**Case Studies**

**Spontaneous coronary artery dissection associated with coughing**

S. Sivam, V. Yozghatli, R. Dentice, M. McGrady, C. Moriarty, J. Di Michiel, P.T.P. Bye, D. Rees

*Department of Respiratory and Sleep Medicine, Royal Prince Alfred Hospital, Missenden Road, Camperdown, NSW 2050, Australia*

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### 1. Introduction

Coughing is common in cystic fibrosis (CF). It is often related to progressive disease or CF exacerbations, and is frequently part of routine airway clearance measures in patients with impaired mucociliary function. In fact, intensification of chronic daily therapies which include airway clearance techniques, is a key element in the management of CF exacerbations.

A wide range of complications related to recurrent coughing have been published [1]. They involve multiple organ systems and vary in their impact on health related quality of life. Cardiovascular complications of coughing include syncope, arrhythmias and rupture of subconjunctival and nasal veins. Chronic cough related to pulmonary infection or chronic inflammation has also been shown to be associated with an increased risk of coronary artery disease or myocardial infarction, although controlled studies are still necessary to demonstrate causality [1].

The incidence of spontaneous coronary artery dissection (SCAD) can vary widely, with one case series reporting figures ranging between 0.07 and 1.1% in patients referred for coronary angiography [2]. The mean age at presentation is 30–45 years and more than 70% of patients diagnosed with spontaneous dissection are female. Coronary atherosclerosis and vascular changes occurring during the peripartum period are most commonly associated with SCAD, however, other disease entities including connective tissue disease, vasculitides, and oral contraceptive use have also been implicated [2].

### 2. Case presentation

A 45 year old mother with cystic fibrosis on the verge of being evaluated for lung transplantation awoke with a coughing spasm in the middle of the night, which progressed to excruciating dull central chest pain, radiating to neck and left arm. She was presented immediately to the emergency department for this unusual symptom complex, which was unlike her prior musculoskeletal pain associated with repeated coughing.

Her past medical history encompassed the many expected complications associated with adult CF including pancreatic insufficiency, chronic sinusitis, mild liver cirrhosis related to cholestasis, low normal BMI (18), malabsorption resulting in osteopenia, arthropathy and impaired glucose tolerance. Her other issues were gestational diabetes, mild hypertension, polycystic ovaries, gastro-esophageal reflux disease (GERD) and oligomenorrhea. Of note, she began menstruating 2 days after her admission suggesting that she was in the luteal phase of her menstrual cycle at the time. For the above conditions, she was managed with...
maintenance azithromycin and nebulized tobramycin, nebulized dornase alfa, vitamin and pancreatic enzyme supplements, ursodeoxycholic acid, irbesartan, saline nasal rinses, ciclesonide and efomoterol. There were several antibiotic related allergies resulting in wheezing and reactive airways, necessitating regular corticosteroid and anti-histamine pre-treatment during hospital admissions. Hypertonic saline was not used regularly due to similar intolerances including coughing. She had no significant bronchodilator response on lung function testing and had negative skin prick testing.

The patient never smoked and consumed minimal alcohol. She had a 6 year old son, who was healthy. Her family history included a sister with Addison’s disease and a brother with CF. In addition, she also had a maternal aunt with hypertrophic cardiomyopathy and a paternal aunt with Takotsubo’s cardiomyopathy.

While she remained hemodynamically stable, the chest pain persisted and her electrocardiogram demonstrated anterolateral ST elevation (Fig. 1). Based on these findings, she was urgently taken for a coronary angiogram. While all her arteries were atheroma free, she was found to have a spontaneous complete left anterior descending (LAD) coronary artery dissection with associated moderate apical hypokinesis. The distal true lumen could not be entered, thus making stenting not possible. The highly sensitive troponin T was elevated at 55 ng/L (normal <14 ng/L) and peaked at 1476 ng/L postangiography. Her platelet count (259 × 10^9/L), INR (1), PT (12.5 s), APTT (35 s) and white blood cell count (9.1 × 10^9/L) were in the normal range. The hemoglobin level (113 g/L) was slightly reduced.

