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# PARANEOPLASTIC SYNDROME AS A POSSIBLE CAUSE OF PULMONARY THROMBOEMBOLISM IN A FEMALE PATIENT WITH NEPHROTIC SYNDROME -CASE REPORT

*Jasmina Mrgud (1,) Ana Jevrić (2), Vlastimir Vlatković (3), Branislav Gašić (3)*

(1) INTERNATIONAL DIALYSIS CENTRE ISTOČNO SARAJEVO; (2) JZU "DR MLADEN STOJANOVIĆ" PRIJEDOR; (3) UNIVERSITY CLINICAL CENTRE OF REPUBLIKA SRPSKA

**SUMMARY:** A 59-year-old female patient was admitted to the hospital due to suffocation, lower leg swelling, and general weakness. She had been treated previously with immunosuppressive therapy for several years because of focal segmental glomerulosclerosis with nephrotic syndrome. The expected therapeutic response was not accomplished. Upon admission, the following were determined in the laboratory: hypoalbuminemia, hyperlipidemia and nephrotic range proteinuria. X-ray of the lungs showed bilateral pleural effusion, because of which a pleural puncture was performed and which drained 800 mL of fluid. Tumor markers test, breast echosonography and mammography were performed, along with bone scintigraphy, which was done upon the recommendation of an oncologist. Mammography described microcalcifications bilaterally while bone scintigraphy showed pathological accumulation of radiopharmaceuticals in the V thoracic vertebra and sternum corpus, and III and IV ribs on the left. On the fifth day of hospitalization, there was a deterioration of patient's general condition with hypotension, tachycardia and angina, as well as an increase in D-dimer. On the ECG sinus rhythm, f 80 / min, low voltage in standard and unipolar leads. Upon the recommendation of a cardiologist, CT was performed according to the program for pulmonary thromboembolism (PTE), which showed submassive PTE. Low molecular weight heparin therapy was used, along with oxygen therapy with dopaminergics, bronchodilators, human albumin and plasma infusions, statins and transient treatment of hypervolemia by means of hemodialysis. The patient was hospitalized for 61 days due to multiorgan dysfunction. Breast magnetic resonance imaging was not performed due to the poor general condition of the patient. Most likely it was breast cancer with secondary deposits, which was recognized late. PTE, as a probable consequence of paraneoplastic nephrotic syndrome, was diagnosed and treated in a timely manner.

**Key words:** nephrotic syndrome; pulmonary thromboembolism; paraneoplastic syndrome

## INTRODUCTION

Pulmonary thromboembolism is a vascular disease that occurs as a complication of venous thrombosis and a thrombus breaking loose and reaching the lungs through circulation. The clinical picture also depends on the degree of occlusion and the number of affected pulmonary arteries (massiveness of the embolism). Annual frequency is 2-3 / 1000 inhabitants. The most common embolizations are proximal DVT 40%, VCS - 10-20%, distal DVT - 20-30%, upper extremities (CVC). Risk factors: trauma, orthopedic surgery (particularly hip and knee), major abdominal, thoracic, gynecological surgeries, vein surgery, cardiovascular diseases accompanied by cardiac decompensation and arrhythmias, septic conditions, long-term immobilization, childbirth, autoimmune diseases, as well as malignant diseases (pancreatic, breast, prostate and bronchus cancer).

## CASE REPORT

Material used from the patient's medical history, medical data from the hospital information system KIS-UCC of Republika Srpska, patient's letter of discharge from UCC of Republika Srpska.

Results: The patient had a positive family history of malignant diseases and a significant weight loss. Objectively of cachectic appearance. Cor: Heart action rhythmic, fast, tones quieter, no noise, TA 120 / 70mmHg. Pulmo: Ausculatory over the lungs bilaterally diminished respiratory murmur. DE: Mutual pretibial edema.

