Case Report

Coexisting cystic lung disease as a rare extra-renal manifestation of autosomal dominant polycystic kidney disease

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ABSTRACT

Autosomal dominant polycystic kidney disease (ADPKD) classically presents with multiple bilateral renal cysts and ultimately progresses to end stage renal disease. While many of the extra-renal manifestations of ADPKD are well-documented, associated pulmonary findings are particularly rare, having only been recently been reported in a handful of studies to date. A 69-year-old female with ADPKD presented to our hospital with respiratory complaints. High resolution computed tomography revealed bronchiectasis, cystic lung disease, and interstitial fibrosis. The patient did not have concurrent risk factors or coexisting disease processes to explain the etiology of her airway and cystic lung disease, which we suggest are manifestations of ADPKD. We have not found a previous report of interstitial lung disease in this setting.

1. Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is a systemic disease affecting approximately 500,000 people and accounts for 5–10% of the dialysis population in the United States alone [1,2]. Predominantly characterized by multiple large bilateral renal cysts, ADPKD typically presents in the third or fourth decade of life. As the renal cysts grow and distort the normal renal parenchyma, progression to end stage renal disease results with an incidence of about 50% by 60 years of age [1,2].

Extra-renal manifestations of ADPKD are prevalent, including cysts affecting the liver, pancreas, central nervous system, and genitourinary tract [1–4]. While many of these extra-renal manifestations have been well documented, until recently, there has been little mention of coexisting pulmonary pathologies [3–8]. In the few reported cases of synchronous lung pathology, the most common pulmonary manifestation of ADPKD has been bronchiectasis with even fewer case reports describing associated pulmonary cysts [4,6,8]. To date, concurrent interstitial lung disease has not been linked to ADPKD nor has it been reported in the literature. We herein report a rare case of airway and cystic lung disease as the pul-
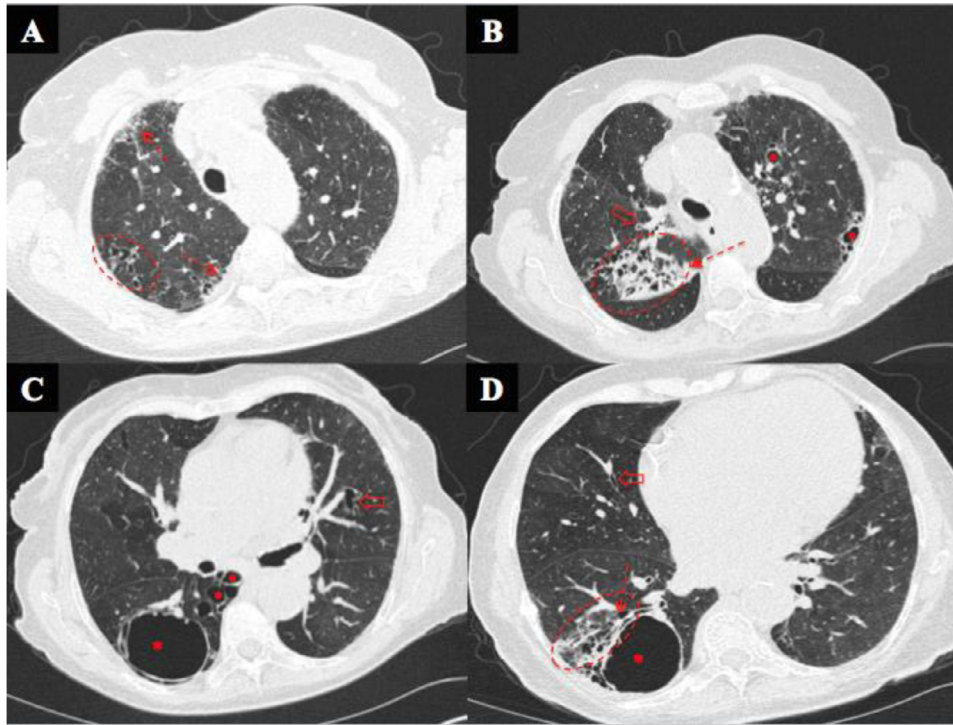

Fig. 1 – Axial non-contrast computed tomography images of the thorax at the level of the mid trachea (a), distal trachea (b), mainstem bronchi (c), and in the lower lung zones (d) show scattered areas of interstitial fibrosis (dashed arrows), honeycombing (dashed ovals), cylindrical and cystic bronchiectasis (open arrows), and pulmonary cysts (asterisks).

monary manifestation of ADPKD as well as the first reported case of coexisting interstitial lung disease in this setting.

