# Pulmonary Papillomatosis: a Rare Case of Recurrent Respiratory Papillomatosis Presenting with Multiple Nodular and Cavitary Lesions

*Diah Martina, Andree Kurniawan, Ceva W. Pitoyo*

Department of Internal Medicine, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

***Correspondence mail:***
*Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia - Cipto Mangunkusumo Hospital. Jl Diponegoro No. 71, Jakarta 10430, Indonesia. email: diahmartina@yahoo.com.*

**ABSTRAK**

*Papilomatosis paru adalah varian papilomatosis respiratorik rekuren yang sangat jarang dijumpai, sulit diobati, menimbulkan morbiditas jangka panjang, dan dapat mengalami transformasi menjadi ganas. Oleh karena gejala dan temuan radiologis yang tidak khas, kelainan ini sering terlambat terdiagnosis. Meskipun bersifat jinak, papilomatosis paru memiliki angka mortalitas yang tinggi. Kami akan menyajikan kasus seorang laki-laki berusia 26 tahun dengan keluhan batuk kronik berulang, hemoptisis, nyeri pleuritik, dan demam. Pasien telah didiagnosis menderita papilomatosis laring dan menjalani reseksi endoskopik serial sejak usia kanak-kanak. Pada pemeriksaan radiografi dan skintigrafi dada didapatkan lesi nodular dan kavitas multipel disertai gambaran air fluid level pada kedua lapang paru. Diagnosis papilomatosis paru dengan infeksi sekunder ditegakkan setelah dilakukan endoskopi dan pemeriksaan histologi.*

***Kata kunci:*** *papilomatosis paru, papilomatosis respiratorik rekuren, lesi nodular, lesi kavitas.*

**ABSTRACT**

*Pulmonary papillomatosis is an extremely rare variant of recurrent respiratory papillomatosis which is hard to treat, causes prolonged morbidity, and may transform into malignant disorder in several cases. Since the symptoms and radiologic findings are not specific, pulmonary papillomatosis is often being misdiagnosed. Although considered benign, pulmonary papillomatosis carries the most significant mortality. This is a case report of a 26 year old man who complained recurrent chronic cough, slight hemoptoe, occasional pleuritic pain, and several episodes of fever. He also had laryngeal papillomatosis and undergone serial endoscopic resection since his childhood. Multiple nodular and cavitary lesions, some with air fluid level, were found in both lung fields at chest radiography and scintigraphy. Diagnosis of pulmonary papillomatosis complicated with secondary infection was made after endoscopic and histologic study.*

***Key words:*** *pulmonary papillomatosis, recurrent respiratory papillomatosis, nodular lesion, cavitary lesion.*

## INTRODUCTION

Recurrent respiratory papillomatosis (RRP) is the most common benign neoplasm of the larynx in childhood.[1] It is characterized by recurrent growth of benign wart-like tumor (papillomatous) along the respiratory tract. The causative agent of RRP is human papilloma viruses (HPV), especially type 6 and 11.[2] Most commonly RRP localized in the larynx, but it may also involve several extralaryngeal sites,

such as trachea, bronchus, and lung parenchym in a less frequency.[3] Despite its benign nature, RRP may cause considerable morbidity as it has a tendency to grow and extend throughout the entire respiratory tract causing severe airway obstruction. It also tends to recur after surgical resection.[4]

Downward extension of papilloma is an extremely rare case. Pulmonary papillomatosis has the least frequency of less than 3%, but it also carries the most significant increase in morbidity and mortality.[4] In this article, we present a case of laryngeal papillomatosis in a 26 year old man that involved pulmonary spread causing chronic recurrent pneumonia.

## CASE ILLUSTRATION

A 26-year-old man complained of recurrent chronic cough with green colored, sometimes bloody, and smelly sputum since several years prior to admission. He also complained of occasional left back pain during respiration and intermittent fever without specific pattern.

From the history taking, we discovered that the patient had been diagnosed as having laryngeal papilloma since he was 9 years old after complaining hoarseness and progressive shortness of breath over a year. He was born vaginally. Unfortunately, his mother already passed away several years ago after a complication of heart disease; hence further investigation of genital papilloma was difficult.

