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CASE REPORT: RECURRENT INFECTED BRONCHIECTASIS IN POORLY CONTROLLED PATIENT LEADING TO CARDIO HEPATORENAL SYNDROME

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Abstract

Background: Cardio hepatorenal syndrome is a severe condition due to chronic congestive heart failure complications characterized by liver and kidney function impairment, however, this condition has a potentially reversible complication.Bronchiectasis as a chronic lung disease was a burden for the healthcare system, especially involving other organs like heart, liver, and renal function. Those conditions were complicated and created a quandary regarding the effective treatments to improve the clinical condition and reduce morbidity and mortality.

Case illustration: A 42-year-old man developed cardio hepatorenal syndrome (CHRS), which may have occurred from recurrent infected bronchiectasis that he had. His HRCT scan of the thorax with contrast showed multiple dilated bronchiwith tram track and signet ring appearance with decreased liver and renal function in laboratory findings, and probability of pulmonary hypertension (PH) and right heart failure (RHF) in echocardiography examination. The diuretic, beta-blocker, and antibiotics were given. During hospitalization, there was improvement day by day not only in his clinical condition but also in his liver and renal function. He has used oxygen as needed, and there was no longer any indication for him to be hospitalized.

Conclusion: Patients with chronic lung diseases like bronchiectasis could have decreased lung function, which developed into other connected organ functions, like heart, liver, and renal. In this case, we found reduced heart, liver, and renal function, requiring a multidisciplinary approach to improve the condition.

***Keywords*:** Bronchiectasis, PH, RHF, cardio hepatorenal syndrome.

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Introduction

Bronchiectasis is an abnormal dilatation of the bronchi producing a chronic cough, mucoid sputum and a variety of the ability to breathe [1, 2]. Based on its mechanism is on inflammation responses causing not only epithelial injury but also remodelling process [3, 4]. The effects of inflammation responses reducemucociliary clearance and create a mucous stasis condition, allowing chronic infection, and leading more inflammation and injury of the epithelial [3, 4]. Those conditions occur continuously like nightmare, called vicious cycle [3, 4].

The severe bronchiectasis may leads to impact increased pulmonary venous pressure, called pulmonary hypertension (PH) [5, 6]. An elevated pulmonary vascular resistance (PVR) in PH allows increasedright ventricle (RV) pressures and afterload causing RV dilatation and remodelling [6, 7]. A worsened right heart function can make an impact on liver and kidneydue to retrograde flow of the central vein congestion that reduce the arterial perfusion and hypoxemia of those organs [5, 8]. The potential for heart failure as a complication of chronic lung disease which causes impaired liver and kidney function, allows this condition to be considered as cardiohepatorenal syndrome. Cardio hepatorenal syndrome (CHRS) is a severe condition due to chronic congestive heart failure complication characterized by liver and kidney function impairment but potentially reversible [9].

An awareness of the consequences of bronchiectasis is required because it may decrease those organs functions, thus increasing morbidity and mortality. For these reasons, bronchiectasis is a burden for the healthcare system because the management of bronchiectasis is not only by pulmonologist but also other experts, requiring a multidisciplinary approach.In this paper, we review a case about recurrent infected bronchiectasis in poorly controlled patient leading to cardio hepatorenal syndrome.

Case Report

A 42-year-old man came to our hospital with worsened breathing. He had a purulent cough and fever one week ago, but he had been hospitalized for the last five days in the previous hospital. He also had foot edema and palpitation in the last two months. He admitted having a history of several respiratory tract infections yearly. However, he denied having a history of not only tuberculosis infection. A history of liver or kidney impairment and sinusitis was denied.

Physical examination showed decreased oxygen saturation (94% with a non-rebreathing mask at 10 L/m) measured by oximetry, increased jugular vein pressure, bilateral rales, and bilateral inferior extremity edema. There was no excessive sweating in appearance. Echocardiography examination showed normal left ventricular function (EF 57%), dilated right atrial and ventricular with reduced ventricular function (TAPSE 0.99cm), and high probability of pulmonary hypertension (TR Vmax 3.54 m/s and TR maxPG 50.27 mmHg). Laboratory findings showed elevated liver enzymes and creatinine serum (Table 1). A high-resolution computed tomography (HRCT) scan of the lungs with contrast showed multiple dilated bronchiwith tram track and signet ring appearance and ground glass opacities bilateral. This imaging also showed fibrosis at the apical segment of the right upper lobe and bilateral inferior lobes (Figure 1). There was just one documented imaging by the patient one month ago. The chest x-ray showed a honeycomb appearance (Figure 2).Abdominal ultrasonography findings showed normal hepar and portal veins with dilated hepatic veins and free fluid in the abdominal cavity. Additionally, the oscillometry findings showed small airway obstruction (Figure 3).

