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End-Stage Idiopathic Pulmonary Fibrosis (IPF) Presumably Associated with Biomass Smoke Exposure: A Case Report from Kenya

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Abstract: **Idiopathic pulmonary fibrosis (IPF) is the most serious form of interstitial lung disease and is characterized by chronic fibrosing interstitial pneumonia and the pathognomonic usual interstitial pattern (UIP) on a high-resolution CT (HRCT) scan of the lungs, as well as lung histology. Risk factors associated with IPF include cigarette smoking, environmental exposures to biomass fuel smoke, organic dust, and other air pollutants. IPF is invariably progressive and fatal, with a mean survival of 2-5 years after diagnosis and a mortality rate of up to 85% following an acute exacerbation. Whereas anti-fibrotic agents like nintedanib and pirfenidone may slow down the decline of pulmonary function even in advanced disease, they are not readily affordable for a typical rural Kenyan patient. In this study, we report on the diagnostic process of IPF in a rural Kenyan woman and highlight the challenges of managing end-stage IPF.**

Keywords: **idiopathic pulmonary fibrosis, IPF, usual interstitial pattern, Velcro-type crackles, biomass fuel, *cor pulmonale*, high resolution chest CT scan, Kenya.**

1. INTRODUCTION

Idiopathic pulmonary fibrosis (IPF) is the most common form of interstitial lung disease and is classified as idiopathic interstitial pneumonia (IIP). The other IIPs include nonspecific interstitial pneumonia (NSIP), respiratory bronchiolitis-associated interstitial lung disease (RB-ILD), acute interstitial pneumonia (AIP), etc. (1). IPF is characterized by a spontaneously occurring chronic fibrosing interstitial pneumonia that is limited to the lungs and is associated with the pathognomonic usual interstitial pattern (UIP) on a high-resolution CT scan (HRCT) of the lungs as well as lung histology (though the latter is rarely necessary) (2, 3). Although IPF suggests a lack of a known cause, some risk factors have been associated with the disease. These include cigarette smoking (4), exposures to stone and metal dusts (5), biomass smoke from wood (6), organic dusts and air pollutants (5, 7), etc. Similarities between IPF and post-COVID-19 pulmonary fibrosis are well established (8, 9). The most common clinical manifestations of IPF include a gradual onset of progressive exertional dyspnea and a dry cough. Physical findings include basal lung crackles as well as the pathognomonic Velcro-type lung crackles of established fibrosis (10). These are brief, discontinuous, explosive, and transient pathological lung sounds heard mainly in late inspiration, named after their similarity to the sound generated by Velcro strips separating. Finger clubbing is found in advanced fibrosis (11). Consensus guidelines have been established for the algorithmic diagnosis and management of IPF and include clinical assessment, pulmonary function tests (which show a restrictive pattern with a reduced forced vital capacity [FVC] but a normal ratio of forced expiratory volume in one second [FEV1]/FVC), a reduced DLCO, and, as the disease progresses, a decrease in the six-minute walk distance) (2). The chest imaging of choice is the high-resolution chest CT scan (HRCT). This must be obtained for all patients with suspected IPF. It shows peripheral, basilar-predominant opacities associated with honeycombing and traction bronchiectasis (12, 13). See Figure 1 below from

