รายงานผู้ป่วย • Case Report

โรคพังผืดที่ปอดในพนักงานโรงงานผลิตแป้งมันสำปะหลัง: กรณีศึกษาผู้ป่วย 1 ราย

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Interstitial Lung Disease in Cassava Flour Production Worker: A Case Report

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หลักการ และวัตถุประสงค์: โรคพังผืดที่ปอด เกิดจากหลายสาเหตุ ซึ่งสาเหตุหนึ่งคือจากการสัมผัสสารเคมีจำพวกกรดจากการประกอบอาชีพ แต่มักไม่มีผู้รายงานมากนัก การศึกษานี้มีจุดประสงค์เพื่อศึกษาถึง (ก) ลักษณะทางคลินิกของผู้ป่วยโรคเนื้อเยื่อปอดอักเสบจากการสัมผัสสารเคมีเรื้อรังหลายชนิด โดยเฉพาะการสัมผัสกรดไฮโดรคลอริก และ (ข) เพื่อศึกษาถึงแนวทางการประเมินสุขภาพของผู้ป่วยฯ ก่อนกลับเข้าไปปฏิบัติงาน

วิธีการศึกษา: รายงานผู้ป่วยรายเดียว

ผลการศึกษา: พนักงานชาย อายุ 50 ปี สมรสแล้ว ภูมิลำเนาภาคตะวันออกเฉียงเหนือของประเทศไทยมาพบแพทย์ด้วยผลสมรรถภาพปอดผิดปกติต่อเนื่องติดกัน 5 ปี โดยไม่มีอาการผิดปกติ ตรวจร่างกายไม่พบอาการผิดปกติ ตรวจทางรังสีวิทยาพบว่า ภาพถ่ายรังสีทรวงอกและภาพถ่ายคอมพิวเตอร์ทรวงอกความละเอียดสูงพบลักษณะของพังผืดที่ปอดทั้งสองข้าง วินิจฉัยได้ว่าเข้ากับโรคพังผืดที่ปอด การซักประวัติอย่างละเอียด ตรวจร่างกาย และตรวจวินิจฉัยเพิ่มเติมทำให้สามารถวินิจฉัยแยกโรคอื่นๆ ที่เป็นสาเหตุของโรคพังผืดที่ปอดออกไป และนึกถึงสาเหตุจากการทำงานสัมผัสกรดไฮโดรคลอริกอย่างสม่ำเสมอเป็นระยะเวลานาน จากหลักฐานทางพยาธิวิทยาสามารถบอกถึงผลของการสัมผัสสารจำพวกกรดเรื้อรังว่าทำให้เกิดการอักเสบของเนื้อเยื่อในปอดได้ การประเมินความพร้อมของผู้ป่วยก่อนกลับเข้าไปปฏิบัติงานกับสารเคมีอีกครั้งพบว่า จากผลสมรรถภาพปอดที่ผิดปกติ ถือว่ามีความเสี่ยงต่อการใส่หน้ากาก

Background and Objectives: Interstitial lung disease (ILD) can be caused by many diseases or through occupational exposure to various hazardous chemicals. Our study presents (a) the clinical information on a patient diagnosed with occupational ILD likely caused by exposure to multiple chemicals—in hydrochloric acid—and (b) an approach for assessing fitness for duty of workers with occupational ILD.

Method: Single case report

Results: A 50-year-old northeastern Thai male worker came to hospital with a complaint of 5 years consecutive abnormal spirometry based on annual periodic examination. All elements of the physical examination were within normal limits. The chest X-ray and HRCT revealed pulmonary fibrosis of both lungs, which fulfills the diagnostic criteria for interstitial lung disease, and a history, physical examination, and laboratory investigation can rule in/out the specific cause. ILD can result from chronic occupational exposure to hydrochloric acid; evidenced by pathological assessment of lung parenchyma, confirming that chronic exposure of irritant gas affects the tissue. Our patient had been assessed that there is some risk to wear a respirator based on his abnormal pulmonary function.

Conclusion: The ILD of this patient may have been caused by occupational exposure to hydrochloric acid where there is some risk to wear respirator.