Supplemental oxygen was used with a non-rebreathing mask, started at 10 L/m, maintaining a saturation of 88-92%.The patient was given double antibiotics for nine days, meropenem as the main antibiotic, and an adjusting-dosed levofloxacin. Meropenem was used for five days at the previous hospitalization and continued until the blood culture, sputum culture, and procalcitonin results were released.Additional therapies to improve respiratory symptoms were given such as high-dose acetylcysteine, steroid, and bronchodilator inhalation. The patient also got a diuretic and beta-blocker from a cardiologist to improve the liver and renal perfusion by reducing venous congestion. In addition, the patient was given albumin supplementation and curcuma by an internist. The patient showed improvement in clinical appearance day by day and in liver and renal function every three days evaluation. The specific pathogen was undetected in blood and sputum culture. The procalcitonin result showed no indication to continue the antibiotic. For these reasons, there was no longer any indication for the patient to be hospitalized.

Table 1. Laboratory results : Showing elevated liver enzymes and creatinine on admission and the evaluation every 3 days.

	On admission	Evaluation every 3 days		
		3rd day	6th day	9th day (last day of hospitalization)
Leucocyte (10^3/µL)	17.43			
Hemoglobin (g/dL)	13.1			
Hematocrit (%)	40.3			
Thrombocytes (10^3/µL)	248.000			
AST (U/L)	872	424	256	178
ALT (U/L)	969	937	691	297
Creatinine (mg/dL)	2.5	1.6	1.4	1.3
Blood Gas Analyze	pH 7.42 PCO2 55 mmHg PO2 67 mmHg HCO3 36 mmol/L ABE 11 mmol/L SBC 37 mmol/L SO2 94%			
Albumin (g/dL)	2.8			
Procalcitonin (ng/mL)				0.05
HBsAg	Negative			
Anti-HCV	Negative			
Blood culture				No specific pathogen
Sputum culture				No specific pathogen

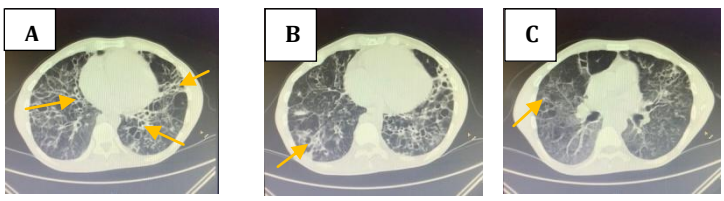

Figure 1. Axial HRCT scan of the thorax : (a) multiple dilated bronchi; (b) fibrotic appearance; (c) ground glass opacities.

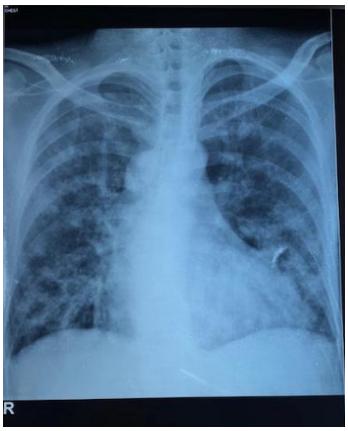

Figure 2. Chest X-ray result : Showing honeycomb appearance.

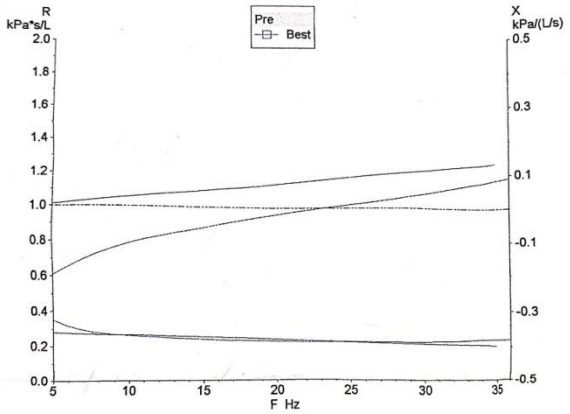

Figure 3. Oscillometry results: Showing increased resistance and negative reactance at lower frequencies. R5Hz : 0.35 of best value (0.28 of pred). X5Hz : -0.20 of best value (0.01 of pred).