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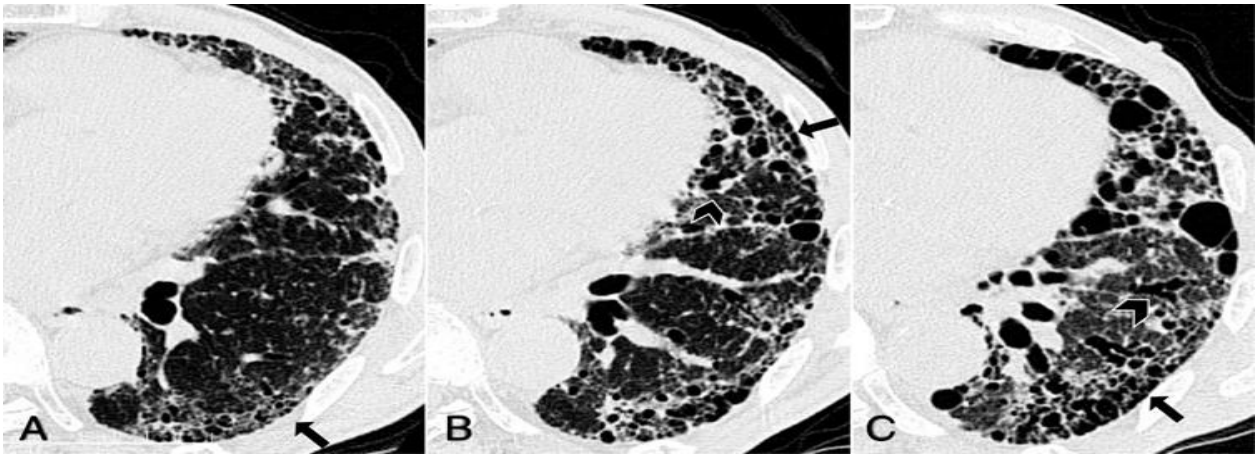
Oda K. *et al.* (14). IPF is a progressive disease with a poor prognosis. The median survival is 2-5 years following diagnosis (15). The natural history is marked by acute exacerbations due to recurrent chest infections. Patients progressively develop respiratory failure, pulmonary hypertension, *cor pulmonale*, and eventually left sided heart failure due to a reverse Bernheim effect (15). This progression is accelerated by cardiovascular diseases, chronic obstructive lung diseases, and other comorbidities (16). The management of IPF is thus aimed at minimizing inflammation and the progression of fibrosis, prompt treatment of acute exacerbations and comorbidities, and supportive care (2). Some of the specific therapies for IPF include the antifibrotic agents nintedanib and pirfenidone (17); and lung transplantation (18). The use of steroids in IPF has had mixed results but remains a cornerstone in managing acute exacerbations (19, 20).

Figure 1: HRCT Findings in IPF



Key: *High-resolution CT findings of a patient with an adverse prognosis. The patient was a 78-year-old man with IPF. HRCT scan at the level of lower left lobe shows fibrosing changes from the baseline (A) at six (B) and 12 months (C). HRCT images at diagnosis of IPF show subpleural predominant interstitial fibrosis, traction bronchiectasis (arrowheads) and honeycombing (arrows). The overall HRCT fibrosis score at the baseline, six and 12 months were 151.3, 162.5 and 185.8, respectively. This patient died 20 months after initial diagnosis. Adapted from Oda K. et al. (14).*

2. CASE SUMMARY

Presenting illness and physical examination

A 77-year-old widowed mother of five, a farmer from Naivasha, Nakuru County, Kenya, first presented to us in April 2023 with clinical features of biventricular congestive heart failure on a background of uncontrolled hypertension. She had no other cardiovascular risk factors. At presentation, she had a 2-week history of progressive cough productive of white sputum but no constitutional symptoms, exertional dyspnea (New York Heart Association grade 2-3), grade 3 pedal edema, orthopnea, paroxysmal nocturnal dyspnea, chest tightness, and recurrent nocturnal wheezing. The latter two symptoms had also been on-and-off for three years prior. She had no history of asthma, was a life-time non-smoker (as was her late husband), and had never been treated for tuberculosis or recurrent childhood chest infections. She had no history of COVID-19 infection and had been vaccinated and boosted against SARS CoV-2 infection. She lived in a typical Kenyan rural village where she had a lifetime of subsistence use of firewood and charcoal for fuel and had no memory of exposure to quarry work sites, dusty road construction, or working in any factory or mining sites. Her physical examination was significant for a baseline hypoxia with an oxygen saturation of 86-88% in room air by pulse oximetry, mild cyanosis of the nails, and a blood pressure of 172/65 mmHg. She had grade 3 finger clubbing (see Figure 2) and bipedal pitting edema up to the sacrum. She had Velcro-type crackles involving up to half of both lungs, with scattered wheezes in the upper lung fields bilaterally. She had normal volume, regular peripheral pulses, an elevated jugular venous pressure of about 10cm, a left parasternal heave, normal S1 and S2 heart sounds but an S3 gallop and a loud P2, and a grade 4/6 murmur of tricuspid regurgitation. She had a tender pulsatile hepatomegaly about 4cm below the right costal margin but no obvious ascites. She was confused with a GCS of 13/15 but had no other focal neurology. The rest of the exam was unremarkable.

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Figure 2: Finger clubbing grade 3: -the nails take an obvious curvature and appear as biconvex laterally.

Grading of finger clubbing: -

Grade 1: The nail bed becomes soft.
Grade 2: There are changes in the angle of the nail fold with loss of Schamroth window.
Grade 3: The nail takes on a more obvious curve.
Grade 4: The end of the finger becomes thicker (club-like).

