasound - Dilated right ventricle

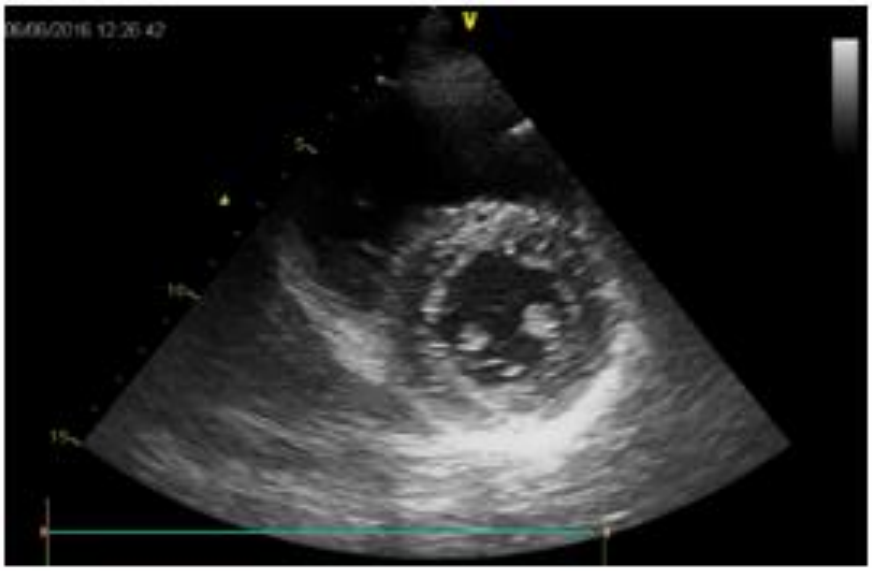

Figure 2: Transthoracic cardiac ultrasound - Dilated right ventricle

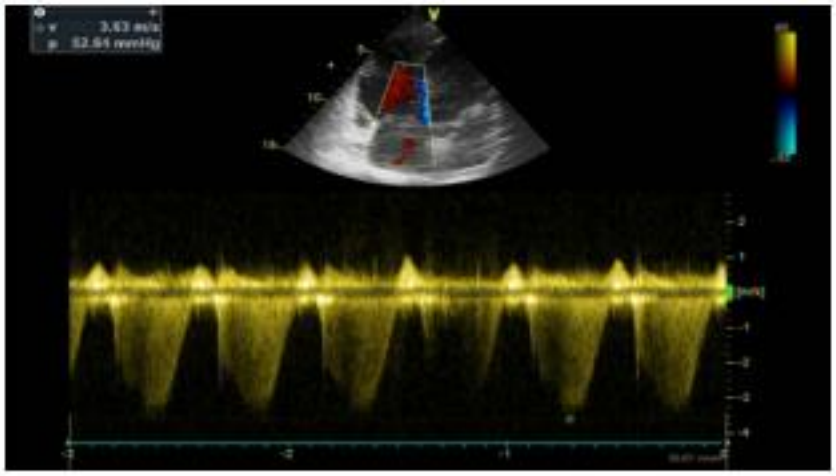

Figure3: Transthoracic cardiac ultrasound - systolic pressure in pulmonary artery 52 mmHg → pulmonary Hypertension

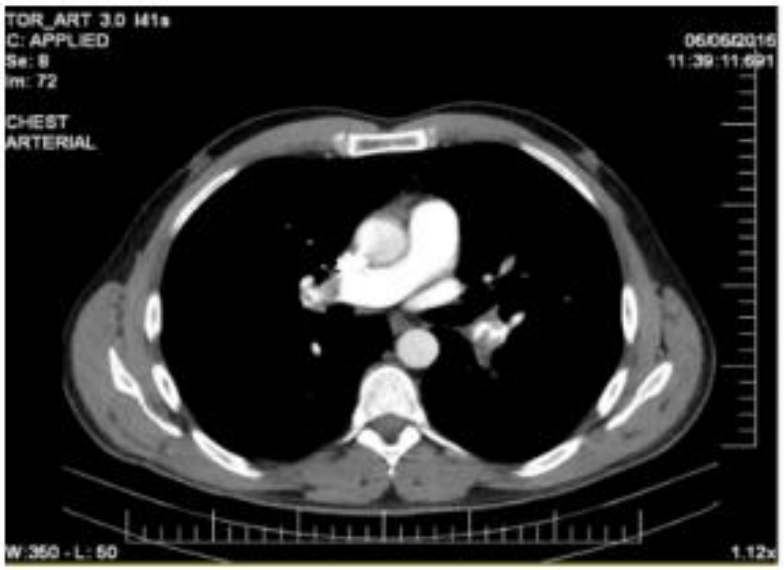

Figure 4: Chest CT angiography - no filling defects in the right main pulmonary artery or branches

