Acute pulmonary hypertension as a symptom of Bard’s syndrome and pulmonary lymphangitis carcinomatosa – rare manifestation of malignant gastric cancer

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Abstract

Introduction. Acute pulmonary hypertension leading to right ventricular failure and circulatory collapse is usually caused by a pulmonary embolism. However, in extremely rare cases, similar clinical manifestations can be related to another diseases, such as lymphangitis carcinomatosa.

Aim. The purpose of this paper is to report on the case of a 29-year-old male patient presented with rapidly progressing dyspnoea.

Description of the case. The diagnosis of pulmonary embolism was made on the basis of echocardiographic signs of pulmonary hypertension and right ventricular (RV) dilatation, and the recommended therapy was introduced. On the suspicion of bronchopneumonia, antibiotics and steroids were applied. However, the previously stated diagnosis of pulmonary embolism was not confirmed by the angio-CT scan, which showed small diffusive lung parenchyma intra-biliary nodules (ground glass opacity) with the peripheral appearance of a tree-in-bud sign. Consecutive CT of pelvis and abdomen along with endoscopy revealed a metastatic gastric cancer with the presence of lymphangitis carcinomatosa and miliary dissemination to the lungs.

The presence of pulmonary metastases in the course of disseminated gastric cancer is known in literature as Bard’s syndrome.

Conclusion. Extrapulmonary malignancies, particularly gastric cancer, should be taken into consideration in differential diagnosis in patients with an acute right ventricular failure and nonspecific lesions in the respiratory system.

Keywords: Bard’s syndrome, malignant gastric cancer, pulmonary hypertension
Introduction

Acute right ventricular (RV) failure can be defined, as a rapidly progressive syndrome with a systemic congestion, resulting from an impaired RV filling, and/or reduced RV flow output. Most often, it is associated with increased RV afterload, or preload and consequently RV frequently among males. Military metastases of adenocarcinoma of the stomach, called also as Bard’s syndrome, were described by Samson et al. at 1962. Apart from single, or multiple tumors in the parenchyma of the lungs, metastatic lesions may manifest themselves as the lymphangitis carcinomatosa, and the pleuritis carcinomatosa. These kinds of metastases of gastric cancer share the feature, that the symptoms in the respiratory system dominate over the symptoms in the alimentary tract.

Description of the case

A 29-year-old patient without past comorbidities, was admitted to the Emergency Unit (EU) with dyspnoea, dry cough, shortness of breath, and reduced exercise tolerance. Such complaints occurred three weeks ago and increased over two days.

Examination revealed: pallor, tachycardia (110 bpm), tachypnoea (breathing rate average 30/min) with oxygen saturation of 92% and BP 110/70mmHg. The respiratory examination provided evidence of crackles at the base of both lungs. The ECG record was normal. The laboratory tests revealed significant D-dimer elevation with slightly increased level of troponin and CRP (Table 1). Symptomatic treatment was introduced: hydrocortisone i.v., fenoterol and ipratropium in nebulisation, supplemental oxygen with a slight improvement of patient’s condition.

Due to D-dimer increment transthoracic echocardiography (TTE) was performed. The following abnormalities occurred: right ventricle overload (RVd=34mm) RV>LV, ACT on the pulmonary valve 35mmHg, with moderate tricuspid valve regurgitation (VC=5mm), TAPSE 18mm. According to the 2014 ESC Guidelines, on the diagnosis and management of acute pulmonary embolism, the CT angiography of pulmonary arteries was requested. Meanwhile, the patient had been admitted to the Intensive Care Unit of Cardiology Department with preliminary diagnosis of not high-risk pulmonary embolism, and echocardiographic symptoms of acute pulmonary hypertension.

The CT angiography of pulmonary arteries revealed widening of the pulmonary trunk (approx. 28.5 mm), and arteries (left-23 and right-22mm). Narrow contrast deficits were observed only in more peripheral pulmonary arteries at the level of the lower lobes.