An emergency tracheostomy had been performed immediately after he experienced severe dyspnea few days following diagnosis to release obstruction. A laryngoscopy showed multiple nodular growths at the larynx and tissue biopsy showed squamous cell papillomas. The diagnosis of laryngeal papillomatosis was then made. Since then, the patient had regular checkups in ear, nose, and throat (ENT) specialist and underwent serial endoscopic resection of papillomas three times a year.

Five years before admission, multiple cavities were found coincidentally after chest X-ray examination prior to routine endoscopic procedure. The patient was then treated with antituberculous regiments although negative sputum microscopy. Patient was also given antifungal considered no improvement after the completion of antituberculous treatment. At the next ENT checkup, the X-ray showed multiple thick-walled cavities with air-fluid level and nodular lesion in the right lung. Diagnosis of suspected pulmonary papillomatosis with secondary infection and possibility of segment 10 aspergilloma of the right lung (**Figure 1**) was made. Patient then underwent direct laryngoscopy, previous to bronchoscopy, which showed multiple granular tumors in vocal cord that extended into carina and right main bronchus. However, a more distal visualization through bronchoscopy was failed since the patient became bradycardia and underwent low oxygen saturation when the scope entered the bronchus. Repeated bronchoscopy was reported to have the same event. A tissue examination of nodules in the larynx and carina showed squamous cell papilloma. After that, the patient was hospitalized several times due to recurrent pneumonia.

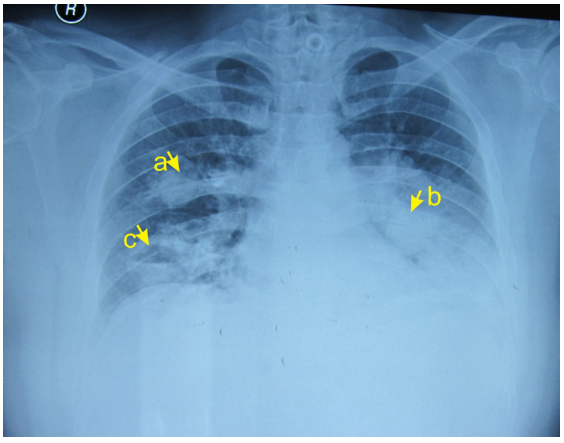


**Figure 1.** Chest X-ray was taken 5 years before admission. Note: the nodules (a, b) and cavity (c) with an air-fluid level (abscess).

On the day of admission, the physical examination of the patient was tachypnea, tachycardia, with an increased in axillary temperature. An auscultation of the lungs showed rales in both lungs with a slight decreased of breath sounds of the left lung. Chest X-ray showed bleak area in both hilus, multiple solid and cavitated nodules in both fields, bleak left hemidiaphragm, and bleak left costophrenicus angle (**Figure 2**).

Chest-CT showed multiple nodules and cavitary lesion, and some abscesses in both lung fields with enlargement of the lymph nodes in the 4R and 7R and perihilar, also lobar pneumonia in lower left lung. (**Figure 3**)

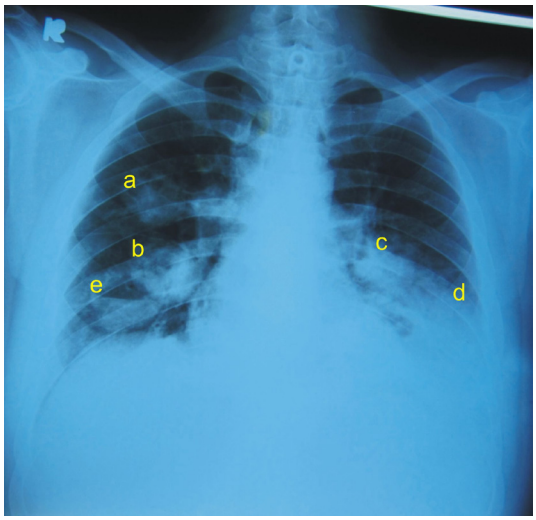


**Figure 2.** Chest X-ray at the time of admission showed more nodules (a, b, c), bleaky area in the left diaphragm (d) and a cavitary lesion with air-fluid level appearance (e).