Discussion

The patient exhibits cardio hepatorenal syndrome (CHRS) stemming from coexisting chronic lung disease and heart failure (cor pulmonale), along with liver and renal impairment that may be potentially reversible [9]. Bronchiectasis, a chronic lung disease characterized by abnormal and thick-walled bronchi leading to permanently dilated bronchi, manifests with chronic cough, mucoid sputum, and progressive respiratory symptoms that worsen during infectious exacerbations [1,2]. Terminology of bronchiectasis came from “broncos” implying airways, and “ectasia” indicating dilatation [1]. Bronchiectasis in this patient was identified through a high-resolution computed tomography (HRCT) scan of the thorax, which depicted multiple dilated bronchi with tram track and signet ring appearances, termed as the bronchiectasis sign.The widely accepted explanation of the bronchiectasis mechanismis known as the vicious/vortex cycle (Figure 4) [3,4]. In this cycle, transmural inflammation resulting from airway infection or injury damages the epithelium due to enzymes (neutrophil elastase and metalloproteinases) released by white blood cells, including neutrophils, macrophages, and lymphocytes [4]. These cells induce ciliary dysfunction, mucous gland hyperplasia, mucous hypersecretion, reduce mucociliary clearance, and impaired bacterial opsonization, thereby reducing phagocytosis and bacterial killing by releasing proinflammatory chemokines and cytokines [4]. These structural abnormalities create mucous stasis condition, a suitable environment for microbes, resultingin reinfection and inflammation. The ineffective tracheobronchial clearance in bronchiectasis patients further complicated this condition [3,4]. Furthermore, thiscycle leads to increased damage and progression of bronchiectasis, ultimately resulting in elevated pulmonary venous pressure [3–6].

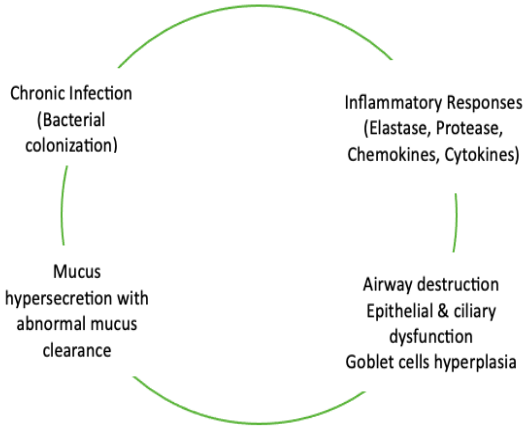

Figure 4. Vicious cycle mechanism of bronhiectasis [3,4].

The bronchiectasis appearance in imaging can mimic diffuse panbronchiolitis (DPB). DPB typically manifests with bilateral, diffuse, small nodular shadows and pulmonary hyperinflation, with ring-shaped or tram-line shadows appearing in advanced cases. Over 80% of DPB patients have a history of chronic sinusitis or currently experience it [10]. However, this patient, lacks evidence of sinusitis and does not exhibit the characteristic small nodular shadows with pulmonary hyperinflation in the imaging.Cystic fibrosis is another condition that can mimic bronchiectasis, but in this case, pancreatic insufficiency and obvious abnormalities in sweat electrolytes are absent [10]. Additionally, the patient has no history of excessive sweating.The imaging also reveals ground glass opacity, indicative of a potential acute infectinve process. Groundglassopacityis a non-specificfindingwith a widerangeofunderlyingcauses, oftenassociated with infection in acutecases. To make a suggestive diagnosis based on thegroundglassopacitypattern, it shouldbecorrelatedwiththepatient'sclinical data andothersupporting examinations [11]. Although previous CT scans were unavailable for comparison, and there was only one previous x-ray showing a honeycomb appearance, the presence of clinical signs of acute infection (a purulent cough with fever and bilateral rales) and leukocytosis allows for considering the appearance of ground glass opacity in this patient as suggestive of an infectious process.

Additionally, the presence of fibrotic tissue in the patient’s high-resolution CT scan may be associated with recurrent inflammation due to a vicious cycle. According to a recent study on idiopathic pulmonary fibrosis, recurrent damage to

pulmonary epithelial cells from microbes, inhaled/systemic toxins, or other sources and inadequate repair of these cells, disrupt the defense mechanism of the epithelium. This disruption can lead to abnormal fibroblastic responses [5]. Injuries of the epithelium not only affect inflammatory and structural cells, but also impact matrix synthesis and the deposition of fibroblasts due to the release of cytokines, growth factors, and mediators [12]. Ultimately, pulmonary parenchymal fibrosis can disrupt the structure and function of pulmonary gas-exchange, leading to reduction in lung function and impacting morbidity and mortality [12].