**Laboratory findings:**

- Haematologic parameters: Leukocytes $14,3x10^9$/L0; Erythrocytes $4,43x10^{12}$/L;

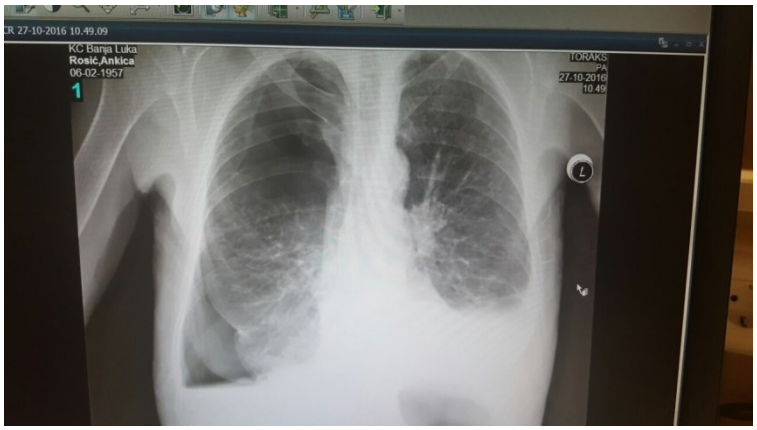
Haemoglobin 137 g/L, Thrombocytes 528 x $10^9$/L;

- Byochemical basic parameter: AST 38 U/L, ALT 26 U/L, LDH 300 U/L;, total serum proteins 41 g/L, albumins 21 g/l, cholesterol 4,6 mmol/l, triglycerids 3,9mmol//L,
- Cardio-byomarkers: CK 84 U/L; CK-MB 19 U/L; TnT 69,7; D-dimer 8,93;
- Blood Nitrogen substances and creatinine clearance: urea 11,9mmol/L, creatinin 101 ɥmol/l (eGFR by formula Cockcroft: 41,7ml/min, MDRD 51,7 ml/1,73$m^2$/min), uric acid 317 ɥmol/l,
- Serum electrolytes and acid-base status parameters: K 3,7, Ca 2,12, Na 140, Cl 100, P 0,94, ASTRUP: pH 7,482, cHCO3 26,8, ABE 3,6.
- Urine analysis: albumin+++, erythrocytes. 3-4; leukocytes: 6-10; BIURET 4,3 g/24h
- Tumor markers: CA 125: 586, CA 15-3: 98, CA 19-9: 1,2, CYFRA 21-1 2,8, CEA: 9,4, NSE: 9,4, HE4 241,5: , ROMA 90,7%.
- Hormone status: TSH 2,75; FT4 17,75; Thyroglobulin: 41,91; calcitonin 0,694;

We conclude that the patient had thrombocytosis, grade III renal insufficiency, normal mineral status, hypoproteinemia and hyperlipidemia, nephrotic range proteinuria, metabolic alkalosis, and elevated tumor markers for the breast and genital tract. Gynaecology ultrasound findings were normal. On the fifth day of hospitalization, the patient's clinical condition sharply deteriorated. as problems, she reported suffocation, chest tightness and dry cough. Objectively dyspnoeic at rest with central cyanosis present, tachycardic heartbeat, quieter tones, no murmur, TA 80 / 60mmHg. ECG showed sinus rhythm, f 80 / min, low voltage in standard and unipolar leads. Oxygen therapy was administered, Dobutamine 5mcg / kg / min (250mg Dobutamine in 250mL 0.9% NaCl), Clexane 0.6 ml 1x1 s.c; blood was taken for D dimer and cardiospecific enzymes.