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สรุป: สาเหตุของโรคพังผืดที่ปอดของผู้ป่วยรายนี้น่าจะเกิดจากการสัมผัสกรดไฮโดรคลอริกจากการทำงาน การประเมินก่อนกลับเข้าทำงานพบว่าผู้ป่วยมีความเสี่ยงต่อการสวมอุปกรณ์ปกป้องระบบหายใจประเภทปกป้องสารเคมี

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Background

Interstitial lung diseases (ILDs) are a group of diseases characterized by inflammation and fibrosis of lung parenchyma, alveola, alveolar epithelium, pulmonary vascular endothelium, perivascular tissues, and related lymphatic tissues. It can be caused by more than 200 individual diseases including connective tissue disease[1]; some drugs such as amiodarone or bleomycin; occupational exposure to dust or chemicals like silica, asbestos, ionizing radiation[2]; some irritant gases like ammonia[3], chlorine, and phosgene[4]; and, idiopathic—the most common cause[5]. Most patients are asymptomatic until there is acute inflammation of the lung tissue or there is loss of lung function to some degree.Common signs are dyspnea, chest discomfort, restless, and weight loss[1].

Diagnosis of occupational ILD depends upon occupational history of chemical exposure, signs and symptoms of respiratory distress, and radiological data. The common chest X-ray finding is reticulonodular infiltration, while nodular or mixed infiltration are less common[6]. High resolution computed tomography (HRCT) would help diagnosis with better accuracy but HRCT has some limits vis-à-vis inter-reader variation[7]. Spirometry can indicate the severity of the disease. Most patients with ILDs present some restrictive pulmonary defect; producing a proportional reduction of FVC and FEV1, and possibly both an elevated and/or normal ratio of FEV1 to FVC[8].

Case report

A 50-year-old, married,Thai, male worker, from northeastern Thailand, went to the Occupational Medicine Clinic with a social insurance claim. The chief complaint was that he had had 5 consecutive abnormal spirometry tests at his annual health check up. He had no complaint of difficulty breathing, dyspnea, chronic cough, sneeze, or conjunctivitis. His general living was normal, functional class I. He had no symptoms in other systems such as dysphagia, motor weakness, lethargy, arthralgia, hematuria, or hematochezia. The first chest radiograph taken at the first presentation revealing an abnormality was suspected of being pulmonary tuberculosis; however, no anti-tuberculosis drugs or other treatments were given. In the latest chest radiograph finding (i.e., the fifth of five), the patient was referred to the Occupational Medicine Clinic to determine whether the abnormal chest radiograph could be attributable to his work.

Evaluation at occupational medicine clinic

Based on the previous histories taken, there was no prior medical condition, medicine (s), or admission with respiratory disease that required long-term antibiotics. The patient was non-smoker, but was exposed to second hand smoke at the workplace. He was an occasional drinker.

The occupational history revealed that he had worked as an agricultural products driver. There was no history of any other occupation such as construction laborer or sand stone worker. There was no history of exposure to beryllium or silica. Twenty years prior, he started working in a cassava flour production factory as production unit worker.The job task was mixing various chemicals such as hydrochloric acid, sulfuric acid, and phosphorus oxychloride. He worked in this unit for 10 years, and the only personal protective equipment he used was a cloth facemask. He complained that he always experienced nasal irritation and burning when working with these chemicals and that he could smell the odor. In the 2 years before transferring to a new job, he got use of a half-face mask respirator with a cartridge, which was shared among 10 work mates. This was used only when they were being exposed to

chemicals. The company monitored the workplace environment for light, noise, dust, and ambient mold, but not ambient acid concentration in the air.

Ten years after working in the saltpeter unit, he moved to work with disulfide. Here he also received a half-face mask respirator with cartridge for use when exposed to chemicals.This mask was shared workmates as it was in the previous unit. Since working in a new unit, the respiratory symptoms have subsided.

Five years after moving to the sulfide unit, during an annual health check up, he was told that his chest X-ray was abnormal, and that the physician suspected pulmonary tuberculosis. He denied any history of chronic cough, night cough, night sweating, weight loss, or any other abnormality indicating pulmonary distress. He denied any history of household tuberculosis. He was sent to a general hospital for further work up, which confirmed no evidence of infection; thus, there was no treatment by anti-tuberculosis drugs. This abnormality occurred at each subsequent annual check-up.

