Eur Respir J 2007; 29: 608–611
DOI: 10.1183/09031936.00099706

CASE FOR DIAGNOSIS

A 35-year-old male with chronic cough

C. Moschos, I. Kalomenidis, C. Roussos and G.T. Stathopoulos

CASE REPORT

A 35-yr-old male was examined in the outpatient clinic of the present authors' department. He complained of a dry paroxysmal cough of indeterminate origin that he had noticed 3 months earlier. The cough was associated with a tickling feeling in the throat. There was no association between coughing flares and meals, nasal discharge, season, time of day or body posture. The patient did not recall having symptoms compatible with an upper airway viral infection in the past 3 months and reported no gastro-intestinal symptoms like daily heartburn and regurgitation. He lived in the city, was a lifetime nonsmoker, his previous medical history was unremarkable and he was not taking any medication. He worked as an electronic engineer in a smoke- and dust-free environment and exhibited a type A personality. Upon appearance of the cough 3 months earlier, he had been examined by a physician and had since received inhaled salmeterol (50 μg *b.i.d.*) and fluticasone (250 μg *b.i.d.*), without improvement.

A thorough physical examination and routine laboratory tests, including white blood cell count and differential, red blood cell count, erythrocyte sedimentation rate, liver and renal function tests, serum C-reactive protein and an ECG were normal. Chest (fig. 1) and paranasal sinus (image not shown) radiographs were taken. Ear, nose and throat assessment was unremarkable. After discontinuing treatment with inhaled salmeterol and fluticasone, simple spirometry pre- and post-bronchodilator (four puffs of 100 μg salbutamol) and bronchoprovocation challenge with methacholine were performed (fig. 2). The patient was given a peak flow meter and during a monthly observation period his diurnal peak flow variation was below 5% (data not shown).