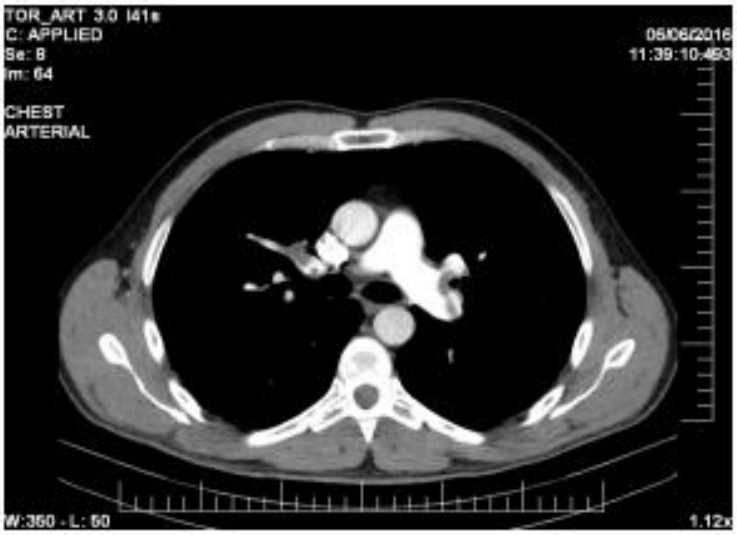

Figure 5: Chest CT angiography - total filling defect in left main pulmonary artery, amputated image of left main pulmonary artery → endoluminal thrombosis