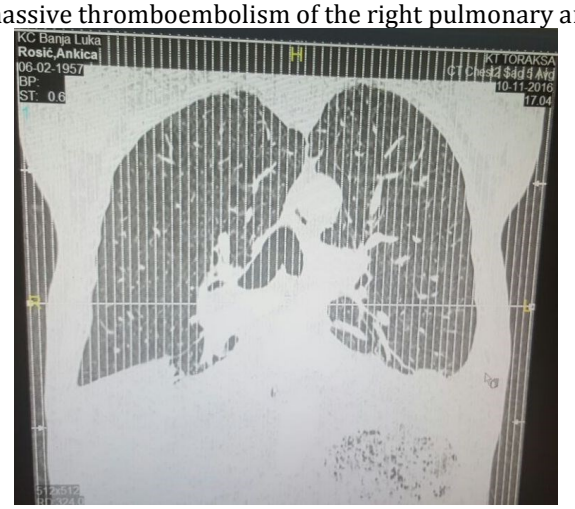
Chest X-ray reveals bilateral pleural effusion (pleural effusion) to the level of the V rib as well as an encapsulated effusion in the projection of the lower lung field to the right (Figure 1).

Figure 1. Chest X-ray (X-ray of the heart and lungs) shows bilateral pleural effusion up to V rib as well as encapsulated effusion in the projection of the lower lung area to the right

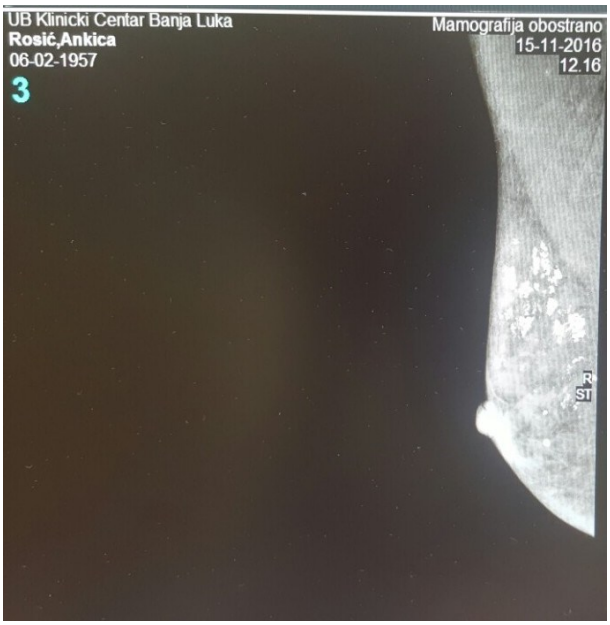


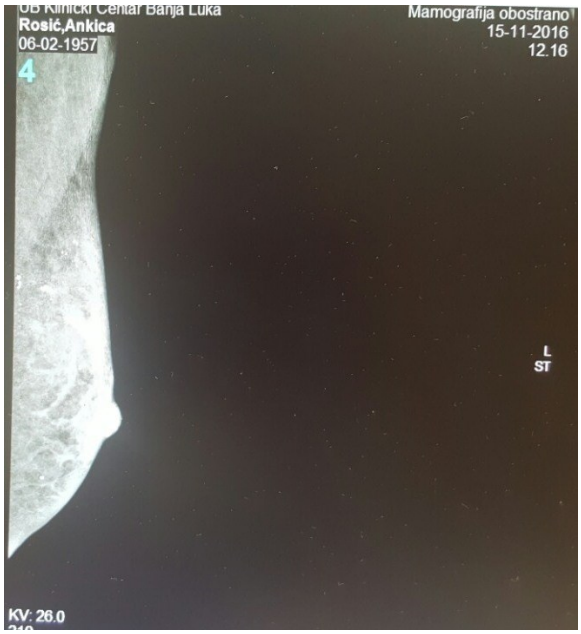

Computed tomography of the thorax (CT) according to the PTE program showed submassive thromboembolism of the right pulmonary artery (Figure 2). The defect in the lumen is differentiated - thromboembolism of the branch of the right pulmonary artery for the upper lung lobus with extension into segmental branches for the anterior segment as well as incomplete thrombosis of the intermediate branch of the right pulmonary artery. Pulmonary artery tree width 23mm, right pulmonary artery 21mm, left pulmonary artery 18mm. There is no consolidation or infiltration in the parenchyma shown. Posterobasal pleural effusion right about 5 cm wide, left up to 6 cm with consequent compressive atelectasis of the basal segments of the lower lung lobes.

