


Expectoration of bronchial casts in association with Ramipril treatment

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Case Report

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Abstract

We report of a 26-year-old female patient who was referred to our centre with congestive heart failure (CHF). Acute myocarditis with a high Parvovirus B19 virus load was diagnosed by myocardial biopsy. CHF improved after start of ramipril 5 mg/d, metoprolol, diuretics, immunoglobins, and a 24-hour infusion of levosimendan. Soon after initiation of medical therapy, the patient started to expectorate bronchial casts with varying frequencies (three times per week to five times daily). Thorough pneumological workup, including histology of the casts, microbiology, and a CT scan of the lungs, did not reveal any cause for bronchial cast formation. Inhalative corticoids were started without any benefit. Two years later, cardiac catheterisation demonstrated normalised left ventricular function. LV end-diastolic pressure, however, was still elevated at 14 mmHg. Endomyocardial biopsies at this time were negative for virus genome. Finally, we changed afterload reduction therapy from ramipril to candesartan. Within 24 hours, expectoration of bronchial casts terminated. Four weeks later, re-exposition to ramipril prompted immediate re-appearance of cast formation, which again stopped with switching back to candesartan. Finally, we were to prove that treatment with ramipril resulted in bronchial cast formation in this patient.

Case report

A 26-year-old female patient was referred to our centre with congestive heart failure (CHF). She had a history of hypothyroidism, adipositas and thrombophlebitis. In addition, she had a psychiatric disorder and received quetiapin.

On admission she presented with acute distress with tachydyspnea at rest and tibial edema. Symptoms had started after an infection of the upper airways, which had been treated with amoxicillin. Surface ECG demonstrated atrial fibrillation and repolarisation abnormalities. Echocardiography showed markedly reduced left ventricular ejection fraction (LVEF 20%) and dilatation of all cardiac chambers. Atrial fibrillation was terminated by DC cardioversion. Apixaban was started for the prevention of thrombosis. Endomyocardial biopsies demonstrated acute myocarditis with a high Parvovirus B19 virus load, and left ventricular end-diastolic pressure (LVEDP) was 12 mmHg. Cardiac function improved after initiation of hydrochlorothiazide, spironolactone, bisoprolol, ramipril (5 mg/d) and a 24-hour infusion of levosimendan.

Shortly after starting anticongestive medication, the patient started to expectorate bronchial casts with varying frequencies (three times per week to five times daily; Fig 1). Pneumologic workup, including histology of the casts, microbiology, and a CT scan of the lungs, did not reveal any cause for bronchial cast formation. Inhaled corticosteroids were started without any benefit regarding expectoration of bronchial casts.

Two years later, re-evaluation of haemodynamics revealed a persistently elevated LVEDP of 14 mmHg. Repeat endomyocardial biopsies were negative for virus genome but revealed mild myocardial fibrosis resulting from former myocarditis.

Finally, afterload reduction therapy was switched from ramipril to candesartan in an attempt to reduce cast formation. Expectoration of bronchial casts stopped within 24 hours thereafter. At that time no other modification of the medical regimen had been performed. Four weeks later, re-exposition to ramipril prompted immediate re-appearance of cast formation, which again immediately stopped after switching back to candesartan.

Discussion

Bronchial casts are mucoid, gelatinous formations in the airways consisting of bronchial mucus. Symptoms vary from cough to potentially life-threatening suffocation.¹

Generally, bronchial cast formation has been described in patients with congenital heart disease (CHD) or pulmonary disease.² Among patients with CHD, those with Fontan circulation have a particularly high risk for formation of bronchial casts with a reported incidence of 1–4%.² In addition, bronchial casts can result from severely impaired haemodynamics after surgery for CHD.³ Asthma bronchiale, tuberculosis and cystic fibrosis are the main pulmonary diseases



Figure 1. Expectorated bronchial cast of our patient.

associated with plastic bronchitis.³ Furthermore, it is assumed that noxious agents such as smoke are risk factors for the development of plastic bronchitis.⁴

Therapeutic attempts to control bronchial cast formation have been performed with medical therapy, catheter interventions and surgery. Therapeutic agents included inhaled fibrinolytics, inhaled mucolytics, inhaled or systemic corticosteroids or systemic immunosuppressants with reduction of symptoms in only few patients.⁵ To improve haemodynamics, sildenafil or bosentan as well as interventional methods or repeat surgery have been employed in patients after corrective surgery of CHD.⁶ However, our patient had elevated filling pressures (LVEP, CVP) as known risk factors for bronchial cast formation. There was no hint for an inflammatory process as an underlying cause.

In conclusion, we were able to identify ramipril as one cause for bronchial cast formation. This side effect has not been described yet for ramipril as well as any other angiotensin-converting enzyme (ACE) inhibitor.

The underlying pharmacological mechanism is unclear. We speculate that cast formation was related to the well-described activation of bradykinin by ACE inhibitors. Bradykinin induces microvascular leakage at all airway levels. Due to its vasodilative action, bradykinin increases blood flow to the airways. Thus, it has a stimulatory effect on airway mucus secretion, which is the main

component of bronchial cast formations.⁷ Furthermore, bradykinin itself stimulates C-fiber nociceptors, which causes chronic dry cough.⁸ In our patient, however, cough was only present in cast expectoration.

Conclusion

Bronchial cast formation is a potentially life-threatening complication often associated with complex CHD. In our patient, cast formation occurred in the absence of CHD or any other cause known so far. To the best of our knowledge, this is the first report of bronchial cast formation due to ramipril treatment. Our case report may encourage colleagues involved in care of patients with bronchial cast formation to focus on ramipril or other ACE inhibitors as part of their therapeutic regimen, as cast formation may stop after switching to an alternative treatment. Further studies may elucidate possible pharmacological mechanisms resulting in bronchial cast formation.

Conflicts of Interest. All authors declare no conflict of interest (K. S. P., T. P., M. S.).

Ethical Standards. The patient gave written informed consent for publication of this report.

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