Bronchiectasis is considered a chronic lung disease capable of not only decreasing pulmonary function but also affecting heart function through the development of pulmonary hypertension (PH), which in turn leads to elevated right ventricle (RV) afterload, eventually progressing to right-sided heart failure (RHF) [2,5]. PH is a common complication of chronic lung disease and a common denominator of all the diseases that lead to chronic cor pulmonale, a condition in which the right ventricle undergoes morphological and/or functional changes due to diseases impacting the lungs, pulmonary circulation, or the breathing process [2,6]. Pulmonary hypertension is defined as an increased mean pulmonary arterial pressure (PAP) >20 mmHg at rest in right heart catheterization as a gold standard assessment, but the echocardiographic can evaluate the probability as an alternative tool [5,6]. Due to limited facilities, a heart catheterization examination was not carried out. Nevertheless, the echocardiography findings in this patient provided a high probability of pulmonary hypertension with severe tricuspid valve regurgitation (TR) and decreased RV dysfunction, while left ventricle function was normal.

In severe and long-term bronchiectasis, pulmonary hypertension may result from vascular pruning, hypoxic vasoconstriction, or vascular remodeling [2]. In chronic severe lung diseases, such as obstructive or restrictive conditions, chronic alveolar hypoxia triggers endothelial cell responses, releasing vasoconstrictors and growth factors that cause pulmonary vessels to constrict and increase vasculartone [13]. In this patient, the presence of small airway obstruction in the oscillometry result may lead to chronic hypoxia, causing pulmonary vessel responses and ultimately leading to pulmonary hypertension.While spirometry is the gold standard for assessing lung function, oscillometry offers a noninvasive alternative when a patient is unable to perform the maneuvers. It aims to identify changes in small airway function, providing valuable information for early diagnosis and monitoring of respiratory tract diseases. This technique, based on forced oscillation (FOT), is performed passively during tidal breathing using sound waves, typically transmitted through the mouth using an oscillation application. As it does not require effort from the subject, oscillometry can be an alternative test to spirometry in various conditions where spirometry is not feasible [14,15].

Furthermore,remodeling of the pulmonary vasculature, characterized byfibromuscular intimal thickening, results in a reduction of the cross-sectional area of the pulmonary vasculature, developing into an elevated pulmonary vascular resistance (PVR). Consequently, this increase in PVR raises the pressure and afterload of the right ventricle (RV), prompting RV dilatation and remodeling [6,7]. Continuous pressure elevation in the pulmonary vasculature induces a range of mechanical changes in the RV [7]. In the early stage of cardiac remodeling, RV hypertrophy enables the RV to remain isovolumic, as increased cardiomyocyte growth facilitates heightened contractility to correspond to elevated pulmonary arterial elastance [5,7]. Subsequently, RV dilatation induces tricuspid annular dilatation, compromised valvular motion, and functional tricuspid regurgitation (TR). Substandard systolic function renders the right heart incapable of offsetting the heightened pulmonary arterial pressure, consequently resulting in elevated right arterial pressure, known as right heart failure (RHF) in the ultimate stages [7]. In the case of this patient, the presence of tricuspid valve regurgitation (TR) and reduced RV function may be construed as an outcome of the remodeling process, creating a high probability of pulmonary hypertension.

Pulmonary hypertension and right heart failure (RHF) can affect the liver by causing venous congestion, reduced arterial perfusion, and decreased oxygen levels [5]. Liver dysfunction is more closely associated with RHF than left ventricular (LV) dysfunction, and hepatic venous congestion from RHF may raise the risk of acute ischemic hepatitis [5]. Congestive hepatopathy is a liver damage condition resulting from RHF or other cardiovascular conditions that lead to passive venous congestion in the liver. It is typically suspected from abnormal liver biochemical test results during routine evaluations, even if it does not cause symptoms [16]. Patients with congestive hepatopathy usually have severe and prolonged right-sided heart failure [5]. Symptoms may include dull pain in the upper right quadrant, jaundice, ascites (fluid in the abdomen), or jugular venous distention [16]. This patient manifested elevated jugular vein pressure, a common clinical sign in individuals with heart failure. Serum alkaline phosphatase is typically normal or slightly elevated in acute heart failure, but it may be elevated in chronic heart failure, whereas serum aminotransferase levels may be notably elevated [16]. Notably, Kyle et al documented a case of congestive hepatopathy with heightened aminotransferase levels, indicative of acute ischemic hepatitis [16]. Elevated levels of AST (872 U/L) and ALT levels (969 U/L) in this patient were observed, further supporting the diagnosis of acute ischemic hepatitis while concurrently excluding liver infection (absence of HBsAg and negative anti-HCV tests).Characteristic congestive hepatopathy findings in abdominal ultrasound include abnormalities in the inferior vena cava and hepatic veins with the clinical history [16]. In this patient, the ultrasonography examination showed signs of congestive hepatopathy, including dilated hepatic veins and free fluid with a normal-sized liver.