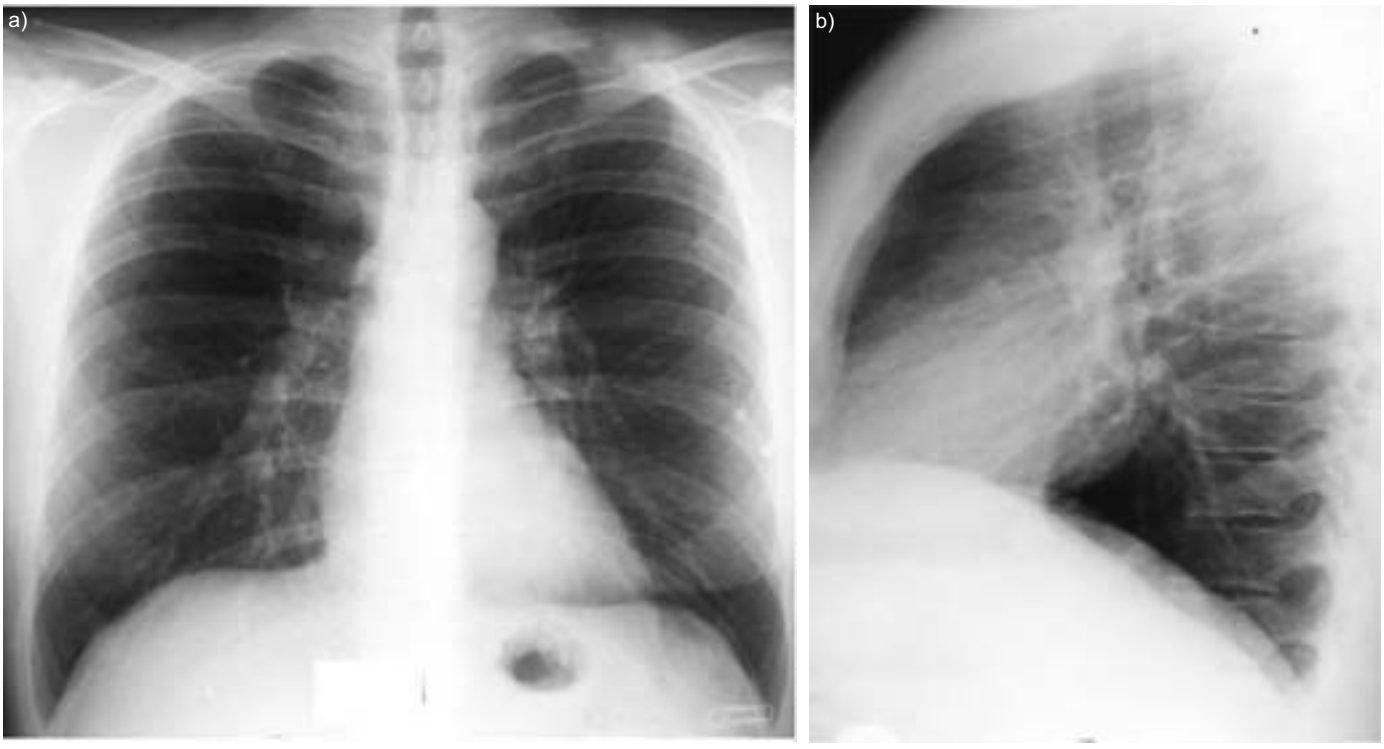

FIGURE 1. Chest radiograph showing a) posterior-anterior view and b) lateral view.

Dept of Pulmonary and Critical Care Services, General Hospital ''Evangelismos'', School of Medicine, National and Kapodistrian University of Athens, Athens, Greece.
STATEMENT OF INTEREST: None declared.
CORRESPONDENCE: G.T. Stathopoulos, Dept of Pulmonary and Critical Care Services, General Hospital ''Evangelismos'', School of Medicine, National and Kapodistrian University of Athens, 3 Ploutarhou Str., 10675 Athens, Greece. Fax: 30 2107235521. E-mail: gstathop@med.uoa.gr

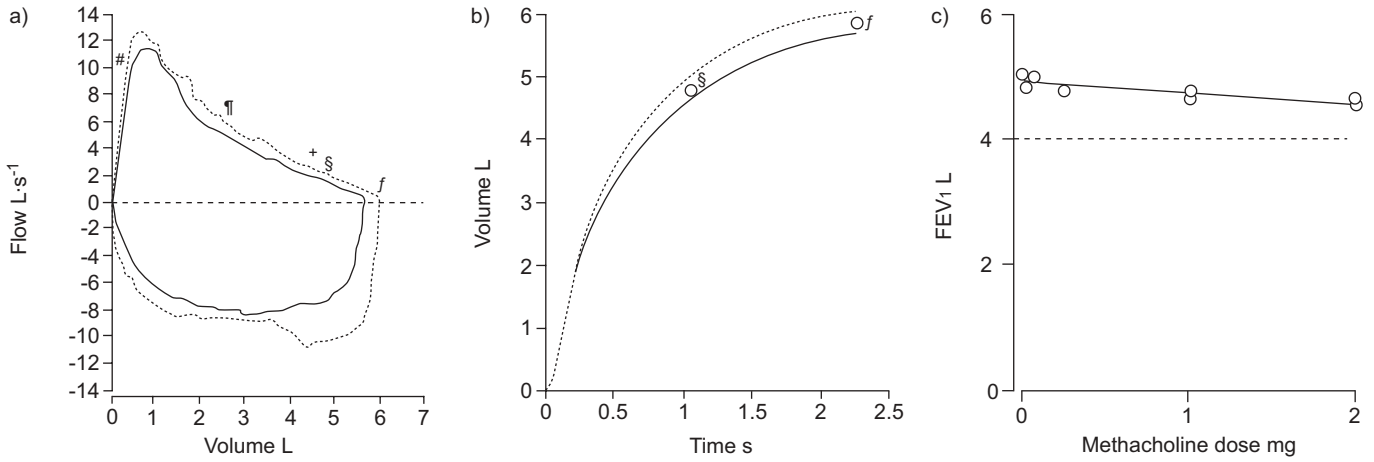

FIGURE 2. Pulmonary function tests of a) flow–volume plot and b) volume–time curve. ——: pre-bronchodilator; ·····: post-bronchodilator; ○: predicted value. c) Methacholine dose–forced expiratory volume in one second (FEV_1) curve. #: peak expiratory flow rate; ¶: forced expiratory flow (FEF) at 50% of forced vital capacity (FVC); +: FEF at 75% of FVC; §: FEV_1; *f*: FVC.