Physical examination revealed: a body weight of 68 kg; a blood pressure of 141/89 mmHg; a regular pulse 59 bpm; and, other signs within normal limits. There were no signs of anemia or jaundice. He had normal auscultation of the lungs, normal heart sounds (without murmur), normal abdominal palpation, no hepatosplenomegaly, no abdominal point of tenderness, no other signs of chronic liver disease, no skin lesions or rash, no hardening of the skin, no clubbing of fingers, and a normal neurological examination. The chest radiographs revealed reticulonodular infiltration at the left upper lung field, suggesting pulmonary tuberculosis. There was no organism found in the sputum gram stain (representing 3 days collection). The pulmonary function test—using spirometry—showed a mixed type ventilatory defect (FEV1, FVC, FEV1/FVC ratio, and FEF25-75 was 68.2%, 69.7%; 0.73, and 46.78% of predicted, respectively). The patient was sent to a pulmonologist for consultation, who suggested further high resolution computed tomography (HRCT) of the chest. The HRCT demonstrated fibrosis, pulmonary nodules, and bronchiectasis of the left upper lung and both lower lungs, suggestive of ILD. A further serologic test was done to rule out evidence of autoimmune disease. The rheumatoid factor was within the normal range, the anti-nuclear antibody was positive for the coarse speckle type, and the anti-double stranded DNA was negative.

The occupational physician and pulmonologist evaluated the evidence and concluded that this patient might be suffering from ILD, caused by occupational exposure to acids.

Figure 1, Patient chest radiograph demonstrating reticulonodular infiltration of the left upper lung.

Figure 2-5, Patient HRCT of chest demonstrated fibrosis, pulmonary nodules, and bronchiectasis of the left upper lung and both lower lungs.

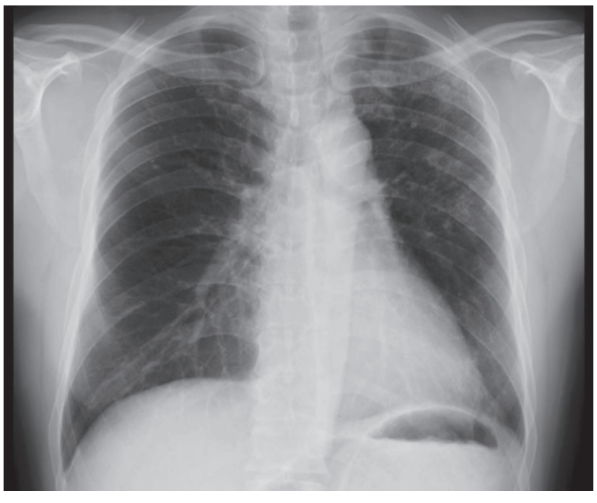
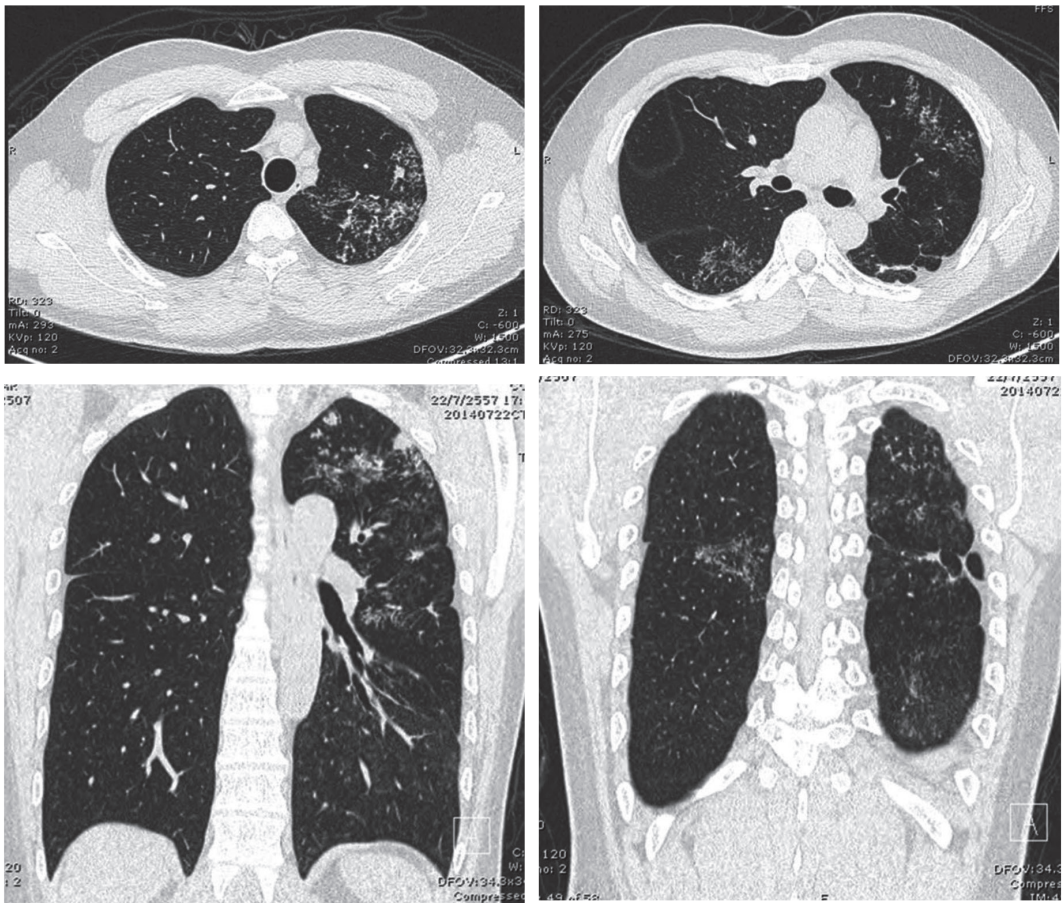