In the Coronary Care Unit, she was medically managed with a glyceryl trinitrate infusion, opioid based pain relief, aspirin, clopidogrel and bisoprolol, a selective β-antagonist. The CF service was consulted for a decline in lung function and symptoms consistent with a respiratory exacerbation, despite a largely unchanged chest X-ray reflecting chronic CF related pathology. Spirometry was not obtained in the acute setting of a dissection knowing that it often resulted in recurrent coughing in this patient. Her baseline FEV1 shortly before this event was 0.66 L (26%) and her FVC was 2.08 L (69%). The spirometric ratio was reduced (0.32). Intravenous ticarcillin, clavulanate and tobramycin were commenced based on her prior sputum cultures which demonstrated chronic colonization with *Pseudomonas aeruginosa*. Chest physiotherapy was administered cautiously considering the circumstances of her dissection, which appeared temporally related to vigorous coughing.

Major surgery requiring general anesthesia was discouraged for a 6 month period, as advised by the cardiology service. With her family history, a genetic consultation was also obtained, however, expert opinion was that the family history was not relevant to the acute dissection. Connective tissue diseases associated with SCAD, including Ehler–Danlos IV were excluded as such diagnoses would be highly relevant for future transplantation and surgery due to poor healing and hemostasis.

With no documented arrhythmias or QT prolongation during her course in hospital, maintenance azithromycin was continued considering her *Pseudomonas* colonization. A follow-up cardiac stress test 3 months after the event revealed a transmural apical infarct of limited extent, with no at risk myocardium. A stress echocardiogram was also performed demonstrating cardiac function within normal range.

### 3. Discussion

In a patient with cystic fibrosis and spontaneous coronary artery dissection temporally related to repeated coughing, several important issues were raised. The first was the inclusion of SCAD, albeit unusual, in the differential diagnosis of a patient with chest pain and recurrent intense coughing spasms, with or without a history of coronary artery disease. This is particularly pertinent in the CF population as controlled coughing is a modality for airway clearance, often administered as part of a chest physiotherapy session.

![Fig. 1. ST elevation myocardial infarction.](image-url)
In selected circumstances, these clearance strategies are temporarily withheld. Vigorous coughing may worsen a pneumothorax or hemoptysis related to a CF exacerbation. Current guidelines on CF related pulmonary complications recommend some caution in hypertonic saline use in these situations as it may aggravate coughing [3]. With our patient’s competing therapeutic goals, we elected to reduce the frequency of her chest physiotherapy but not discontinue it altogether in view of her deterioration in lung function. She had already discontinued nebulized hypertonic saline prior to the incident and reported no worsening of cough in relation to her angiotensin receptor blocker for hypertension or recently added selective β-antagonist.

Chronic infection and inflammation increase the risk of atherosclerotic coronary artery disease, however, the absence of atherosclerosis supports causes other than plaque rupture. The contribution of frequent corticosteroid use to her dissection remains unclear. While it is associated with increased atheroma formation, which she did not have, it may also have adverse effects on the connective tissue of arteries [4]. In her case, her corticosteroid use was reduced as a cautionary measure but could not be discontinued altogether.

The long term use of maintenance azithromycin was also reviewed following the myocardial infarction [5]. In our patient, there was no prolongation of the QT interval, or arrhythmias and the ejection fraction normalized. She did not have a high baseline risk of cardiovascular disease prior to the SCAD. Thus, in view of her severe lung disease, the drug was cautiously reintroduced without apparent complications.

The characteristic profile for SCAD in the general population appears to fit that of our patient — most are females, in their fourth decade and the LAD vessel is implicated in approximately 60% of cases [2]. The prognosis is usually good but an associated mortality rate is described in the longer term [2]. In general, it is unusual for patients with CF to be excluded from lung transplant in Australia because of significant cardiac disease with the possible exception of older patients with atherosclerosis. With her excellent progress, she is now actively listed for bilateral lung transplantation and is managed in parallel by the cardiovascular, respiratory and lung transplantation services.

References