Furthermore, the results of the CT scan presented diffused, small intralobular nodules (ground glass opacity) in lung parenchyma with the peripheral appearance of a tree-in-bud sign. The presence of nonspecific findings in the lower lobes, directed differential diagnosis of allergic alveolitis, interstitial disease, or others. The notes included also several abnormalities such as the slightly enlarged lymph nodes in the lung cavities, enlarged sub-nodal nodes, the right lower lobe bronchus and lymph nodes in the mesenteric fat tissue, up to 15 mm.

The treatment was enriched by low molecular weight heparin injections in therapeutic doses, fluids and supplemental oxygen with a slight improvement of patient’s condition.

The imaging examination with ultrasonography of lower limbs veins, thyroid gland and abdomen was established. Following pathological findings were described: asymmetrical widening of gastric antrum, cervical lymphadenopathy, a small normoechogenic tumor in the left lobe of the thyroid. It needs to be mentioned: viral markers, including HIV, HBV and HCV, EBV, cytomegaloviruses, were non-reactive for serology. Other scans appeared to be negative for atypical infections such as: Mycoplasma pneumoniae, Chlamydiophila pneumoniae, and Legionella pneumophila. In addition to that, blood and sputum cultures, cancer markers as CA 125, CA19-9, were negative as well.

Other, more relevant laboratory tests results, are presented in the Table 1.

Table 1. Laboratory results of patient

<table>
<thead>
<tr>
<th>Test</th>
<th>At the day of admission</th>
<th>Fifth day of hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP mg/l [0.0–5.0]</td>
<td>29.3</td>
<td>17.6</td>
</tr>
<tr>
<td>WBC 10^3/µl [4.00–11.00]</td>
<td>8.23</td>
<td>14.6</td>
</tr>
<tr>
<td>D-DIMER ng/ml [0–500]</td>
<td>14300</td>
<td>3795</td>
</tr>
<tr>
<td>NT-proBNP pg/ml [0–125]</td>
<td>409</td>
<td>5444</td>
</tr>
<tr>
<td>TNThs pg/ml [3.0–1.4]</td>
<td>90.32</td>
<td>31.01</td>
</tr>
</tbody>
</table>

The patient’s condition improved slightly after the symptomatic treatment composed of inhaled bronchodilators, intravenous steroids, diuretics. Moreover, wide spectrum antibiotics were administered intravenously. On the fourth day of hospitalization, the patient’s condition deteriorated, and sudden respiratory and cardiac arrest occurred. Resuscitation activities (CPR) were successful. Full consciousness returned however symptoms
of hypoxemia (oxygen saturation up to 70%), and tachycardia (150/bpm) remained.

The TTE presented significant right-sided ventricular overload, with features of severe pulmonary hypertension, and tricuspid valve gradient up to 90mmHg (Fig. 1, 2).

Repeated chest angiography revealed widening of the pulmonary trunk up to 31mm, without central or peripheral embolization.

Further diagnostic process, enriched by abdomen and pelvis contrast CT, confirmed pathological findings in the area of the gastric antrum (Fig. 3).

The diffused lymphangitis was found in the following areas: the antrum (18mm), pylorus (15mm), lesser curvature of the stomach, hepatic hilum, mesentery, near the celiac trunk and aorta (13mm).

Gastroscopy uncovered gastric mucosa infiltrations in the area of greater curvature of stomach. Histopathologic study of preantral part of stomach demonstrated poorly cohesive carcinoma, with inclusion of signet ring cell carcinoma. (Fig. 4)

On the sixth day of hospitalization, a respiratory and a cardiac arrest occurred. The resuscitation was unsuccessful.

The diagnosis was established based on the clinical presentation and investigations.

The cause of the death was cardiogenic shock due to acute RV failure, as a consequence of poorly differentiated carcinoma of the stomach with diffuse pulmonary metastasis, and lymphangitic carcinomatosis.

