

## Severe Pulmonary Embolism with Negative D-Dimer-Testing

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Received: July 14, 2014 Revised: December 18, 2014

Accepted: December 23, 2014

Published online: February 10, 2015

### ABSTRACT

A 46 year old female Caucasian was admitted with shortness of breath on exertion, productive cough and hemoptysis few days of duration without any other chronic diseases. She had recent history of sigmoid diverticulitis treated with antibiotic and hysterectomy a year ago because of hypermenorrhoe. Vital signs were stable without any clinical signs of a deep venous thrombosis. The electrocardiogram (ECG) showed sinus rhythm with an incomplete right bundle branch block. Laboratory tests revealed a negative d-dimer (Latex-method). We assessed a contrast enhanced computed tomography scan (CT) of the chest illustrating surprisingly a severe pulmonary embolism in the right lung (main bronchus of the lower lobe). Several further examinations ruled out malignant diseases or favorable thrombosis. Treatment of the patient was established using low molecular weight heparin (subcutaneously administered), switched to rivaroxaban at the end of the in-hospital duration. Discharge was carried out after eight days in stable conditions. Anticoagulation was prescribed for three months. D-dimer testing is clinically established to rule out embolism/thrombosis laboratorial despite of arterial or venous location. This is a unique case, where the laboratorial testing failed to detect a severe pulmonary embolism while the sensitivity for

the d-dimer testing tends in general high. Clinically, the imaging approach (computed tomography scan of the chest) reflects “the gold standard” for pulmonary embolism in contrast to the d-dimer testing.

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**Key words:** Severe pulmonary embolism; Negative d-dimer testing; Hemoptysis

Dagkiran H, Atas R, Tomic I, Plachtzik C, Geisler T, Gawaz MP, Oberhoff M, Anger T. Severe Pulmonary Embolism with Negative D-Dimer-Testing. *Journal of Cardiology and Therapy* 2015; 2(1): 265-268 Available from: URL: <http://www.ghrnet.org/index.php/jct/article/view/1033>

### INTRODUCTION

Due to the high sensitivity of the d-dimer-test<sup>[1]</sup> - in general, the d-dimer test is used to demonstrate the specific diagnosis of pulmonary embolism or deep vein thrombosis<sup>[2]</sup>. In contrast, a negative d-dimer-testing rules out severe pulmonary embolism in high probability<sup>[1,2]</sup>. Here in this specific case report, we are demonstrating a 46 year old female Caucasian suffering acute severe pulmonary embolism identified through thoracic CT without elevated d-dimer levels in the laboratory. This case is important and needs to be reported due to the lack of elevated d-dimer testing even when severe pulmonary embolism occurred.

### CASE REPORT

A 46 year old female Caucasian was admitted with shortness of breath on exertion, productive cough and hemoptysis since few days without any other chronic diseases. She had recent history of sigmoid diverticulitis treated with antibiotic and hysterectomy a year ago because of hypermenorrhoe. Patient was still active on nicotine (2 pack years). Orally informed consent was obtained from the patient for publication of this case report and any accompanying images.

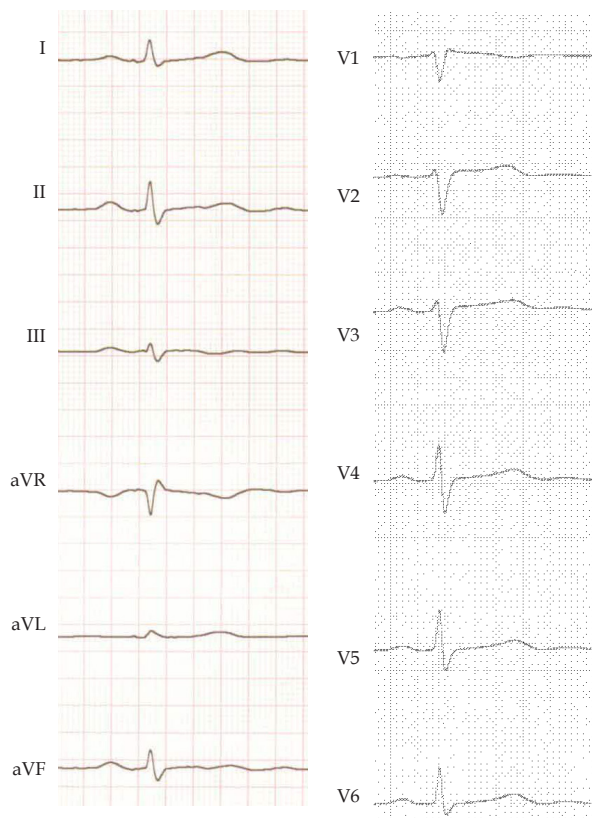
Clinically we found a woman in a good general condition and normal nutritional status, awake, oriented, her blood pressure 100/70

