

Pulmonary Tumor Thrombotic Microangiopathy: A New Paraneoplastic Syndrome?

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Key Words

Pulmonary tumor thrombotic microangiopathy · Paraneoplastic syndrome · Diagnosis · Adenocarcinoma

Abstract

This report, based on data from a clinical case, proposes that pulmonary tumor thrombotic microangiopathy, an underdiagnosed cause of pulmonary hypertension and death in patients with adenocarcinoma, is a paraneoplastic syndrome (PNS). Clinicians in general must be alert to the presence or development of PNS that may precede, coincide with, follow, or herald the recurrence or the primary diagnosis of malignancy since early recognition facilitates prompt diagnosis and treatment.

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Introduction

Clinicians in general must be alert to the presence or development of paraneoplastic syndromes (PNS) that may precede, coincide with, follow, or herald the recurrence or the primary diagnosis of malignancy since early recognition facilitates prompt diagnosis and treatment. PNS is defined as a ‘pathology caused by tumor cells, which systematically produce a large amount of hormones, growth factors, cytokines and a variety of specific symptoms’ [1]. Examples of PNS, associated with metabolic, mucocutaneous, hormonal and neurological symptoms [2], include dermatomyositis-polymyositis, Cushing syndrome, carcinoid syndrome, myasthenia gravis and syndrome of inappropriate antidiuretic hormone [3]. To this list of distinct PNS we would add a rare, fatal and likely underdiagnosed cause of pulmo-

nary hypertension known as pulmonary tumor thrombotic microangiopathy (PTTM) that is seen in patients with adenocarcinomas [4].

Case and Discussion

Herein, we report a case of PTTM in a 47-year-old female with triple-negative breast cancer. Initially, this patient who developed fever and tachycardia during treatment on a clinical trial was hospitalized to rule out/treat infection. The next day she developed dyspnea, hypoxemia, and ground glass opacities on a CT scan. The lack of a response to broad-spectrum antibiotics suggested an alternate diagnosis to pneumonia. On transthoracic echocardiography, which was ordered over 1 week later, the cause of her dyspnea was revealed to be acute cor pulmonale. Together with an elevated D-dimer and a prolonged prothrombin time in the setting of a V/Q scan with a low probability for pulmonary embolism a diagnosis of PTTM, a rare arteriopathy associated with coagulation cascade activation and vascular remodeling [5] was made.

Based on the pathogenesis of PTTM, which is related to the secretion of vascular remodeling factors [6] including vascular endothelial growth factor, fibroblast growth factor, and platelet-derived growth factor the plan was to treat the patient with sunitinib [7], a multitargeted tyrosine kinase inhibitor that blocks vascular endothelial growth factor and platelet-derived growth factor receptors. While she unfortunately died before treatment with sunitinib could begin, it is reasonable to assume that earlier diagnosis and treatment would have resulted in a better outcome.

Due to this paraneoplastic-like secretion of vascular and vascular smooth muscle mitogens, we suggest that PTTM meets the definition of a PNS. In the absence of a biopsy, echocardiographic and coagulation studies [8] are the diagnostic tests of choice.

As PTTM is a heretofore potentially unrecognized PNS, we suggest that the acute or subacute development of cor pulmonale should prompt an evaluation for new, recurrent, or worsening malignancy.

Statement of Ethics

The clinical research behind this report complies with the guidelines for human studies. Any subjects have given their informed consent and the study protocol has been approved by the relevant institute's institutional review board (IRB).

Disclosure Statement

The authors declare that they have no conflicts of interest to disclose.

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