Case Report

The risk-benefit balance of anticoagulant treatment: case report

Andreea Teodorescu[1]

[1]*Department of Internal Medicine, Clinical Emergency Hospital of Bucharest, Bucharest, Romania*

Correspondence to: Andreea Teodorescu, Department of Internal Medicine, Clinical Emergency Hospital of Bucharest, Romania; e-mail: aandreeateodorescu@yahoo.com

Abstract: *A 76-year-old female presents at the emergency department with dyspnea and pleuritic, sharp right laterothoracic pain that started suddenly. Her medical history includes stage 2 hypertension, diabetes mellitus type 2, chronic obstructive pulmonary disease stage IV GOLD with home oxygen therapy, chronic pulmonary heart disease, diffuse interstitial lung disease with a previous episode of alveolar hemorrhage, chronic renal disease stage 2, and paroxysmal atrial fibrillation, for which she had a Watchman device implanted, taking into consideration her anticoagulation contraindication due to the previous alveolar hemorrhage episode. The biological findings reveal hypoxemia and hypocapnia, a positive D-dimer test, an inflammatory syndrome, mild hypopotassemia, acute decompensation of chronic renal disease, and a positive urine culture with Enterococcus faecium. Emergency thoracic computed tomography reveals bilateral pulmonary thromboembolism. Immediate parenteral anticoagulation and antibiotic therapy are initiated with favorable evolution. At discharge, concerning the risk-benefit balance of anticoagulation in a senior patient with multiple comorbidities, the anticoagulant therapy is changed to a novel oral anticoagulant for at least three months, with reevaluation needed after that period.*

Keywords: *thromboembolism, warfarin, stroke, atrial fibrillation.*

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Introduction

Thrombosis is the formation of a blood clot that causes complete or partial blockage within an arterial or venous vessel, limiting normal blood flow. In developing countries, this pathology is associated with the three most common causes of death: myocardial infarction, stroke, and pulmonary embolism [1]. The mainstay of treatment for this spectrum of pathologies is anticoagulation.

Jay McLean discovered the first anticoagulant, unfractionated heparin, in 1916; it was the only substance used until 1940, when Warfarin, a compound that inhibited the synthesis of vitamin K-dependent coagulation factors II, VII, IX, and X, become available [2]. After 1980, new research on the coagulation cascade led to the development of novel oral anticoagulants that target the X factor [2].

Case Presentation

A 76-year-old female, an ex-smoker, presents at the emergency department with dyspnea and a sharp right laterothoracic pain that started suddenly. The patient was discharged from our hospital one week prior to the current presentation, when she was treated for urosepsis.

Her medical history includes stage 2 hypertension, diabetes mellitus type 2, chronic obstructive pulmonary disease stage IV GOLD with home oxygen therapy, chronic pulmonary heart disease, diffuse interstitial lung disease with a previous episode of alveolar hemorrhage, chronic renal disease stage 2 and paroxysmal atrial fibrillation. After the first episode of atrial fibrillation, which was over ten years ago, she had a catheter ablation of the arrhythmogenic foci, with a recurrence of the arrhythmia two years later. In order to prevent thromboembolic events, warfarin was added to her medication at that time; however, an episode of diffuse alveolar hemorrhage confounded the case, so the anticoagulant therapy was discontinued. Considering the relative contraindication to oral anticoagulation, a Watchman device was implanted to prevent embolic events by blocking the left atrial appendage.

Her at-home medications include a beta blocker, a statin, a diuretic, an antiplatelet agent, and a bronchodilator.

The clinical examination reveals deterioration of the patient's general condition, atrial fibrillation with a rapid ventricular response of 120 beats per minute, arterial hypotension with a blood pressure of 100/50 mmHg, symmetrical vesicular breath sounds without additional rales, oxygen saturation of 80% in breathing room air, corrected to only 91% with oxygen mask with a debit of 15 liters/minute, and no signs of deep venous thrombosis.