2. Case report

A 69-year-old woman with a history of ADPKD, end stage renal disease on dialysis, hypertension, and diabetes mellitus presented to our outpatient lung center with complaints of dyspnea, wheezing, and a worsening cough with yellow sputum production for several weeks. The patient denied any smoking history, inhaled drug use, or inhaled allergen exposure. There was no known history of pulmonary infection. At the time of admission, aside from an elevated blood pressure of 160/69, the patient's vital signs were within normal limits. Physical examination demonstrated crackles throughout both lungs with bronchial breath sounds noted at the right lung base. Laboratory data were unremarkable. Spirometry demonstrated an FVC of 1.56 L (62% of predicted), FEV_1 of 1.14 L (59% of predicted), FEV_1/FVC of 73% of predicted, none of which were significantly changed with bronchodilator treatment, and a TLC of 3.44 L (78% of predicted), overall in keeping with a very mild restrictive pattern.

Non-contrast high resolution computed tomography imaging of the chest was performed and demonstrated numerous cysts of varying sizes throughout both lungs (Figs. 1 and 2). Findings at the lung bases appeared grossly unchanged when compared to the prior computed tomography (CT) abdomen 9

years prior, but no comparative imaging was available for the remainder of the pulmonary parenchyma (Fig. 3). The largest cyst was irregularly shaped and located in the right lower lobe, measuring approximately 5.7 × 5.6 × 8.0 (AP x TV x CC) without air–fluid levels (Figs. 1 and 2). Several areas of cylindrical and cystic bronchiectasis without a lobar distribution with coexisting bronchial wall thickening and air trapping were identified (Figs. 1 and 2). In addition, predominantly subpleural reticulation, traction bronchiectasis, and honeycombing were found in the dependent portions of both lungs, consistent with interstitial fibrosis (Figs. 1 and 2). There was no significant change in the imaging appearance of this patient's pulmonary findings when compared to the study from several years prior. Within the visualized upper abdomen, numerous peripherally calcified hepatic and renal cysts were identified in keeping with the patient's known diagnosis of ADPKD (Fig. 4).

The patient was subsequently started on a short course of oral antibiotics and was recommended to continue her inhaled bronchodilators. An acute pulmonary infectious etiology was considered unlikely given the clinical, laboratory and imaging findings; therefore imaging findings were attributed to pulmonary sequela of ADPKD.

3. Discussion

ADPKD is the most common form of polycystic kidney disease, with an incidence between 1:500 to 1:1000, and clas-
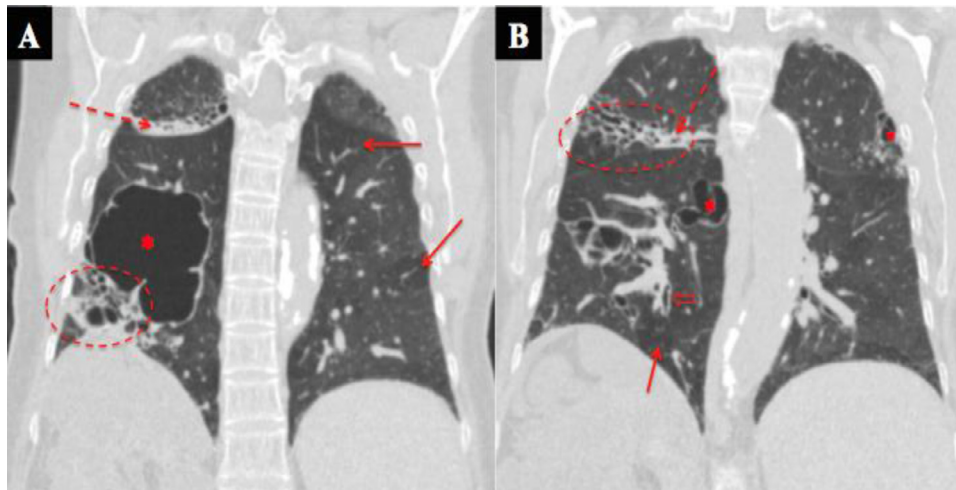
Fig. 2 – Coronal non-contrast computed tomography of the thorax demonstrates multiple pulmonary cysts, with a dominant large, irregular cyst in the right lower lobe (asterisks). Areas of interstitial fibrosis (dashed arrows), cylindrical bronchiectasis (open arrows), honeycombing (dashed ovals), and air trapping (solid arrows) are also seen bilaterally.
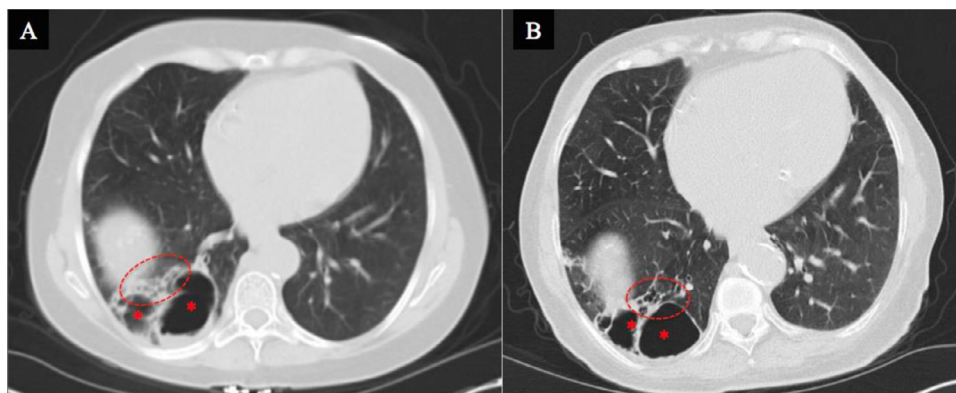

