Tracheobronchial calcification on bronchoscopy in a patient with end stage renal failure: an unusual cause of chronic cough

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Abstract
Pulmonary calcification can develop as a complication of end-stage renal failure. Most patients are asymptomatic, with characteristic parenchymal changes incidentally detected on computed tomography (CT) imaging and a clinical course that is usually benign. In this report, we describe a 64-year-old female with a history of inadequate peritoneal dialysis who presented with severe chronic cough, a symptom that persisted despite treatment for respiratory tract infection. On follow-up bronchoscopic examination, white nodular tracheobronchial mucosal changes persisted. The presence of calcium deposits within these nodules was histologically confirmed, although CT imaging had not suggested the presence of calcific tracheobronchial changes. We believe that the bronchoscopic findings represent a highly unusual presentation of metastatic pulmonary calcification and an uncommon cause of chronic cough amongst patients with end-stage renal failure.

Introduction
Extra-skeletal deposition of calcium is a well-known complication of end-stage renal failure and occasionally manifests as metastatic pulmonary calcification (MPC) of the alveolar parenchyma [1]. In this report, we describe an adult patient in whom mucosal calcification was identified in the trachea and bronchial tree following mucosal biopsy in the context of insufficient dialysis.

Case Report
A 64-year-old female presented with subjective fevers and a 14-month history of dry cough. Her past medical history was significant for chronic kidney disease secondary to hereditary glomerulonephritis, for which she commenced peritoneal dialysis 11 months earlier.

Clinical examination and chest X-ray were unremarkable. Computed tomography (CT) chest showed upper lobe-predominant ground-glass opacification and collapse of the right middle lobe (Fig. 1). On bronchoscopy, there was ulceration affecting the anterior aspect of the distal trachea and the posterior tracheal wall and extensive white nodular mucosal abnormality. Similar nodular lesions extended into the right main bronchus. The mucosa was friable with easy-contact bleeding, especially in the right middle lobe. The opening of the right middle lobe was narrow, possibly due to the extent of mucosal inflammation in this region. Bronchoscopic biopsies from the ulcerated tracheal mucosa showed focal ulceration and regenerative hyperplasia, with no evidence of fungal infection.

Culture of washings from bronchoscopy yielded positive bacterial culture for Streptococcus pneumoniae. Following treatment for infection, the patient re-presented with constipation and nausea and was found to have pericardial and parapneumonic effusions. These clinical findings, together with objective markers of inadequate dialysis, prompted the urgent commencement of haemodialysis via an existing arteriovenous fistula. Although the patient’s uraemic symptoms and effusions resolved following commencement of haemodialysis, the cough persisted.
Repeat bronchoscopy 10 weeks from the initial assessment and 6 weeks from the commencement of haemodialysis showed resolution of the tracheal ulceration. The nodular appearance of the mucosa was diminished but persistent, extending from the distal trachea to involve both main bronchi, lingua, right middle lobe bronchus, and both lower lobe bronchi (Fig. 2). Right lower lobe endobronchial biopsy showed prominent subepithelial calcifications, mild patchy acute and chronic inflammation, focal squamous metaplasia, and mild fibrosis (Fig. 3). No granuloma or malignant change was identified. The calcifications were believed to relate to dialysate calcium and hyperphosphataemia. Repeat bacterial and fungal cultures were negative.

Phosphate, calcium, and parathyroid hormone (PTH) level remain elevated [44.8, reference range (RR) 0.8–5.5 pmol/L], suggesting tertiary hyperparathyroidism. Table 1 shows key biochemical values before and after the commencement of haemodialysis. A non-calcium based phosphate binder has been commenced. Several months following the commencement of haemodialysis, the patient’s cough has subsided.

Figure 1. Computed tomography (CT) chest showing right middle lobe collapse prior to initial bronchoscopy (left) and improvement in the extent of right middle lobe (RML) collapse after several months of regular haemodialysis (right).