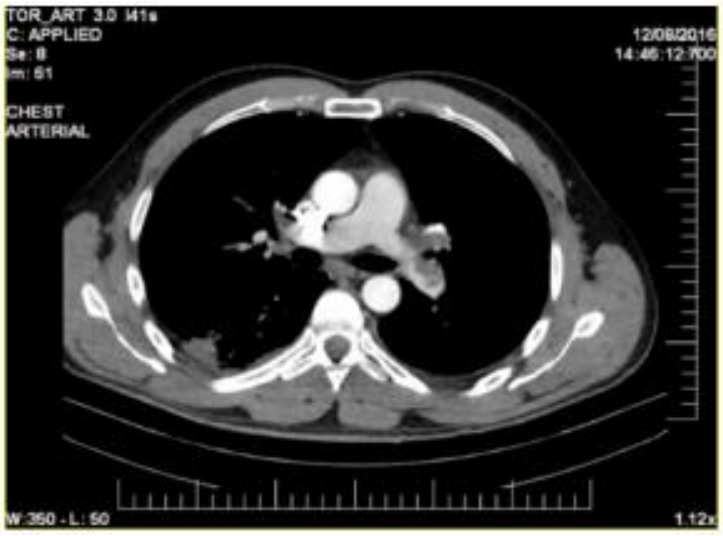

Figure 6: Thoracic CT angiography - left main pulmonary artery re-permeability

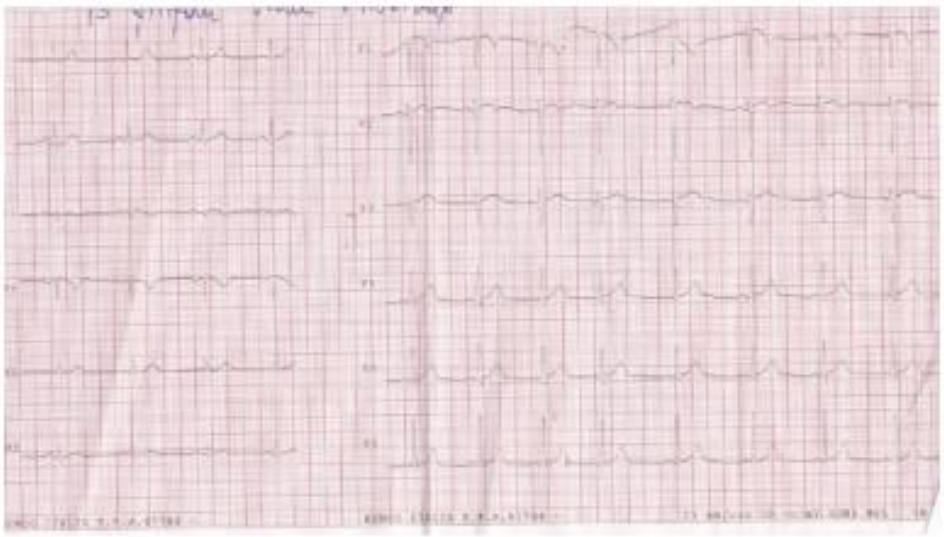

Figure 7: Electrocardiogram 12 leads at discharge – unchanged

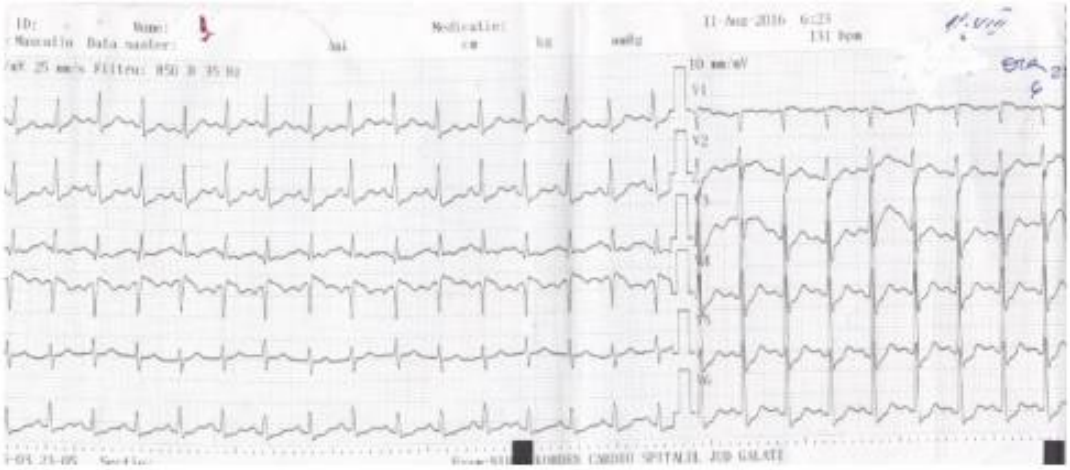

Figure 8: Electrocardiogram 12 leads - sinus tachycardia

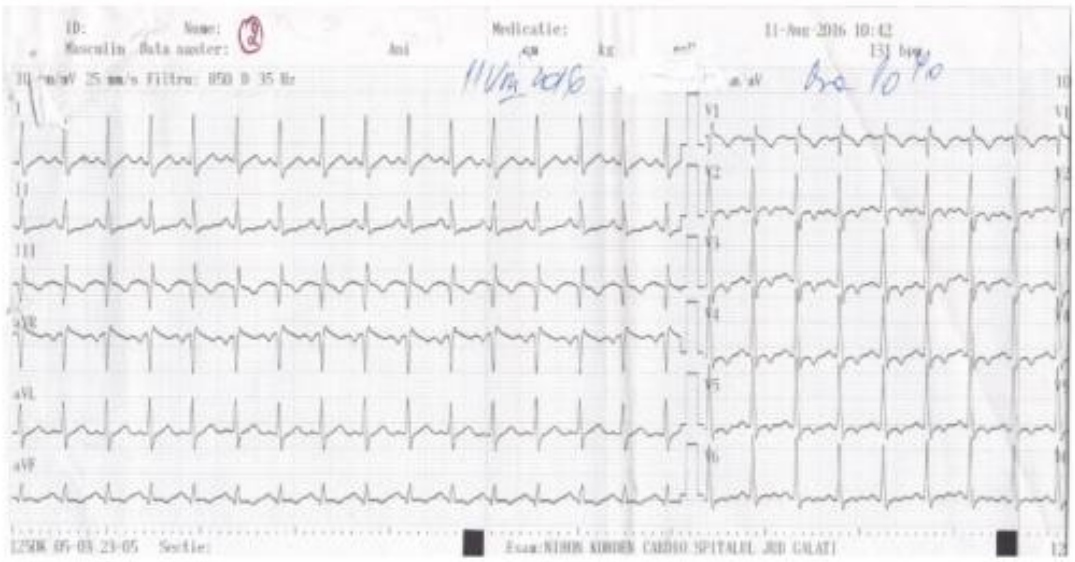