Figure 1 The chest radiograph demonstrating reticulonodular infiltration of the left upper lung.



Figures 2-5 The HRCT of chest demonstrated fibrosis, pulmonary nodules, and bronchiectasis of the left upper lung and both lower lungs.

Discussion

Based on history taking, patient denied any abnormal symptoms such as dyspnea, dysphagia, weakness, fatigue, joint pain, abnormal defecation, or abnormal urination. Connective tissue disease—such as systemic lupus erythematous and systemic sclerosis—was, therefore, ruled out.The patient also denied history of any underlying disease, long-term antibiotic injection, antihypertensive drugs use (i.e., amiodarone).The patient had never undergone any chemotherapy nor rheumatoid treatment; thus, several causative drugs were also ruled out. Additional occupational history-taking revealed the denial of any work in the sand stone industry, tunnel drilling, or construction/demolition; therefore, pneumoconiosis was also ruled out. The patient had, however, worked in a cassava flour production factory, suggesting possible exposure to disease-carrying rodents in the workplace environment. Obadina et al. found *Aspergillus spp*. is one of the most common organisms in cassava waste, and causing hypersensitivity pneumonitis[9]. History-taking and occupational hygiene data, however, showed a normal range of ambient rodent level, making organic dust an unlikely cause of ILD.

Based on the physical examination, connective tissue disease was not likely the cause of the disease. The history and physical examination did not rule out sarcoidosis; however, the radiographic data showed no evidence of hilar adenopathy in either lung, sosarcoidosis was unlikely the cause of ILD[10]. The lack

of serological data—such as angiotensin converting enzyme (ACE), adenosine deaminase, amyloid A or soluble interleukin-2 receptor level—make the conclusion difficult to rule out.

Based on radiologic data, the chest X-ray showed reticolonodular pattern and HRCT demonstrated fibrosis, pulmonary nodules, and bronchiectasis of the left upper lung and both lower lungs, pulmonary tuberculosis was the first differential diagnosis that has to rule out. The 3-days sputum was all negative for any organism. Cultivation of sputum for TB was also no growth. Moreover, an unaltered of pulmonary symptoms and no progression of radiological presentation can encourage pulmonary tuberculosis may not be a cause of ILD albeit difficult to conclusion because lacking of serological data such as sputum PCR for TB.

An additional serologic test showed that the rheumatoid factor was within the normal range; that the anti-nuclear antibody was positive for the coarse speckle type; and, that the anti-double stranded DNA was negative. The possibility of systemic lupus erythematous was, thus, weakened. Even if the ANA were positive for the coarse speckle type, that would not be specific for any connective tissue disease. All of the symptoms and signs, however, were normal, strongly suggesting that connective tissue disease was unlikely the cause of disease.