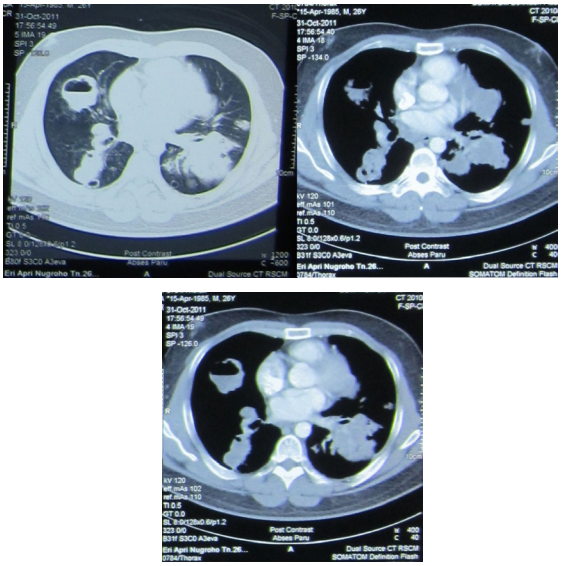

**Figure 3.** Chest-CT showed multiple nodules, cavitary lesions, lymphadenopathy, and abscess.

Diagnosis of pulmonary papillomatosis with secondary infection was made after laboratory and sputum examination. Since the history of previous bronchoscopy was unsuccessful, we planned an elective bronchoscopy with the intensive care team after the infection resolved.

Pneumonia was treated with antibiotic based on the culture and resistance test result, bronchodilator, and mucolytic. During hospitalization, infections signs and symptoms were improved. Physical examination and laboratory evaluation were within the normal range. An evaluation of chest radiograph showed improvement of infiltrates and decreased water level in the cavity. (**Figure 4**) Patient discharged after had an education about healthy lifestyle and hygiene maintenance to prevent reinfection. The bronchoscopy was then planned to be done during outpatient.

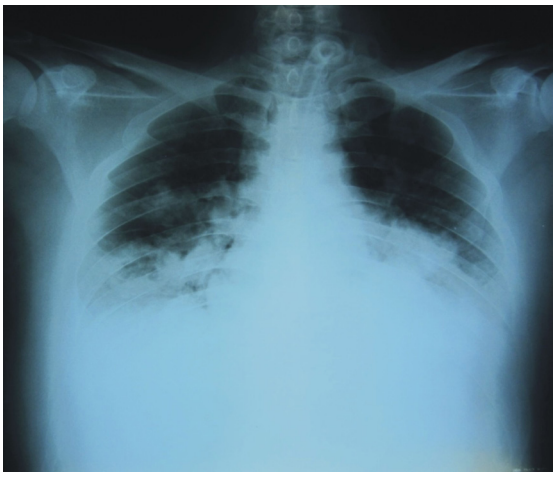

**Figure 4.** Chest X-ray after treatment

## DISCUSSION

Recurrent respiratory papillomatosis (RRP) is a benign growth of papilloma, most commonly juvenile onset and localized in larynx. Therefore, this disorder was formerly known as juvenile laryngeal papillomatosis. However, this term began to be abandoned since it may arise in adulthood with lower frequency. Age of presentation of disease is usually in teens for the juvenile-onset form but can be as early as the first year of life. Initial presentation in the adult form tends to peak in the third and fourth decades.[2] Its tendency to recur and extend downward along the respiratory tract made lead to term "recurrent respiratory papillomatosis".[6] This disorder is exclusively caused by human papilloma virus (HPV) infection, especially type 6 and 11, which is most likely transmitted during transit through the birth canal during vaginal delivery by a

mother with infected cervical tissue.[1,7-9]

A history of persistent hoarseness with progressive difficulty in breathing especially in a child is a pathognomonic symptom.[10] In this case the symptom had been felt since the age of 8 years and had worsen over time. Chronic and progressive symptoms in this case indicate recurrent pattern of papilloma's growth despite serial endoscopic resection.[4,11] These complaints may be misdiagnosed as asthma, chronic bronchitis or vocal cord nodules that may delay the diagnosis with resultant acute airway obstruction.[3,12] Some of these patients may require tracheostomy for immediate breathing and further airway management, such as in this case. Tracheostomy, on the other hand, is also suspected as one of causes of further spread to the bronchial and lung parenchym.[3,6,13]

Although about 75% of RRP remained stable without the extension of papilloma, there is still a possibility to spread to another location.[11] RRP may extend into other respiratory tract, such as trachea in 3-26% of cases and lung parenchym in 1-3% of cases.[4,14] Being the least common, pulmonary papillomatosis carries the most significant mortality and invariably fatal within 10 years.[14]

Precise pathogenesis of lung involvement is unknown. It is believed that the expansion to the lungs is caused by aerial dissemination of the fragments removed at the time of endoscopic surgery and following tracheostomy, with seeding into the lung tissue.[14] Types of HPV and younger onset of RRP are also suspected to be the factors that causes the spread to the lungs, although there are no studies that can prove it.[3] In this case, the patient diagnosed at 8 years old and underwent repeated endoscopic resection up to three times a year by then.