Using drugs that may potentially harm the liver can increase liver enzymes [17]. In the presented case, the patient had a history of meropenem use, however, liver injury due to meropenem is typically mild, rare, transient, and self-limited [18]. Congestive hepatopathy lacks a specific treatment but can be managed by addressing the underlying heart disease [16]. The majority of cases are reversible upon resolution of the underlying causes [5]. This liver impairment is caused by heart

dysfunction called cardio-hepatic syndrome, as an acute or chronic dysfunction of the heart or liver dysfunction that can be impacted to each other [19]. Those organ interactions have wide interrelated components [19].

The other potential consequence caused by venous congestion is renal dysfunction. This condition may increase renal interstitial pressure and renal hypoxia, even without significant prior sodium and water retention from high RV afterload and reduced RV output in the early stage [8]. Furthermore, it results in decreased not only renal blood flow but also glomerular filtration rate (GFR) [8]. Elevated central venous pressure caused by RHF can allow renal congestion from backward pressure and flow, thus decreasing renal perfusion and glomerular filtration rate [5]. In this case, the patient had elevated creatinine serum level (2.5 mg/dL) with decreased GFR (32ml/min/1.73m2). There are no specific clinical manifestations, but it usually depends on the underlying disease [8]. Cardiorenal syndromecan be considered in right-sided heart failure patients with deteriorated renal function at any time of presentation because the terminology of this condition involves impairment in acute or chronic dysfunction between the heart and renal, which may induce acute or chronic dysfunction in the other one [8,20].

Based on the probability of venous congestion and the presence of pulmonary hypertension and right heart dilatation in this bronchiectasis patient, and there is no specific therapy for liver and renal impairment in cardio hepatorenal syndrome (CHRS), the patient got diuretic therapy and a beta-blocker from a cardiologist to reduce the congestion. Curcuma and albumin supplementationwere given to support the liver and to settle the hypoalbuminemia from an internist.Liver and renal function tests were evaluated every three days and showed an improvement. A bronchoscopy examination was not performed due to considering the stability of the patient's condition regarding right heart failure. Treatment for the infection also was given.Because there were limited hospital facilities for culture examination and the patient had a good response to meropenem, we considered continuing meropenem from previous hospitalization besides the adjusting dose of levofloxacin until the blood culture result was released. There was no specific pathogen in blood and sputum cultures, which may be caused by the antibiotics used. During hospitalization, the patient showed an improvement in clinical condition day by day. Respiratory symptoms such as cough and shortness of breath had improved, and the oxygen was used as needed.Moreover, the procalcitonin result showed a low level that indicated stopping the antibiotics used [21]. For these reasons, there was no longer any indication for the patient to be hospitalized.

A better understanding of the bronchiectasis mechanism is required to decide on appropriate management through a multidisciplinary approach, especially when involving other related organs like the heart, liver, and renal. Without an awareness of those consequences, considering the efficiency of therapy would be hardbecause bronchiectasis is not onlya burden to the patients caused by reduced quality of lifebut also a burden to the healthcare system [22].

Conclusion

People with chronic lung disease have the potential to develop cor pulmonale due to increased pulmonary resistance. This condition is closely related to other organs like liver and renal through the central venous system. People with chronic lung disease need to be evaluated regularly to monitor their condition, thus preventing complications in the connected organs.

In this case, poorly controlled bronchiectasis had developed and caused related organ complications such as heart, liver, and renal. Furthermore, it was possible to increase morbidity and mortality. A multidisciplinary approach in advanced chronic lung disease is necessary to evaluate and manage the complications, thus improving quality of life and also considering other condition related.

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Conflict of Interest

The author declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Informed Consent

Informed consent was obtained prior to performing the procedure, including permission for publication of all photographs and images included herein.

Ethical Statement

This case report was conducted in accordance with the National Health Research and Development Ethical Guidelines and Standards. The collection and evaluation of all protected patient health information was perfomed in a Medical Practice Act-compliant manner.

Author Contribution

M.C designed the project, analysed the data and wrote the manuscript. N.M.Y conceived the original idea. W.W.S.P supervised the project and provided critical feedback. M.C wrote the manuscript in consultation with W.W.S.P and N.M.Y.

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