The clinical examination of the abdomen shows tenderness in the epigastrium and right hypochondrium upon superficial palpation.

The biological findings include a positive D-dimer test, an inflammatory syndrome, significant leukocytosis with neutrophilia, mild hypopotassemia, a glomerular filtration rate of 67 ml/min/1.73 m^2 (calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation) and normal amylase and lipase levels. The arterial blood gas analysis reveals the presence of hypoxemia and hypocapnia. The urine culture is positive for Enterococcus faecium.

The chest X-ray reveals a fine reticular pattern with left-sided pleural effusion and an increased cardiothoracic ratio (Fig. 1).

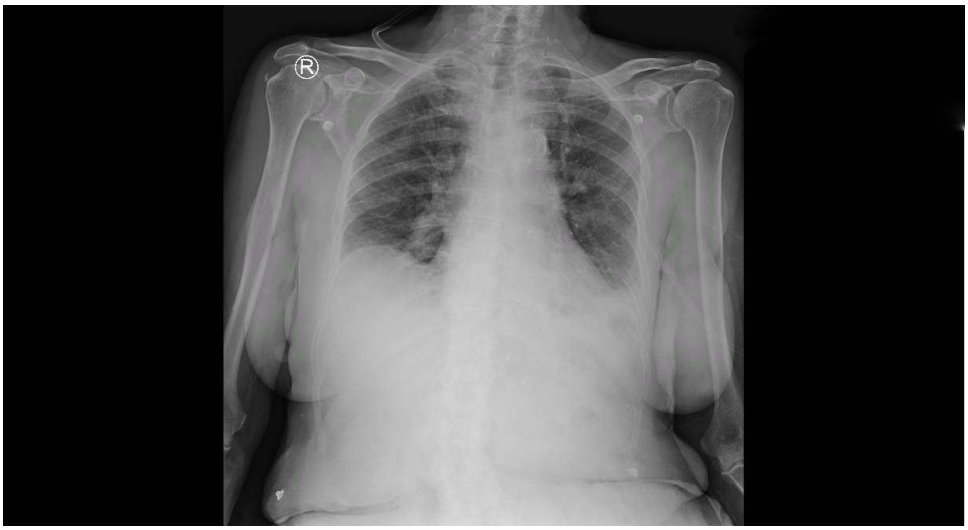

Fig. 1. Chest X-Ray image showing fine reticular pattern and left-sided pleural effusion

The electrocardiogram shows atrial fibrillation with a rapid ventricular response of 150 beats per minute, ST-segment elevation of 1 mm in aVR and diffuse ST depression.

The cardiac ultrasonography reveals a non-dilated left ventricle with concentric hypertrophy and preserved ejection fraction, a dilated right ventricle of 38 mm with tricuspid regurgitation jet gradient of 51 mmHg and dilated inferior vena cava. No pericardial effusion was present. Venous Dopper ultrasound confirms no signs of deep vein thrombosis. The abdominal ultrasonography is normal.

We continue the investigations with emergency thoracic computed tomography, which reveals a contrast agent filling defect in the terminal portion of both pulmonary arteries extending over the lobar ramifications. Other findings include bilateral pleurisy, a well-placed Watchman device, and aortic valve calcification (Fig. 2).