Figure 9: Electrocardiogram 12 leads after fibrinolysis

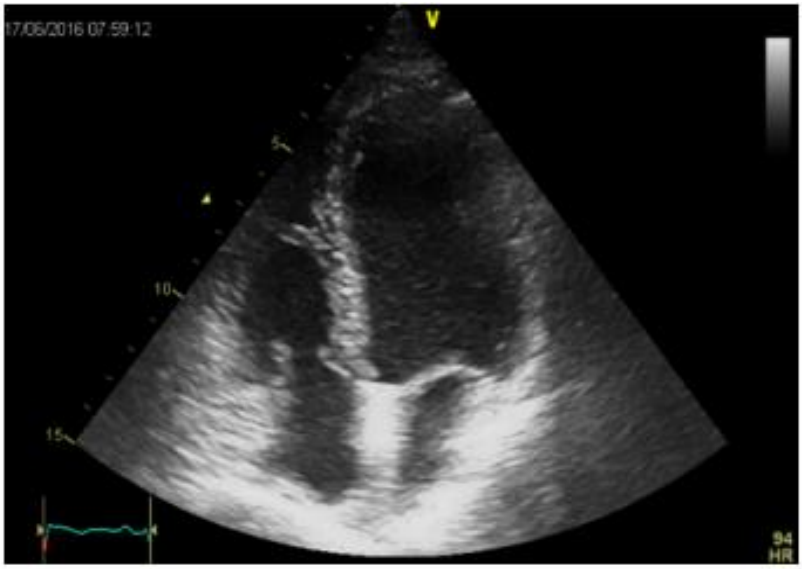

Figure 10: Transthoracic cardiac ultrasound at discharge – unchanged

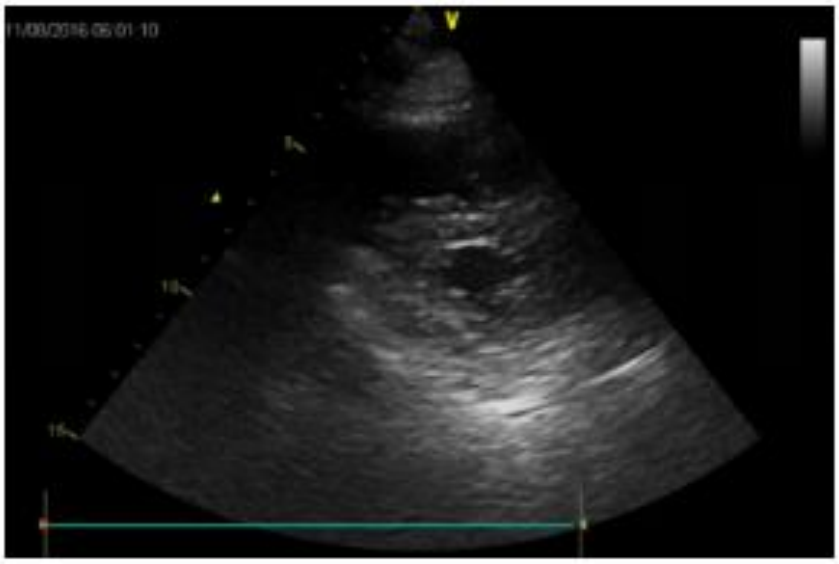

Figure 11: Transthoracic cardiac ultrasound - right ventricular dilatation

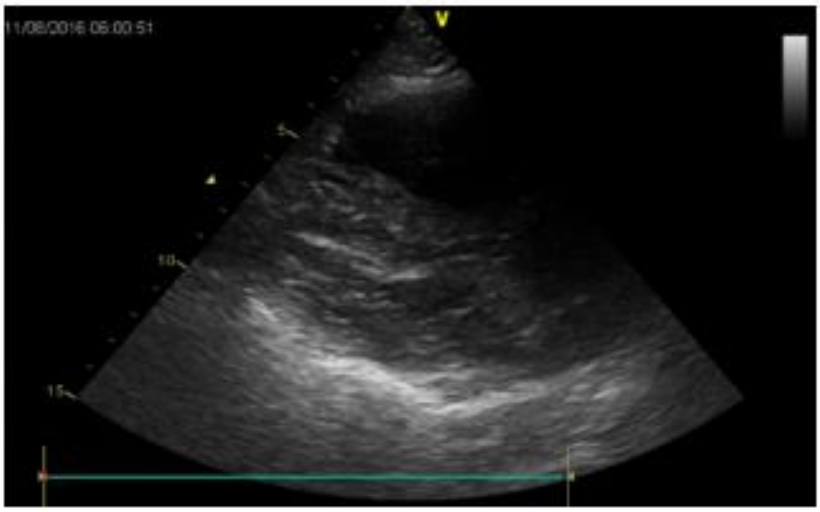