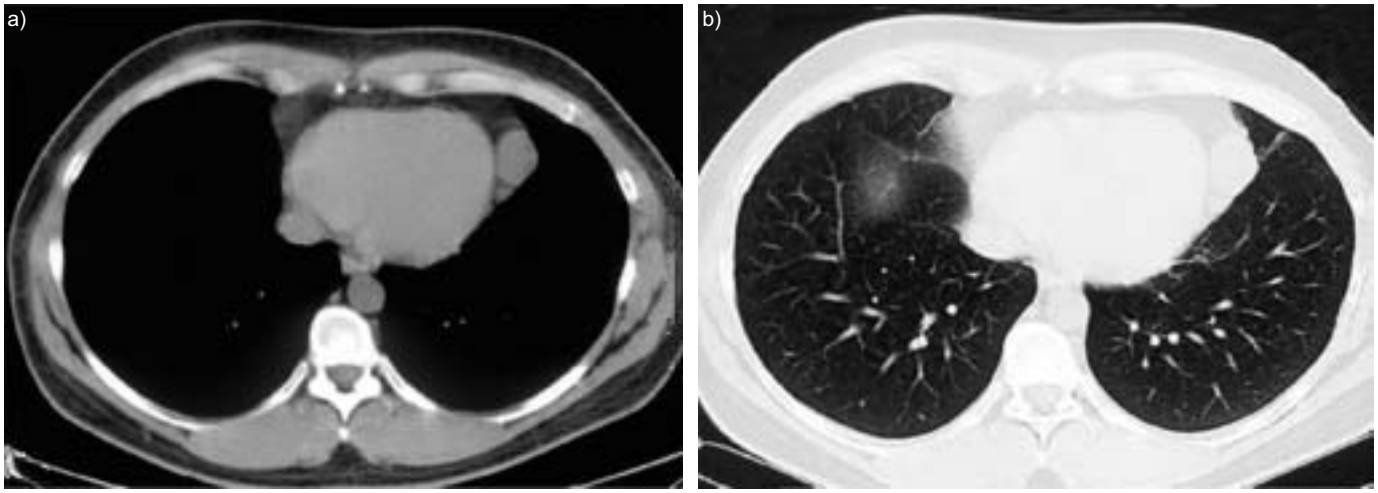

FIGURE 3. a and b) Computed tomographic scans of the chest.

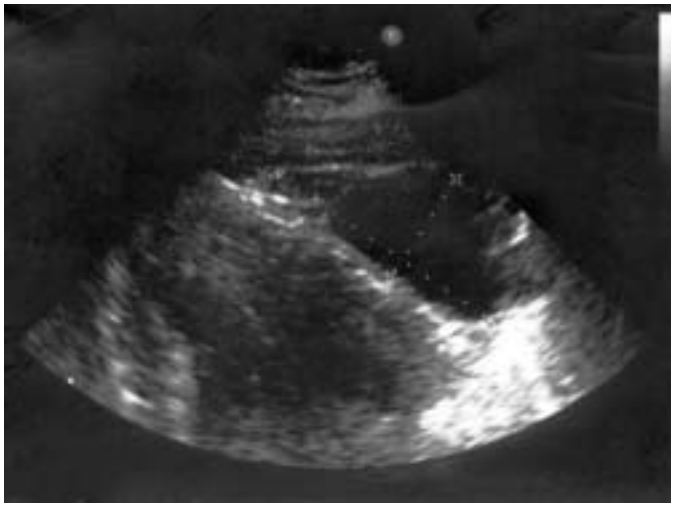

FIGURE 4. Transthoracic ultrasound.

Since an empiric trial of inhaled corticosteroids had already been administered, treatment was discontinued and empiric treatment for gastro-oesophageal reflux disease was administered with a proton pump inhibitor (omeprazole, 20 mg *b.i.d.*) over a period of 2 months. Neither withholding inhaled steroids nor omeprazole administration had any effect on the patient's symptoms and coughing persisted. Therefore, a computed tomographic (CT) scan of the chest was ordered (fig. 3), followed by transthoracic echocardiography (fig. 4).

BEFORE TURNING THE PAGE, INTERPRET THE CHEST RADIOGRAPHS, PULMONARY FUNCTION TESTS, COMPUTED TOMOGRAPHY AND ULTRASOUND, AND SUGGEST A DIAGNOSIS.