Fig. 3 – Axial non-contrast computed tomography images of the thorax in the lower lung zones obtained 9 years prior (Fig. 3A) show honeycombing (dashed ovals) and pulmonary cysts (asterisks). There is also a small amount of dependent fluid/debris visualized in the larger cyst. Axial non-contrast computed tomography images of the thorax at the same level in the lower lung zones obtained at the time of admission (Fig. 3B) show a similar degree of honeycombing (dashed ovals) and pulmonary cysts (asterisks).

sically presents in the third and fourth decades of life. Renal manifestations of ADPKD have been well characterized by the development of large bilateral renal cysts. As the cysts grow and distort the normal healthy renal parenchyma, patients may present with hypertension, abdominal pain, and hematuria. Gross specimens and histopathology demonstrate diffuse cystic enlargement of the kidneys, with hundreds to thousands of epithelium-lined cysts. This leads to compression, and later atrophy, of the normal renal parenchyma. Over time, as healthy renal parenchyma is replaced, approximately 50% of patients will progress to end stage renal disease by 60 years of age [1,2].

Pathogenesis of ADPKD has been linked to mutations of either the *PKD1* or *PKD2* gene, which encode for the polycystin 1 and 2 proteins, respectively [9,10]. Mutations of the *PKD1* gene have been reported in 85–90% of patients with ADPKD, with the remaining minority having mutations of the *PKD2* gene,

which typically presents with a milder disease course [4,5,9]. These proteins have been implicated as important components of a variety of epithelial and endothelial mechanosensory ion channel complexes leading to renal cyst formation [9–11]. Fluid filled outpouchings or diverticula form in the renal tubules and later wall off to become the epithelial lined cyst that the disease is known for. The polycystin proteins are located in the renal tubules and in epithelial and endothelial surfaces elsewhere in the body, thus resulting in both the renal and extra-renal manifestations of this disease [1,2,4,9–11].

Several extra-renal manifestations of ADPKD have also been described including hepatic cysts, pancreatic cysts, central nervous system arachnoid cysts, intracranial aneurysms, cardiac valvular abnormalities, colonic diverticulosis, abdominal wall hernias, seminal vesicle cysts, and infertility [1–4]. While the majority of these extra-renal manifestations of ADPKD have been well described, understanding of the pul-

Fig. 4 – Non-contrast axial computed tomography image of the abdomen showing multiple cysts in the liver (solid arrows) and kidney (asterisks) with some peripheral calcifications in keeping with autosomal dominant polycystic kidney disease.

monary manifestations of ADPKD has been limited due to the relative rarity, having only been described in a handful of case studies [3,5–8]. The most commonly reported synchronous pulmonary pathologies are bronchiectasis and pulmonary cyst formation, which are thought to be secondary to polycystin mutations resulting in ciliary dysfunction involving the airway epithelium and smooth muscle [5,9–12].