Figure 12: Transthoracic cardiac ultrasound - right ventricular dilatation

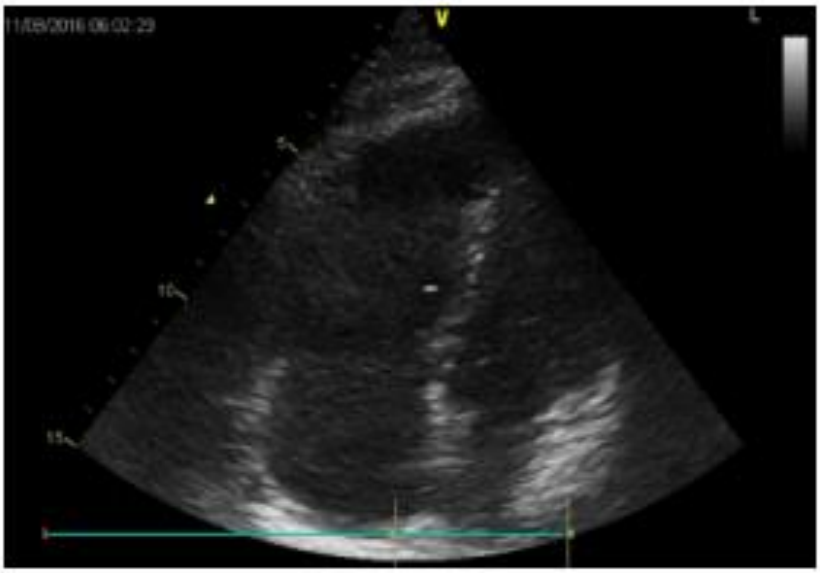

Figure 13: Transthoracic cardiac ultrasound - flattening of the interventricular septum

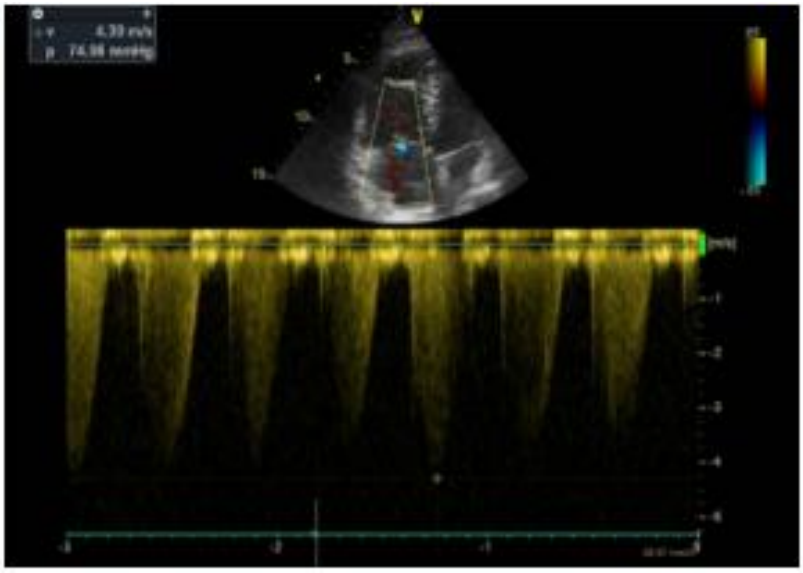

Figure 14: Transthoracic cardiac ultrasound increased systolic pressure in the pulmonary artery - 74 mmHg