INTERPRETATION

Chest radiography

Figure 1 shows near-normal normal chest radiographic films. After careful evaluation, and with some difficulty, a round, homogeneous opacity can be identified in the lateral projection, located well above the diaphragm and superimposed on the cardiac opacity.

Pulmonary function and bronchoprovocation challenge tests

Figure 2a and b show normal flow–volume and volume–time curves, respectively, with no response to bronchodilation. Figure 2c shows a normal forced expiratory volume in one second (FEV_1)–methacholine dose plot, without significant bronchoconstrictor response (~8% drop in baseline FEV_1), even at maximal methacholine dosage (2 mg).

Computed tomography

The CT images in figure 3 (soft-tissue gating (a); and lung parenchymal gating (b)) show a solitary, unilocular, thin-walled, round cyst, sized 3×4 cm, situated along the left inferior cardiac border, exhibiting an attenuation coefficient between those of water and fat. No other lesions were seen.

Transthoracic ultrasound

Transthoracic ultrasonography showed a cyst measuring 3×4 cm in close association with the pericardium, and ruled out any haemodynamic changes, cardiac compression, right ventricular outflow obstruction or atrial enlargement.

Diagnosis: Left-sided pericardial cyst.

CLINICAL COURSE

After consultation with the patient on the possibility that his cough may be caused by the pericardial cyst, a decision was made to proceed to surgical removal of the cyst. Pre-operative bronchoscopy, performed to rule out coexisting endobronchial lesions, was unremarkable. The cyst was thereafter removed *via* video-assisted thoracoscopic surgery. Pathological examination of the cyst concurred with the diagnosis of pericardial cyst. The patient's cough resolved immediately after surgery and has not reappeared after 6 months of follow-up.

DISCUSSION

Cough is the most common respiratory symptom encountered by clinicians [1]. Acute cough is usually easier to diagnose and resolves after proper therapy. Chronic cough is defined as cough lasting >8 weeks, and can be a significant problem, interfering with important daily activities. The most common causes of chronic cough are asthma, gastro-oesophageal reflux disease, upper airway cough syndrome, nonasthmatic eosinophilic bronchitis or a combination of the above [2]. Although some authorities suggest that the cause of chronic cough can be identified in up to 95% of cases, in ~20% of patients a diagnosis cannot be established even after ruling out uncommon causes of chronic cough [1]. Diagnostic tests limited to the respiratory system do not always provide a diagnosis, since cough can be the major or presenting symptom in a large percentage of patients with common and uncommon non-pulmonary diseases. Mediastinal lesions commonly cause cough by impinging the adjacent airways or the vagal afferent nerves that regulate involuntary coughing, but cough is rarely the main or sole manifestation. The most common mediastinal lesions that can cause cough are oesophageal cysts and tumours, lymphomas, mediastinal lipomatosis, and neuromas and neurilemmomas of the vagus or internal laryngeal nerves [2].

Pericardial cysts are the second most common type of primary mediastinal cysts after bronchial cysts and constitute 7% of all mediastinal lesions [3]. They are most frequently congenital, arising from aberrant fusion of pericardial lacunae in approximately one in 100,000 individuals; however, some may be acquired. They remain unchanged in size or slowly enlarge over a period of many years and are often discovered in routine chest radiographs of asymptomatic adults, usually in the fourth to fifth decade of life. They are usually unilocular cystic lesions with a wall of varying thickness with fat cells, lymphocytes, blood vessels and muscle fibres and clear fluid contents, hence the name ''clear water'' or ''spring water'' cyst [4]. Of all pericardial cysts, 70% are located in the right cardiophrenic angle, 22% in the left cardiophrenic angle and the remaining 8% elsewhere in the pericardium (*e.g.* the posterior mediastinum, the right or left hilar region, the right paratracheal area or the para-aortic region) [3]. The differential diagnosis of pericardial cyst includes foramen of Morgagni diaphragmatic hernia, large right pericardial fat pad, mediastinal or diaphragmatic tumours, and tumours of the heart or pericardium [5]. Thymomas are a relatively common cause of mediastinal mass in young patients, and while thymoma usually resides just anterior to the aortic root, it can occur anywhere from the neck to the cardiophrenic angle. Most thymoma patients are asymptomatic, although one third experience chest pain, cough, dyspnoea and/or other symptoms related to compression or invasion of adjacent structures [6]. Although the majority of patients with pericardial cysts are asymptomatic, about one third exhibit symptoms.