Figure 2. Bronchoscopic appearance of right main bronchus; multiple 1–2 mm nodular lesions extended from distal trachea to the lobar bronchi.

Figure 3. H and E slide at 400x magnification showing bronchial wall tissue demonstrating bronchial epithelium with prominent subepithelial stromal calcification (arrows) and mild acute and chronic inflammation.
Diagnosis of MPC and the presence of non-specific findings on cross-sectional imaging of the abdomen. This is the first instance in which bronchoscopic findings have led to the diagnosis of MPC and the first case in which a patient has presented with chronic cough. We propose that this case extends the known spectrum of presentations related to pulmonary calcification in renal failure.

Tracheobronchial calcification is a possible cause of chronic cough amongst patients with severe renal failure, even in the absence of typical radiological abnormalities of MPC. Bronchoscopy should be considered in patients with chronic renal failure and persistent cough, where no clear alternative cause has been identified, even in the absence of radiological evidence of bronchopulmonary calcification.

Discussion

Soft-tissue calcification is a well-documented complication of end-stage renal failure [1–4]. Periarticular tissue is most commonly affected, but other sites may be involved. Pulmonary and cardiac calcifications have a prevalence of 40–80% in an autopsy series of haemodialysis patients [1]. Pulmonary involvement is known as MPC, usually diagnosed following incidental detection on cross-sectional pulmonary imaging. Individuals are generally asymptomatic, and the process follows a benign course, although abnormalities of gas exchange and associated restrictive pathology have also been reported [1], possibly due to an interstitial fibroproliferative response to the presence of the calcium deposits [2].

Radiological patterns of MPC include diffuse bilateral calcific nodules, centrilobular upper zone nodules, regions of persistent patchy consolidation, ground-glass infiltrates, or confluent change resembling lobar pneumonia [4]. Calcification of the bronchioles, bronchi, and trachea has been occasionally reported on radiological assessment [5]; however, notably such changes were not present in this case. Calcium deposits in MPC consist of calcium phosphate or, less commonly, whitlockite, together with smaller amounts of calcium pyrophosphate [3].

The mechanisms of calcium deposition in renal failure are complex. It is proposed that relative alkalinity at the apex of the lung due to lower PaCO₂ and higher blood pH at this site predisposes to calcification with an upper lobe predilection [3]. However, the mechanism for tracheobronchial deposition of calcium is not known.

Very few reports have documented tracheobronchial calcification as a bronchoscopic finding in this disease process [6,7]. In this case, the bronchoscopic findings occur in the presence of non-specific ground-glass changes in the upper lobes but none of the typical radiological findings of MPC. Notably, there was no evidence of calcium deposition elsewhere on cross-sectional imaging of the abdomen. This is the first instance in which bronchoscopic findings have led to the diagnosis of MPC and the first case in which a patient has

Table 1. Key biochemical and hormonal values before and after the commencement of haemodialysis.

| Key biochemical and hormonal values (normal reference interval) | Values at time of initial bronchoscopy (pre-haemodialysis) | Values at time of repeat bronchoscopy (following initiation of regular haemodialysis) |
|---------------------------------------------------------------|----------------------------------------------------------|-----------------------------------------------------------------------------------|
| Bicarbonate (22–33 mmol/L)                                   | 24                                                       | 21                                                                                |
| Phosphate (0.75–1.5 mmol/L)                                  | 2.84                                                     | 1.88                                                                              |
| Urea (2.7–8.0 mmol/L)                                        | 20.2                                                     | 15.3                                                                              |
| Creatinine (umol/L)                                          | 1076                                                     | 579                                                                               |
| Corrected calcium (2.25–2.62 mmol/L)                         | 3.0                                                      | 2.7                                                                               |
| Parathyroid hormone (0.8–5.5 pmol/L)                         | 52.7                                                     | 44.8                                                                              |

Disclosure Statement

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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