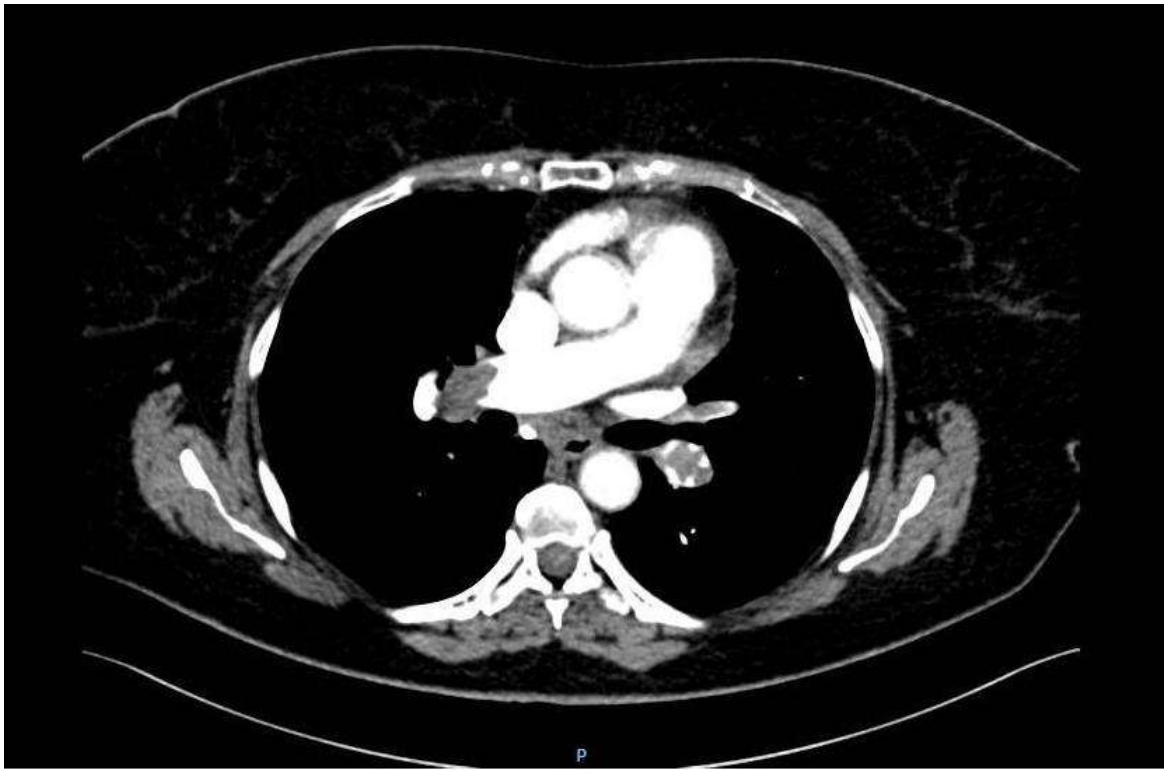

Fig. 2. Contrast-enhanced computed tomography image showing contrast agent filling defect in the terminal portion of both pulmonary arteries

The final diagnosis is acute respiratory failure due to bilateral pulmonary embolism and urinary tract infection. In addition to her previous doses of diuretics, angiotensin-converting enzymes, and bronchodilators, parenteral anticoagulant therapy and oxygen therapy were initiated, to maintain an oxygen saturation of 88-92%, antibiotic therapy, an increased dose of beta-blockers, and proton pump inhibitors. During the first few days of hospitalization, the patient develops severe hypotension, necessitating noradrenaline vasopressor support. Over the following days, the clinical and biological evolution is positive, the vasopressor support is discontinued, and the biological panel returns to normal. The oxygen requirement to maintain optimal saturation drops to 10 liters per minute.

At discharge, the parenteral anticoagulant is switched to a novel oral anticoagulant – Apixaban, in a low dose of 2.5 mg twice a day due to a creatinine level over 1,5 mg/dl and body weight of less than 60 kg and receives a recommendation for continuing aspirin, beta blockers, diuretics, angiotensin-converting enzyme inhibitors, statins, bronchodilators and home oxygen therapy. The oral anticoagulant is recommended for at least three months, with further need for reassessing the risk-benefit balance of anticoagulation in a senior patient with atrial fibrillation with a Watchman device implanted, acute pulmonary thromboembolism, and a history of diffuse interstitial lung disease and alveolar hemorrhage.