The most common symptoms associated with pericardial cysts are vague chest pain, dyspnoea and persistent cough [7–9]. However, complications can be life-threatening, including cardiac compression, right ventricular outflow obstruction, cyst rupture with cardiac tamponade and cyst infection with cardiac or large vessel erosion. There have been reports of pericardial cysts causing atrial fibrillation by obstructing right atrial filling or even sudden death after a stress test, and of hydatid pericardial cysts presenting with circulatory collapse [5, 10–12]. There are no reports of malignant transformation. Traditional treatment includes thoracotomy or thoracoscopic removal, but pericardial cysts can also be diagnosed and treated by percutaneous aspiration and injection of ethanol as a sclerosing agent with no evidence of recurrence upon a 3-yr follow-up [9]. Recurrence has been reported after thoracoscopic removal with successful thoracoscopic re-excision [13].

In the present case, after ruling out common causes of chronic cough according to current guidelines, the diagnostic evaluation suggested that an uncommon extrapulmonary cause, such as a left-sided pericardial cyst, was responsible for the patient's cough, probably *via* stimulation of the afferent vagal receptors from the airways [14]. In this regard, the tickling sensation in the patient's throat associated with the cough, disappeared with the cough after removal of the pericardial

cyst. As hydatid disease is endemic in Greece, antibodies against *Echinoccocus granulosus* were measured in the patient's serum but were not detectable.

In conclusion, although it is rare that a pericardial cyst should present with the sole symptom of cough, it should be considered in the differential diagnosis of patients with chronic cough after excluding other common causes.

REFERENCES

1 Prakash UB. Uncommon causes of cough: ACCP evidence-based clinical practice guidelines. *Chest* 2006; 129: 206S–219S.
2 Diagnosis and management of cough. Executive summary. *Chest* 2006; 129: 1S–23S.
3 Kutlay H, Yavuzer S, Han S, Kayi Cangir A. Atypically located pericardial cysts. *Ann Thorac Surg* 2001; 72: 2137–2139.
4 Strollo D, Rosado-de-Christenson M, Jett J. Primary mediastinal tumors: part II. Tumors of the middle and posterior mediastinum. *Chest* 1997; 112: 1344–1357.
5 Borges A, Gellert K, Dietel M, Baumann G, Witt C. Acute right-sided heart failure due to hemorrhage into a pericardial cyst. *Ann Thorac Surg* 1997; 63: 845–847.
6 Strollo D, Rosado-de-Christenson M, Jett J. Primary mediastinal tumors. Part 1: tumors of the anterior mediastinum. *Chest* 1997; 112: 511–522.
7 Feigin DS, Fenoglio JJ, McAllister HA, Madewell JE. Pericardial cysts, a radiologic-pathologic correlation and review. *Radiology* 1977; 125: 15–20.
8 Jarzabkowski DC, Braunstein DB. Pericardial cyst: an incidental finding. *J Am Osteopath Assoc* 1998; 98: 445–446.
9 Noyes BE, Weber T, Vogler C. Pericardial cysts in children: surgical or conservative approach? *J Pediatr Surg* 2003; 38: 1263–1265.
10 Vlay S, Hartman A, Brook S. Mechanical treatment of atrial fibrillation: removal of pericardial cyst by thoracoscopy. *Am Heart J* 1995; 129: 616–618.
11 Fredman CS, Parson SR, Aquino TI, Hamilton WP. Sudden death after a stress test in a patient with a large pericardial cyst. *Am Heart J* 1994; 127: 946–950.
12 Gossios K, Passas G, Kontogiannis D, Kakadellis J. Mediastinal and pericardial hydatid cysts: an unusual cause of circulatory collapse. *Am J Roentgenol* 2003; 181: 285–286.
13 Horita K, Sakao Y, Itoh T. Excision of a recurrent pericardial cyst using video-assisted thoracic surgery. *Chest* 1998; 114: 1203–1204.
14 Hargreaves M, Channon K. Mechanism of pacemaker induced cough. *Br Heart J* 1994; 71: 484–486.