Introduction

Chronic thromboembolic pulmonary hypertension is a rare and serious medical condition that is severely underdiagnosed. As symptoms including shortness of breath, chest discomfort and fatigue are non-specific; the diagnosis can be difficult and is often missed. However, chronic thromboembolic pulmonary hypertension...
hypertension is potentially curable by means of pulmonary endarterectomy performed at experienced centers [1]. In this work authors retrospectively evaluated incidence, clinical pictures and difficulties in diagnosis and treatment of patients, in whom chronic thromboembolic pulmonary hypertension was confirmed.

**Methods and Results**

In the period of the time from January 1996 to December 2014, at the Department of 1st. Internal Clinic, University Hospital Martin, there were totally hospitalized 54 502 patients, 570 [270 female] with acute pulmonary embolism [PE], who formed 1,05% from total amount of hospitalized patients. In this period, 11 patients were diagnosed with chronic thromboembolic pulmonary hypertension [CTEPH] forming 1,93% of patients with the diagnosis of PE. Diagnosis of CTEPH was confirmed by ventilation-perfusion [V/Q] lung scintigraphy, computerized tomography angiography of lung [CTPA] and/or pulmonary angiography and right heart catheterization. All 11 patients had pulmonary hypertension [PH] confirmed by transthoracic echocardiography. At the ECG, 9 of them had sinus rhythm and 2 of them had atrial fibrillation. Signs of right ventricle hypertrophy and overload at the ECG had 9 of 11 patients, these changes were assessed as ischemic or non-specific, right ventricle hypertrophy was overlooked in all 9 patients at the beginning of the hospitalization. V/Q lung scintigraphy was positive in all 11 patients, and CTPA performed at our hospital were positive in 8 of 11 patients. Levels of D-dimers in all 11 patients were in physiological range. A history of acute pulmonary embolism had 7 [4 female] of 11 patients, incidence of CTEPH after acute PE was 1, 23 % and history of acute PE in 63,6% of CTEPH patients. From 3 months to 2 years had passed since acute PE to first symptoms of CTEPH and from 6 month to 6 years had passed since first symptoms to diagnosis CTEPH was confirmed. In the acute phase of PE, 5 patients were treated with systemic thrombolysis, 2 of them with anticoagulation therapy, all 7 patients after PE continued with oral anticoagulation therapy [warfarin] until the diagnosis of CTEPH was confirmed. 4 of 11 patients had no history of PE and deep venous thrombosis. From Risk factors of venous thromboembolism and CTEPH 10 of 11 patients had elevated factor VIII, 3 of 11 patients had positive anti phospholipid antibodies, 2 patient had low level of protein C, 1 patient elevated homocystein, 1 patient had positive family history of CTEPH and 1 patient was after splenectomy. Major symptoms of the patients with CTEPH before admission to hospital were progressive dyspne, chest pain and haemoptysis. Patients were admitted to hospital with diagnosis as suspected recurrent PE [4 cases], acute coronary syndrome [3 cases], heart failure [2 cases], progressive dyspne in differential diagnosis [2 cases]. 3 patients underwent pulmonary endarterectomy [PEA], 2 patients refused consultation in specialized center with expertise in the medical and surgical management of CTEPH, 2 patients was not suitable for PEA because of their polymorbidity, 3 patients were classified as NYHA II and are monitored by cardiologist and they are planned for consultation in specialized center with expertise in the medical and surgical management of CTEPH for our region is in Prague [Czech Republic]. Basic information about our patients are summarized in the Table 1 below. Figure 1 show ECG from patient No: 1 before PEA, Figure 2 show ECG from the same patient 4 month after PEA. Figure 3 show transthoracic echocardiography from the same patient before PEA and Figure 4 transthoracic echocardiography 4 month after PEA. Figure 5 show V/Q scan from the same patient before PEA, and CTPA performed at our hospital was negative.
Discussion

No specific genetic mutations have been linked to the development of CTEPH. Even if more recent papers suggest that the prevalence of CTEPH is up to 3.8% in survivors of acute pulmonary embolism [2] most experts believe that the true incidence of CTEPH after acute pulmonary embolism is 0.5–2%. CTEPH can be found in patients without any previous clinical episode of acute pulmonary embolism or deep venous thrombosis [3]. In 2011, Pepka-Zaba et al. published registry data reporting a history of acute PE in 74.8% of CTEPH patients [4]. The symptoms of CTEPH are indistinguishable from other subgroups of pulmonary hypertension. Patients with CTEPH typically present in either of 2 scenarios: patients may complain of progressive dyspnea on exertion, hemoptysis, and/or signs of right heart dysfunction including fatigue, palpitations, syncope, or edema after a single episode or recurrent episodes of overt...
Table 1  Summary of patients with chronic thromboembolic pulmonary hypertension (CTEPH) CTPA-Computerized Tomography Angiography of Lung, PE-Pulmonary Embolism, VTE-Venous Thromboembolism, APA-Antiphospholipid Antibodies, PEA-Endarterectomy, FVIII-Factor VIII (range 60-150 IU/dl), Homocystein (range 5-12 umol/l).