Discussion

The particularity of this case consists of the necessity of reassessing the risk-benefit balance of anticoagulation in a senior patient with multiple comorbidities.

While on anticoagulation therapy with warfarin in order to prevent thromboembolic events in atrial fibrillation, the patient presented diffuse alveolar hemorrhage which is an uncommon clinical condition that can be

caused by a coagulopathy induced by warfarin therapy. The narrow therapeutic window and multiple interactions with other medications might have been the cause [3].

Even though anticoagulation is the gold standard in preventing stroke and systemic embolization in atrial fibrillation, in cases of partial contraindication, as in our case with the alveolar hemorrhage, patients can benefit from the Watchman device, which closes the left atrial appendage and prevents further embolization. Studies show that this device is non-inferior to Warfarin in preventing embolic events [4]. Following implantation, anticoagulant management consists of Warfarin and Aspirin for 45 days, followed by dual antiplatelet therapy for six months, and then lifelong Aspirin [4].

As in our case, a new pathological event that might impact this management may be pulmonary thromboembolism. According to the 2019 Guidelines of the European Society of Cardiology on Acute Pulmonary Embolism, therapeutic anticoagulation for more than three months is recommended for all patients with pulmonary embolism as a Class I, Level A recommendation [5]. The significant, temporary, or reversible nature of risk factors influences the decision to continue oral anticoagulant medication after this period. Our patient had no significant risk factors, two moderate risk factors (respiratory failure and urinary tract infection one week prior to the occurrence), and three weak risk factors (aging, arterial hypertension, and limited mobility) as predisposing factors.

Venous thromboembolism, clinically presenting as deep vein thrombosis or pulmonary embolism, is globally the third most frequent acute cardiovascular syndrome after myocardial infarction and stroke [6]. A personal history of pulmonary embolism is one of the most significant risk factors for pulmonary embolism, as the risk is almost eight times greater in individuals aged 80 years than in the fifth decade of life [6]. Other recommendations to prevent a new episode include daily physical activity, which might also prevent muscular deconditioning in the elderly, weight management, avoiding infections and using compression stockings.

Conclusion

In conclusion, this case report emphasizes the importance of reassessing the risk-benefit balance of anticoagulation in a frail patient with multiple comorbidities. The efficacy of anticoagulation therapy in various pathologies remains debatable and is at the center of important decisions. Patient-centered medicine should lead us to provide the most individualized medical care, always considering the patient as an individual who requires a customized therapeutic approach.

Author Contributions:

A.T. conceived the original draft preparation. A.T. was responsible for conception and design of the review. A.T. was responsible for the data acquisition and for the collection and assembly of the articles/published data, and their inclusion and interpretation in this review.

Compliance with Ethics Requirements: *"The author declares no conflict of interest regarding this article".*

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References

1. Ashorobi D, Ameer MA, Fernandez R. Thrombosis 2022. Available online: https://www.ncbi.nlm.nih.gov/books/NBK538430/. Accessed on 10 May 2023.

2. Heestermans M, Poenou G, Hamzeh-Cognasse H, et al. Anticoagulants: A Short History, Their Mechanism of Action, Pharmacology, and Indications. *Cells* 2022;*11(20)*:3214.

3. Borjian S, Hakkak N, Borjian MA. A rare case of Diffuse Alveolar Hemorrhage (DAH) due to warfarin toxicity. *Rom J Intern Med*. 2020;58(1):35-39.

4. Magdi M, Renjithal SLM, Mubasher M, et al.The WATCHMAN device and post-implantation anticoagulation management. A review of key studies and the risk of device-related thrombosis. *Am J Cardiovasc Dis*. 202;11(6):714-722.

5. Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). *Eur Heart J.* 2020;21:543–603.

6. Raskob GE, Angchaisuksiri P, Blanco AN et al. Thrombosis: a major contributor to global disease burden. *Arterioscler Thromb Vasc Biol* 2014;34:23632371.