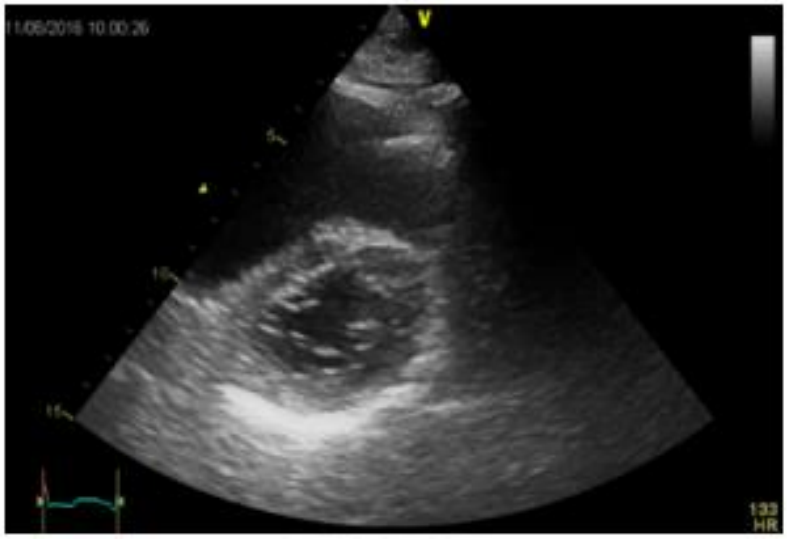

Figure 15: Transthoracic cardiac ultrasound - pericardial fluid slide

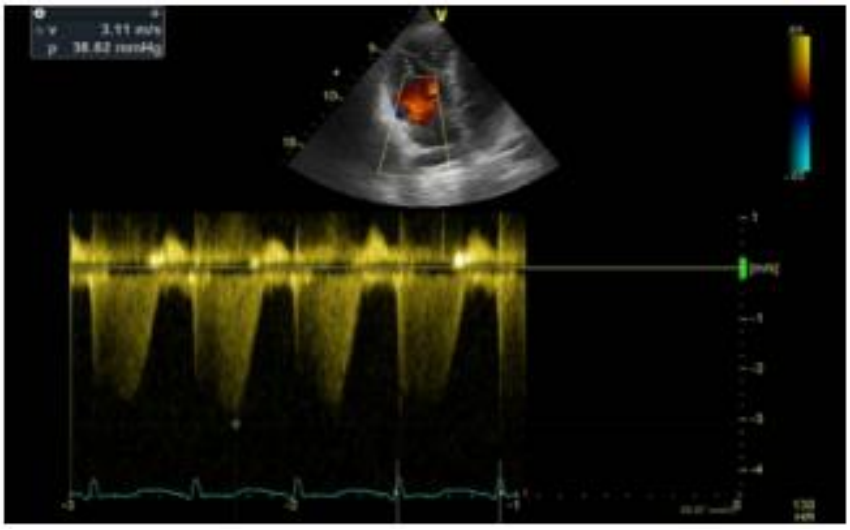

Figure 16: Transthoracic cardiac ultrasound post fibrinolysis, systolic pressure in the pulmonary artery- 38 mmHg

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No funding for the research

Ethical approval

This is not a research study. No ethical approval was necessary.

Consent

Consent for publication was obtained from patient before discharged.

Author contribution

Mihaela ANGHELE -the doctor who received the patient in the emergency room; collected the data and wrote the
clinical part of the article.

MARINA Virginia – wrote the final form of the article; corresponding author.

DRAGOMIR Liliana - collaborating physician

Registration of research studies

This is a case report. Is not a research study.

Guarantor

DRAGOMIR Liliana

ANGHELE Mihaela

Provenance and peer review

Not commissioned externally peer- reviewed.

Declaration of Competing Interest

The author decelerates that there is not conflict of interest regarding the publication of this article.

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