mmHg, her pulse 62/min, her respiratory rate increased 21/min, oxygen saturation of 97%, no pathologic murmurs, auscultation of the lungs reveals no bilateral wheezes and rales, unobtrusive physical examination.

Laboratory tests resulted negative for d-dimer-testing three times with the Latex-method (0.28/0.33/0.45), other laboratory values were within normal range. The ECG showed a sinus rhythm at the rate of 62/min., incomplete right bundle branch block, without excitation abnormalities (Figure 1). X-ray of chest revealed the contour of a diaphragm in regular and deep standing manner, compatible with a pulmonary emphysema, no pneumonia, mediastinum wasn't widened, no stasis and enlargement of the heart, aorta was according to age. The transthoracic echocardiography was completely with normal findings. For further acute analysis, we performed a contrast enhanced CT-scan of the chest and figured out an embolism of the pulmonary artery of the lower lobe without infarction, without round lesions or enlargement of the lymph nodes (Figure 2).

Further examinations (the sonography of deep veins and of complete abdomen; gynecological examination; the CT-scan of the abdomen; the gastroscopy and the colonoscopy) were completely without any pathological findings except for diverticulosis without signs of acute activation, two hemangiomas in the liver, a liver cyst in the left liver lobe.

The appropriate treatment for this patient without cardiovascular instability was anticoagulation with low molecular weight heparin, which was subcutaneously administered during the several examinations. During the in-hospital duration we switched the anticoagulation therapy to rivaroxaban per oral<sup>[3]</sup>. Hospital discharge was carried out after eight days in stable condition.



**Figure 1** ECG of the Patient during admission. Shown the regular sinus rhythm at the rate of 62/min., incomplete right bundle branch block, without excitation abnormalities as indicated in respectively ECG's.



**Figure 2** Contrast Enhanced CT-Scan of the Chest. Pulmonary embolism detected in the main bronchus of the lower lob of the right lung without signs of infarction, infiltrations or tumors. The black arrow marks the thrombosis in the right lower bronchus.

## DISCUSSION

D-dimer is a fibrin degeneration product and is generated during a fibrinolysis reflecting a diagnostic method for assessing coagulation activity<sup>[4]</sup>. Several independent methods to measure the d-dimer activity (quantitative production of d-dimer) such as ELFA, ELISA, Latex- and whole blood assays (Table 1) are established<sup>[5]</sup>. D-dimer-testing is used in the diagnosis of suspected thrombotic disorder (deep venous thrombosis, pulmonary embolism, disseminated intravascular coagulation) (Table 2). A negative d-dimer-test is clinically reducing the probability of thrombotic disorder in patients without severe diseases, anticoagulation therapy, recent surgery and pregnancy<sup>[4]</sup>. In addition there are many causes of quantitative high-level of d-dimer for example: heart diseases, heart attack, pneumonia, cancer, advanced age and infectious diseases (Table 2)<sup>[6]</sup>.