Diagnostic work-up

Her work-up included a normal complete blood count, creatinine, random glucose, and a urinalysis. The EKG showed a normal sinus rhythm with a ventricular rate of 84 bpm, a normal P-wave and QRS axis, left ventricular hypertrophy and P-*pulmonale*, and no features of ischemia or heart block. An interval transthoracic point-of-care echocardiogram showed a concentric left ventricular hypertrophy with diastolic dysfunction, a left ventricular ejection fraction of about 45%, no regional wall motion anomalies, no pericardial effusion, no mural or intracardiac thrombi, moderate to severe tricuspid regurgitation with mild mitral regurgitation, and a right ventricular systolic pressure of about 45 mmHg, consistent with pulmonary hypertension. Her chest x-ray (CXR) showed a cardiomegaly with bibasal reticular infiltrates, interstitial edema, and ground-glass opacities. See Figures 3 and 4. She had negative sputum microscopy for acid-fast bacilli and a negative sputum Gene X-pert test for tuberculosis.

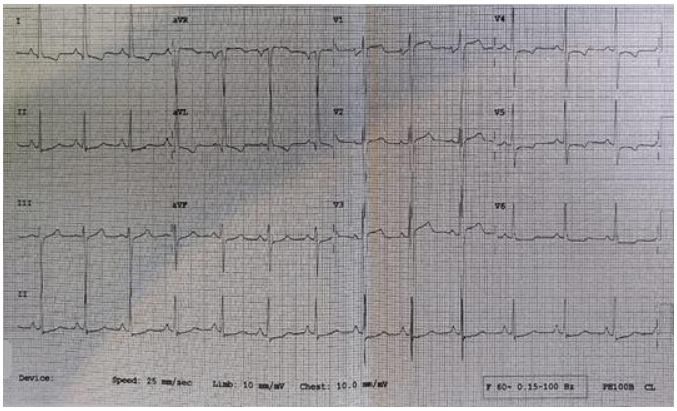

Figure 3: EKG showing a normal sinus rhythm with a ventricular rate of 84 bpm, normal P and QRS axes, left ventricular hypertrophy by voltage criteria, and P-*pulmonale.*

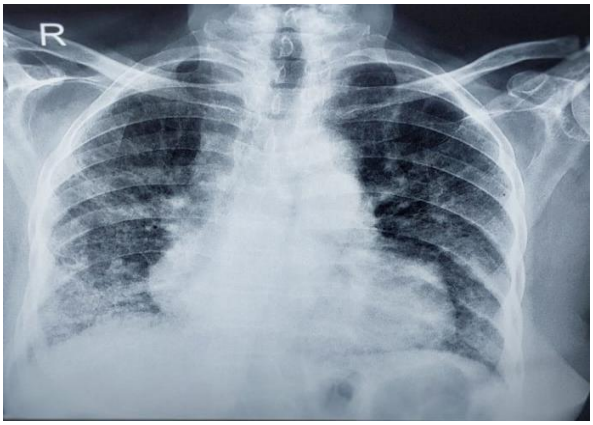

Figure 4: Baseline CXR showing a cardiomegaly with bibasal reticular infiltrates, interstitial edema, and ground-glass opacities

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Diagnosis, Management, and Follow-up

She was assessed to have features of biventricular heart failure complicated with pulmonary hypertension (WHO Groups 2 and 3) and hypoxia. The etiology was deemed to be hypertensive heart disease and possible biomass smoke-induced interstitial lung disease (most likely idiopathic pulmonary fibrosis) complicated with pulmonary hypertension (WHO Group 3) with a reverse Bernheim effect. An interval high resolution CT (HRCT) scan of the chest showed a cardiomegaly with an enlarged pulmonary trunk, ground-glass opacities in both lung fields predominantly in the peripheries, septal thickening with a crazy paving pattern and honeycombing in the right basal lung, no confluent consolidation, no mediastinal adenopathy, no pleural effusion but mild pleural thickening, and prominent upper lobe vessels. (Unfortunately, the HRCT chest images were too damaged to be used in this publication.) The precipitant for the current presentation was assessed to be her uncontrolled hypertension and community-acquired pneumonia. She was admitted and put on comprehensive therapy, including intravenous then oral diuresis with furosemide, intravenous ceftriaxone and oral azithromycin, oral losartan, spironolactone, steroids (initially intravenous hydrocortisone then oral prednisone), sildenafil 25mg twice daily, salbutamol plus ipratropium bromide nebulization, short-term oxygen supplementation, and other supportive care. Additionally, she was given the PCV-13 pneumococcal vaccine (we did not have PPSV-23). An attempted pulmonary function test was unsuccessful several times due to her very poor respiratory effort. She was discharged home stable after 4 days of inpatient therapy, with SPO2 of 89-91% in room air and on comprehensive medications, including steroid and salbutamol metered dose inhalers, sildenafil, and anticoagulation with warfarin. She was followed up on for another 4 months in the clinic. During this time, she was re-admitted twice in anasarca and severe respiratory distress, which was precipitated by recurrent pneumonia. One of the repeated CXRs done 3 months later showed a worsening of reticular infiltrates and pulmonary edema. See figure 5. This led to progressively worsening hypoxia until she became oxygen-dependent, needing long-term oxygen therapy (LTOT). This was achieved by means of an oxygen concentrator machine delivering oxygen through nasal prongs. Unfortunately, she succumbed to severe pneumonia in another facility six months later.