There is no specific symptom to identify pulmonary papillomatosis, although some cases present with chronic cough, hemoptoe, pleuritic pain, or wheezing.[3,4] The typical feature of pulmonary papillomatosis is multiple nodules scattered throughout the lungs, with some evolving to cavitation, and the subsequent risk of chronic infection.[14] Pulmonary involvements may occur and appear in the form of thin-walled cysts, nodules, fibrosis, and bronchiectasis. The mechanism of its formation is still controversial[9,15] and thought due to peripheral airway obstruction by the papilloma which produced emphysematous area, or it may result from necrosis and excavation of solid nodular lesion.[9] In these conditions, a chest-CT to evaluate pulmonary involvement is required. As a standard examination, chest-CT may indicate lung involvement with diffuse spread of lung. Nodules that appear to grow, turn into fluid-filled cysts, and can become large cavities with thin or thick walls. Because the nodules continued to grow, the blood supply to the central nodule disappeared resulting in the occurrence of central necrosis. Communication with an airway causes cavitation. Another hypothesis is bronchial obstruction by the papilloma followed by pneumotoceles or subsegmental emphysema.[16]

In this case, a suspicion of pulmonary papillomatosis began when chest X-ray of a patient with laryngeal papillomatosis showed multiple nodules, cavities, and abscess in both lungs. The history of tuberculosis treatment without clinical and radiological improvement further supports the diagnosis. Patient also complained chronic cough, slight hemoptisis, and occasional pleuritic pain all of which are symptoms of lung involvement of papillomas. Chest-CT showing multiple nodules and cavities, and some abscesses scattered in both lung fields made the diagnosis of pulmonary papillomatosis became more apparent.

Further evaluation of histopathology is the next step. Previous laryngoscopy showed the extension of papillomas into carina and left main bronchus. A bronchoscopy and histological study was required to support the diagnosis. However, bronchoscopy to assess lung involvement failed to reach distal airways due to the problem of oxygen saturation. Therefore, a more careful procedure in intensive care setting was planned to obtain a tissue sample for histology and HPV typing if necessary. The last data of histopathological evaluation obtained from the tissue of the larynx and carina showed the squamous cell papillomas. An ultrasound guided trans-thoracal biopsy revealed no malignant cells which raise the probability that the papilloma had not transformed into malignancy.

Pathological examination in pulmonary papillomatosis is conducted to ascertain whether there is a transformation into a malignant disorder.[3-4,13] Further evaluation of papillomas and possible transformation into carcinoma is considered necessary since RRP possesses risk of malignant transformation in 3-7% of cases.[1,2,4,14,16-18]

Currently there is no standard treatment for lung involvement in respiratory papillomatosis.[14,19] While no medical or surgical cures for RRP, surgical management remains the mainstay of therapy for RRP.[1,20] However, resection can only be done on the disorder that is localized and has not spread. While papillomas in upper airways are amenable to endoscopic excision, those invading the lungs are not.[14] Although several reports have described the effects of different drugs, such as cidofovir, interferon alpha, and indol-3-carbinol, further researches are necessary.[14]

The prognosis of lung papillomatosis is determined by the presence of transformation toward malignancy. However, limitations in determining time of biopsy sampling evaluation make the determination on the patient's prognosis becomes difficult.[14] Age at onset also determine the prognosis. The younger the patient's age at diagnosis, the more likely the patient will have severe disease. Recurrent pneumonia is a common complication which often contributes to its high morbidity and mortality as well.[1]

## CONCLUSION

Lung involvement of recurrent respiratory papillomatosis is a very rare yet fatal case with significant mortality rate. Multiple nodular and cavitary lesions scattered in the lung are the typical pictures of pulmonary papillomatosis. Unfortunately, currently there is no standard therapy for pulmonary papillomatosis. Chronic and recurrent pneumonia is a common complication which contributes to high morbidity and mortality. A careful investigation and endoscopic procedures may help us diagnose and give appropriate treatment needed.

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