A pulmonary embolism is caused through an embolus in the pulmonary artery due to (i) high degree of coagulation<sup>[7]</sup>, high degree of cardiac thrombosis<sup>[7]</sup> or high degree of endothelial disorders of the pulmonary arteries<sup>[7,8]</sup>. A blood gas analysis in patients with pulmonary embolism shows hypoxemia and hypokapnia<sup>[9]</sup>. The ECG shows signs of right sided ventricular strain, SIQIII-type, complete right bundle branch block<sup>[10]</sup>. A contrast enhanced *CT-scan* of the chest is a special diagnostic method to find pulmonary embolisms with a sensitivity of 86-100%<sup>[11]</sup>. This disease is the most common unrecognized cause of death<sup>[9]</sup>. Approximately 95% of pulmonary embolisms derive from thrombosis in the vena cava inferior<sup>[1]</sup>. Typical clinical signs are: dyspnea/ tachypnea, tachycardia, cyanosis, chest pain, cough, hemoptysis, dizziness, sweating, syncope (in the short term)<sup>[12]</sup> The clinical condition ranges from asymptomatic to

threatening condition in cardiac shock<sup>[12]</sup>. There are several risks of pulmonary arterial embolisms: immobility, previous trauma, operations, smoking, varicose veins, congestive heart failure, female gender, pregnancy, contraceptives, obesity, advanced age, drying out and rare vascular anomalies<sup>[12]</sup>. If there is a presence of recurrent thrombosis pathological findings such as antiphospholipid syndrome, protein C and S deficiency ATIII-deficiency, polyglobulia, polycythemia vera and malignant diseases should be ruled out<sup>[6]</sup>.

Due to the high sensitivity of the d-dimer-test<sup>[1]</sup> - in general, the d-dimer test is used to demonstrate the specific diagnosis of pulmonary embolism or deep vein thrombosis<sup>[2]</sup>. Thereby, a negative d-dimer-testing rules out severe pulmonary embolism in high probability<sup>[1,2]</sup>.

## CONCLUSION

Because of the high incidence of early lethality in patients with acute pulmonary embolism reflecting clinically symptoms such as dyspnea/tachypnea, tachycardia, cyanosis, chest pain, cough, hemoptysis, a fast resolving therapy is very important. Therefore, clinically we demand an individual diagnostic concept. D-dimer-test is broadly used to determine pulmonary embolism or deep vein thrombosis. A negative d-dimer-testing rules out a severe pulmonary embolism with high probability<sup>[2]</sup>. Additionally, the sensitivity of the d-dimer-test depends on the used diagnostic method (Table 1) or further malignant and infectious diseases (Table 2).

**Table 1** Systems for d-dimer testing.

Method	Type	Manufacturer
Immunofluorescence immunoassay	ELFA	VIDAS <sup>®</sup>
Immunoabsorption assay microplate immunoassay membran-immunoassay	ELISA	Asserachrom <sup>®</sup> Nycocard <sup>®</sup> Cardiac Reader <sup>®</sup> Instant IA <sup>®</sup>
Latex-method		Tinaquant <sup>®</sup> STA-lia-test <sup>®</sup> HemosIL
Whole blood assay		SimpliRed <sup>®</sup> Simplify <sup>®</sup>

**Table 2** Causes of elevated d-dimer levels.

<b>Permanently increased values in blood</b>	aortic aneurysm
	other vascular aneurysm
	hemangiomas
	Kasabach-Merritt-Syndrome
	other vascular malformation
	several shunts
	malignancies in particular adenocarcinoma
	several hematological cancer
	venous or arterial thrombosis
	pulmonary embolism
	peripheral or coronary arterial embolism
	trauma
	recent surgery
<b>Acute increased values in blood</b>	burns
	hematoma
	aortic dissection
	sepsis
	severe infections
	erysipelas
	HELLP-syndrome
	hemolysis
HIT type2 (heparin-induced thrombocytopenia)	

Hence, we suggest primarily an imaging diagnostic method (CT scan of the chest) to determine pulmonary embolism in regard to the irregularities in the quantitative determination of d-dimer levels. A d-dimer-test alone is not sufficient.

## ACKNOWLEDGMENTS

We grateful thank the patient for the agreement to publish anonymously this case. Additionally, thanks to Ralph Felbinger, MD for the CT scans.

## CONFLICT OF INTERESTS

There are no conflicts of interest with regard to the present study.

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