Diagnosis of occupational cause

Based on the history-taking, the patient came to hospital with a complaint of 5 consecutive years of consecutive abnormal spirometry tests and an abnormal annual chest radiograph, albeit without of any symptoms of pulmonary or others system. Additional history-taking revealed no underlying disease and that the patient never smoked. The occupational history confirmed that the patient was exposed to multi-chemical substances even though there were no signs of any pulmonary disease. The chest radiograph demonstrated reticulonodular infiltration at the left upper lung, but no organism was found in the 3-day sputum collection. The HRCT showed fibrosis and pulmonary nodules in both lungs. Taken together, one concludes that this patient had ILD, and that the likely cause was occupational exposure. Differential diagnosis for finding others causes of disease was necessary.

Potential cause from acid gas exposure

Based on the history-taking, the patient had been exposed to various acidic chemicals such as hydrochloric acid, sulfuric acid, and phosphorus oxychloride. All three acidic substances are used in the degradation of cassava flour to decrease viscosity for processing. The history confirmed irritation of the upper airways and smelling of acidic odor. When phosphorus oxychloride reacts with water or is in solution, it will decompose to hydrochloric acid[11]

$$O=PCl_3 + 3\,H_2O \longrightarrow O=P(OH)_3 + 3HCl$$

Hydrochloric acid is a corrosive strong mineral acid with clear or pale yellow color. It may produce odor when concentration above 0.8 ppm. Hydrochloric acid is mildly to moderately fat-soluble. Exposure to high concentrations may cause acute severe irritation of upper respiratory tract, bronchospasm, pulmonary edema, toxic pneumonitis. After acute bolus exposure, FVC can be reduced within 1-2 years. Chronic low-dose exposure may cause irritation of the upper airway, teeth erosion, perforation of the nasal septum, laryngeal edema[12]. and increasing risk of developing irritant-associated asthma[13]. In pediatric patients, inhalation of hydrochloric aerosol and gas may cause ILD[14].

There is limited research on the effect of chronic low-dose exposure of hydrochloric acid to lung tissue; however, there is research on the effects of chronic low-dose exposure to chlorine gas in animals. There is an influx of inflammatory cells in the peribronchial tissue after long-term exposure, resulting in irritation of the upper airways and causing bronchospasms. The inflammatory cells also increase in other tissue such as the perivascular tissue[15]. In addition to affecting the bronchi and upper airways, chronic low dose exposure of hydrochloric acid may also affect the pulmonary interstitium, resulting in ILD. Interstitial lung disease in our patient may very well have been cause by chronic exposure to hydrochloric acid at his place of work.

Fitness for duty assessment

Fitness for duty is an assessment for evaluating a worker's physical and mental fitness for return to work[16]. The categories include: fit to work; fit with restrictions; fit with some limitations; and, unfit to work. In the current case the patient would continue to be exposed to chemicals like disulfide, so he should only return to work wearing a respirator.

Since the patient has ILD and abnormal pulmonary function (i.e., FEV1 is 60% of predicted), he might be able to wear a respirator but would have to trial it before working in a real environment[18]. Choosing an appropriate respirator requires a medical evaluation and fit test[17] albeit he may be at high risk because of his ILD and high blood pressure. Job modification to avoid of chemical exposure would be a better solution for this worker.

According to Occupational Safety and Health Administration (OSHA), a respiratory protection program is needed whenever workers are required to wear a respirator. Engineering modifications to the workspace to ensure proper ventilation are mandated.

Conclusion

Occupational ILD is an uncommon disease and is usually diagnosed as idiopathic. Taking of occupational history and chemical exposure helps in making a diagnosis. In the current patient, history, physical examination, laboratory investigation, and radiographic data supported the conclusion that the clinical presentation was likely ILD. A thorough occupational history, physical examination, and laboratory investigation helped to exclude other diseases that can cause ILD, suggesting the occupational exposure of hydrochloric acid was causative. The fitness to work assessment evaluates patients before sending the back to work. A respiratory protection program should be conducted for this patient prior to-re-entering areas where risk of chemical exposure exists. Engineering controls—including better mechanical ventilation of the work area—would lessen chemical exposure of employees.

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