Discussion

The term pulmonary lymphangitic carcinomatosis (PLC) was first coined by Troisier in 1873 to describe a condition of diffuse infiltration of the lymphatics of both the lungs by malignant cells. The analysis of literature data performed by Bhattacharya et al. relates to such condition with greater predilection for males (60:40), and has a greater propensity to younger population. The most common locations of the primary tumor are: lungs, breasts, pancreas, stomach and prostate. Li Zhuang explains the pathologic features of PLC as a consequence of primary liver cancer.
Physiologically, cancer in the mediastinal and pulmonary hilar lymph nodes may obstruct lymphatic drainage, resulting in retrograde migration of cancer cells into terminal lung tissues via lymphatic vessels, or anterograde migration of cancer cells in the pleura into the pulmonary hilar lymph nodes through intrapulmonary lymph vessels. Furthermore, fibrosis of an interstitial tissue of the lungs can be interpreted as: intensive inflammation various in degree, and fibrosis of an interstitial tissue of the lungs with further disorders of the perfusion to ventilation ratio. Such malignancy with invasion into deep penetration into the submucosa, lymphatics or venules is associated with an increased risk of nodal metastases. A signet ring histology is an independent predictor of poor prognosis in gastric adenocarcinoma. Poorly differentiated adenocarcinomas, and signet-ring cell carcinomas found in the intra hist-pat study, were classified as “undifferentiated histological types”, according to the Japanese classification of gastric carcinoma. Such malignancy with invasion into deep penetration into the submucosa, lymphatics or venules is associated with an increased risk of nodal metastases. Signet ring histology is an independent predictor of poor prognosis in gastric adenocarcinoma.

Interstitial lung disease (ILD) encompasses a large, and diverse group of pathological conditions that share similar clinical, radiological and pathological manifestations with different aetiologies. Results of CT scans, described as the ground glass with a tree-in-bud sign, can be interpreted as: intensive inflammation various in degree, and fibrosis of an interstitial tissue of the lungs or very rarely miliary neoplastic pulmonary metastases.

On the microscopic level, such metastases are characterized by the presence of single neoplastic cells or their clusters in the lumen of blood and lymphatic vessels of the lungs sometimes accompanied by thrombi consisting of thrombin and platelets. Pathophysiologically lesions lead to constriction of the vessels lumen, thus leading to perfusion disorders of the large area of the lungs with further disorders of the perfusion to ventilation ratio.

In the presented case, narrow contrast deficits were observed only in more peripheral pulmonary arteries in CT scan on the day of admission. The second CT scan did not reveal microembolisms. Moreover, discovered significant decrease of D-dimer, probably, was a result of the heparin treatment, but it was not associated with a clinical improvement.

According to Murry et al. disseminated pulmonary tumor embolism should be suspected in a patient with cancer who has dyspnoea, hypoxemia, and unexplained PH, and is a common autopsy finding in patients with cancer, but it is rarely diagnosed premortem. Contrast-enhanced CT, and pulmonary angiography are not helpful to detect microembolisms, and their negative predictive value is low. In order to confirm the diagnosis of microscopic pulmonary tumor embolism, tissue must be obtained by either open-lung or transbronchial lung biopsy. Such a method was refused due to terminal condition of the patient. However, based on the progression of the disease and the described results of the imaging, reference can be made to those with a related course. Treatment of low-density heparin was included due to primary suspicion of pulmonary embolism based on radiological, and echocardiographic examination. Dexamethasone, and antibiotics were added as the treatment method of systemic connective tissue disease and bronchopneumonia. Thus, surgical treatment remains the treatment of choice for early stage signet ring carcinomas.

Currently, there are no proven effective treatment strategies for PLC. Based on recent studies chemotherapy with a regimen of oxaliplatin, leucovorin and 5-fluorouracil, did not lead to life extension in the case described by Gilchrist et al. Despite that, there are case reports of platinum-based chemotherapy leading to transient remission. Patients with PLC included in the study of Densteed et al. (six patients with an average age 26 and primary gastric tumor), had a mean survival time of 22 days after their first admission to hospital.

Conclusion
Poorly differentiated cancer is believed to show poor prognosis and aggressive behavior. Presented manifestation of malignant gastric cancer with abrupt progression, RV failure with symptoms of pulmonary hypertension, can be a consequence of respiratory and lymphatic systems affection by metastases. Treatment options in high severity are limited and not associated with life extension.

Followed conclusions can be made after analysis of similar, described in literature cases, associated with the microembolisms or pulmonary lymphangitis carcinomatosa or heterogeneous lung metastases.

Finally, extrapulmonary malignancies should be considered in patients with symptoms of acute right ventricular failure and nonspecific lesions in the respiratory system.

References