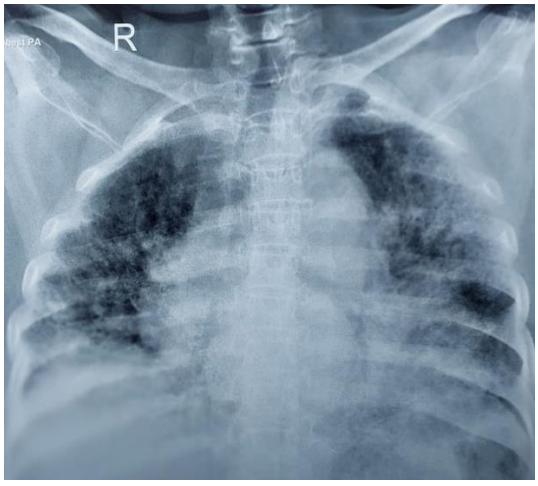

Figure 5: A CXR repeated 3 months from the index admission showing a worsening of reticular infiltrates and pulmonary edema, as well as pneumonia in the left upper lobe.

3. DISCUSSION

A diagnosis of IPF must be suspected in patients who present with progressive exertional dyspnea, a dry cough, finger clubbing, and Velcro-type lung crackles (2). This was the case with our patient. The diagnosis was confirmed by a HRCT of the lungs, which showed advanced features of the usual interstitial pneumonia pattern. We believe that the IPF in our patient was most likely associated with a life-long exposure to smoke from biomass fuel (6). She had been cooking using firewood and charcoal all her life. It is possible that certain genetic factors predisposed her as well (6). At the time of her IPF diagnosis, she had already developed respiratory failure, pulmonary hypertension, and *cor pulmonale* with features of left-sided heart failure (the reverse Bernheim effect). The advanced nature of her disease was compounded by hypertension and exacerbations from recurrent pneumonias, leading to an accelerated decline in her cardio-pulmonary function and eventual death. These recurrent pneumonias occurred despite having been given the PCV-13 pneumococcal vaccine (21), suggesting a possible poor immunogenicity probably partially explained by concurrent systemic steroid use (22). This is

consistent with the poor prognosis of IPF, especially when each episode of an acute exacerbation carries a mortality rate of up to 85% (23). Other poor prognostic indicators in our patient included her advanced age, need for long-term oxygen therapy, a diffuse pattern of involvement on HRCT, and concurrent uncontrolled hypertension (24). We extensively counseled the patient and her family on the end-stage nature of her disease and linked them with a psychological counselor upon discharge for ongoing psychosocial care. Whereas observational data suggest that nintedanib and pirfenidone are efficacious in slowing the decline in pulmonary function (measured by forced vital capacity) across the range of disease severity (25, 26), they were too expensive for our patient to afford. We administered sildenafil and warfarin in accordance with the guidelines for the management of pulmonary hypertension (27).

4. CONCLUSION

IPF is progressive and invariably fatal. Patients need to have a HRCT of the lungs to confirm the usual interstitial pattern. Advanced disease presenting with respiratory and heart failure needs a personalized approach that focuses on long-term oxygen therapy, diuresis, anticoagulation, other supportive measures, and counseling on end-of-life matters. The use of antifibrotic agents must be rationalized.

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INFORMED CONSENT

Informed consent was obtained from the patient to publish this case report.

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