Bronchiectasis tends to be the prevalent feature of ADPKD in the lung with a reported incidence of 19–37% [5,7,11]. A single center retrospective analysis performed by Driscoll and coworkers evaluated the CT findings of patients with ADPKD compared to patients with chronic kidney disease and demonstrated a significantly increased prevalence of bronchiectasis in the ADPKD cohort (37% vs. 13%) [5]. In this cohort, mild cylindrical bronchiectasis was present without a lobar predominance. A similar single center retrospective analysis performed by Moua and coworkers confirmed these findings, demonstrating a higher prevalence of mild bronchiectasis in those with ADPKD, with lower lobe predominance [7]. While the majority of the current literature describes cylindrical bronchiectasis as the predominant pattern in ADPKD, at least one study has demonstrated centrally distributed cystic bronchiectasis [3]. Our patient demonstrated both cylindrical and cystic bronchiectasis without a lobar predominance fitting both patterns.

The incidence of pulmonary cyst formation in ADPKD is much less common than bronchiectasis and has been reported in only a few case reports [6,8]. Pulmonary cysts in the setting of ADPKD tend to be of variable size without a lobar predominance. In all previously reported cases, based on the lack of a reasonable alternative diagnosis, pulmonary cysts were attributed to underlying ADPKD. Based on the rarity of pulmonary cysts associated with ADPKD, it has been sug-

gested that the presence of coexisting tuberous sclerosis complex (TSC) might explain the presence of both pulmonary and renal cysts. Genomic analysis has revealed a close proximity to the TSC2 and PKD2 genes on chromosome 16 and therefore, a TSC2–PKD1 contiguous gene syndrome has been hypothesized in patients with pulmonary cysts in the setting of ADPKD, although, this has not been verified to date [6]. Though our patient did not have identifiable stigmata of tuberous sclerosis, this remains an interesting hypothesis and requires further investigation.

Our patient's CT examination demonstrated the presence of both cylindrical and cystic bronchiectasis, as well as, pulmonary cysts of varying sizes without lobar predominance. Differential considerations for cystic lung disease include lymphangioleiomyomatosis (LAM), pulmonary langerhans cell histiocytosis, lymphocytic interstitial pneumonia, Pneumocystis pneumonia, and desquamative interstitial pneumonia. Our patient was well outside the typical demographic of LAM which classically affects women of childbearing age and was without identifiable stigmata of tuberous sclerosis making LAM unlikely. As our patient was a non-smoker both pulmonary langerhans cell histiocytosis and desquamative interstitial pneumonia were also considered unlikely. As the cysts did not fit a peribronchovascular distribution and the patient did not have a history of connective tissue disorders or immunocompromised status, lymphocytic interstitial pneumonia and Pneumocystis pneumonia were considered unlikely [13]. Therefore, our patient's cystic lung disease was attributed to her underlying ADPKD.

To the best of our knowledge, coexisting interstitial fibrosis with ADPKD has not been described in the literature to date. Our patient had interstitial fibrosis characterized by reticulation, traction bronchiectasis, and honeycombing and while

the overall pattern was suggestive of usual interstitial pneumonia, there were a few scattered areas of air trapping [14]. Given the relatively stable clinical findings without significant disease progression, idiopathic pulmonary fibrosis was considered unlikely and our patient did not have any underlying disease process (eg: collagen vascular disorders) or drug exposure to attribute the findings to secondary UIP from typical causes. Our patient also did not report a history of inhaled allergen exposure, making chronic hypersensitivity pneumonitis unlikely. The overall pattern of fibrosis and the clinical picture do not conform to any other type of interstitial lung disease with findings presumed to be secondary to ADPKD [14]. In general, the other pulmonary manifestations of ADPKD tend to have a mild clinical course, which might explain the relative indolent course of fibrosis in our patient [7,11]. However, the exact relationship or potential casual nature of ADPKD to interstitial fibrosis is unclear at this time, and warrants further investigation.

In conclusion, this is a case of ADPKD demonstrating previously described rare pulmonary manifestations including bronchiectasis and cystic changes, but also to the best of our knowledge, the first case demonstrating concurrent manifestations of interstitial fibrosis [3,6,8]. As there are currently no clear guidelines or recommendations for routine screening for coexisting lung pathology as a manifestation of ADPKD, knowledge of the rare pulmonary manifestations is crucial when evaluating these patients [4].

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