<table>
<thead>
<tr>
<th>AGE</th>
<th>GENDER</th>
<th>INTERVAL FROM PE TO THE ONSET OF SYMPTOMS/ INTERVAL FROM THE ONSET OF SYMPTOMS TO DIAGNOSE</th>
<th>INITIAL DIAGNOSIS</th>
<th>RESULT OF CTPA</th>
<th>RISK FACTORS OF VTE AND CTEPH</th>
</tr>
</thead>
<tbody>
<tr>
<td>56 years</td>
<td>Female</td>
<td>1/5 years Systemic thrombolysis</td>
<td>Acute coronary syndrome</td>
<td>Negat.</td>
<td>Homocystein 20.9 umol/l, FVIII 240 IU/dl, OC</td>
</tr>
<tr>
<td>64 years</td>
<td>male</td>
<td>0/1 year No PE</td>
<td>Progressive dyspea</td>
<td>Pozit.</td>
<td>Pozit. family history for CTEPH FVIII 280 IU/dl</td>
</tr>
<tr>
<td>44 years</td>
<td>male</td>
<td>1/2 years Systemic thrombolysis</td>
<td>Suspected recurrence of PE</td>
<td>Pozit.</td>
<td>Myeloproliferative disease, low level of protein C FVIII 250 IU/dl</td>
</tr>
<tr>
<td>66 years</td>
<td>male</td>
<td>0/3 years No PE</td>
<td>Progressive dyspea</td>
<td>Negat.</td>
<td>Status post splenectomy FVIII 260 IU/dl</td>
</tr>
<tr>
<td>68 years</td>
<td>female</td>
<td>6 months/1 year Systemic thrombolysis</td>
<td>Heart failure</td>
<td>Pozit.</td>
<td>Pozit. APA FVIII 280 IU/dl</td>
</tr>
<tr>
<td>64 years</td>
<td>female</td>
<td>3 months/6 months Systemic thrombolysis</td>
<td>Heart failure</td>
<td>Pozit.</td>
<td>FVIII 292 IU/dl</td>
</tr>
<tr>
<td>61 years</td>
<td>male</td>
<td>1/1.5 year Anticoagulation treatment</td>
<td>Suspected recurrence of PE</td>
<td>Pozit.</td>
<td>FVIII 288 IU/dl Pozit. APA</td>
</tr>
<tr>
<td>62 years</td>
<td>female</td>
<td>2/1 year Anticoagulation treatment</td>
<td>Suspected recurrence of PE</td>
<td>Negat.</td>
<td>FVIII 144 IU/dl Low level of protein C</td>
</tr>
<tr>
<td>69 years</td>
<td>male</td>
<td>0/1 year No PE</td>
<td>Acute coronary syndrome</td>
<td>Pozit.</td>
<td>FVIII 190 IU/dl Pozit. APA</td>
</tr>
<tr>
<td>71 years</td>
<td>Female</td>
<td>0/2 years No PE</td>
<td>Acute coronary syndrome</td>
<td>Pozit.</td>
<td>FVIII 242 IU/dl</td>
</tr>
<tr>
<td>73 years</td>
<td>male</td>
<td>2/6 years Systemic thrombolysis</td>
<td>Suspected recurrence of PE</td>
<td>Pozit.</td>
<td>FVIII 264 IU/dl</td>
</tr>
</tbody>
</table>
provides detailed views of the lung parenchyma and facilitates the diagnosis of interstitial lung disease and emphysema. Contrast CT angiography of lung (CTPA) is helpful in determining whether there is evidence of surgically accessible CTEPH. It can delineate the typical angiographic findings in CTEPH such as complete obstruction, bands and webs, and intimal irregularities as accurately and reliably as digital subtraction angiography. With this technique, collaterals from bronchial arteries can be identified [15, 16]. However, normal CTPA of lung does not exclude a diagnosis of operable CTEPH and screening with CTPA potentially misses CTEPH. The sensitivity rate of detecting chronic thromboembolic disease of just 51% with CTPA versus >96% with a VQ scan. With improving generations of CT scanners, the higher resolution images provide additional details such as vascular wall thickness and surrounding structures not appreciated by conventional angiography and high-quality multidetector CTPA may be a suitable alternative to pulmonary angiography in centers with experience in CTEPH [17, 18]. Pulmonary angiography (digital subtraction angiography) is regarded as the gold standard procedure for assessing suitability for PEA. It defines extent and distribution of disease and distinguishes thromboembolic versus non thromboembolic disease. Furthermore combined with right heart catheterization a correlation can be made between the degree of disease and the degree of hemodynamic impairment. The procedures should always be carried out by experienced staff at a unit with specialist pulmonary hypertension experience [18]. Once the diagnosis of CTEPH is made, all patients should receive life-long anticoagulation therapy unless contraindicated. All patients with CTEPH should be referred for operability assessment by an experienced CTEPH team to determine if the patient is operable and candidate for PEA. If a patient is deemed non-operable, this patient should be repeatedly referred for operability assessment for a second opinion by an experienced CTEPH team. For patients deemed non operable, or patients after pulmonary endarterectomy with persistent symptomatic PH, treatment with PH targeted medical therapy is recommended. Other treatment options in select cases may include lung transplantation or percutaneous transluminal pulmonary angioplasty [18, 19]. Due to the strong association between PE and CTEPH, the European society of cardiology (ESC) guidelines suggest that patients with acute PE, showing signs of PH or RV dysfunction, at any time during their hospital stay, should receive a follow-up echocardiography after discharge [usually after 3–6 months] to determine whether or not PH has resolved [20].

Conclusion

CTEPH is a debilitating disease caused by chronic obstruction of pulmonary artery branches following episodes of pulmonary embolism and incomplete thrombus resolution. The prognosis of these patients is poor unless an early diagnosis is made and treatment is initiated. Nowadays, CTEPH is commonly underdiagnosed and not properly managed. Any patient with unexplained PH should be evaluated for the presence of CTEPH, and a V/Q lung scan is recommended as screening method of choice. If the V/Q scan or CTPA reveals signs of CTEPH, the patient should be referred to a specialized center with expertise in the medical and surgical management of this disease.
References