Figure 2. Chest CT according to the PTE protocol:
submassive thromboembolism of the right pulmonary artery




**Figures 3. and 4.** Native mammography of both breasts and the axillary region: Bilaterally prepectoral and more pronounced in the right breast, multiple intraductal segmental calcifications are observed, completely filling the ducts. Among these amorphous calcifications, multiple individual microcalcifications of suspected malignant characteristics are observed




**DISCUSSION:**

Malignant tumors affect the body locally: by their mass, by infiltrative growth, by destruction of local tissue, by compression, through necrosis, bleeding, secondary infections. By systemically secreting hormones and other substances, they affect distant organs and systems or consume building material and energy. Paraneoplastic syndrome is a group of clinical disorders associated with a malignant disease and which are not a result of direct physical effects of the primary tumor or a metastatic disease [1]. It exists in 10-20% of patients, primarily in small cell lung, breast, ovarian cancer, and in malignant lymphomas; clinical manifestations differ. It is not related to the size of the primary tumor, it may occur late in the evolution of the disease or it may be the first sign of disease

recurrence. The exact mechanism of occurrence of paraneoplastic syndrome is not clear, it is assumed to be related to the production of biologically active substances by tumors (polypeptide hormones and cytokines) or the production of antibodies. Paraneoplastic syndrome includes nonspecific metabolic and endocrine manifestations of a tumor.

**Symptoms and signs of paraneoplastic syndrome may be:**

- **Systemic**: anorexia, cachexia, weight loss, fever, orthostatic hypotension.
- **Dermal**: acquired palmoplantar keratoderma, pemphigus vulgaris, pruritus.
- **Neurological**: peripheral neuropathy, encephalopathy, necrotizing myelopathy, cancer-associated retinopathy, vision loss, visceral neuropathy.
- **Endocrinal and metabolic**: nonmetastatic hypercalcemia, secretion of parathyroid-like hormone (more common in squamous cell carcinoma, microcellular carcinoma 10%), Sy. Cushing, hypercorticism (microcellular carcinoma 1.6-4.5%), the syndrome of inappropriate secretion of antidiuretic hormone, gynecomastia and galactorrhea, excessive secretion of gonadotropic hormone, carcinoid syndrome, hyperthyroidism, hyper and hypoglycemia, hypophosphatemia, hypouricemia.
- **Renal**: glomerulonephritis, tubulointerstitial disease.
- **Haematological**: anemia, leukocytosis and eosinophilia, leukemoid reaction, thrombocytosis and thrombocytopenic purpura.
- **Coagulopathies**: hypercoagulability, Troussean syndrome (more common in adenocarcinoma), thrombophlebitis, disseminated intravascular coagulopathy.
- **Collagen vascular**: dermatomyositis, polymyositis, vasculitis, systemic lupus erythematosus.
- **Bone and joint**: digiti hyppocratic, pulmonary hypertrophic osteoarthropathy (more common in adenocarcinoma).

The literature gives the nephrotic syndrome as a direct cause of thromboembolism due to loss of antithrombotic factors through urine and increased production of prothrombotic factor in the liver [2].

Hemodialysis patients have twice the incidence of pulmonary thromboembolism than patients without renal disease, and hemodialysis patients have a higher incidence of PTE than patients on peritoneal dialysis [3]. Vascular access infection, septic condition and use of temporary and permanent central venous catheters for hemodialysis contribute to this.

**CONCLUSION:**

The incidence of pulmonary thromboembolism has been underestimated due to unreliable clinical picture, diagnosis, and insufficiently accurate tests which would confirm clinically suspected PTE. What is required here is a multidisciplinary approach to the treatment because the real incidence is ten times higher than estimated. The patient most likely had breast cancer with secondary deposits but one which was detected late. PTE as a probable consequence of paraneoplastic nephrotic syndrome was timely diagnosed and treated.

Timely detection of the underlying disease, better survival and patients' better quality of life are possible through good cooperation of cardiologists, nephrologists, oncologists and pulmonologists.

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