# An Atypical Presentation of Pulmonary Tuberculosis in an Asthmatic Adolescent: A Case Report*

**Geannagail O. Anuran, MD, MBA****

## Abstract

Pulmonary tuberculosis (PTB) screening is conventionally done with the use of a chest radiograph. However, immunocompromised patients with PTB could present with a normal chest finding. It is therefore important to probe through the patient's history to determine if sputum smear microscopy would be needed even for screening.

A 15-year-old female, a known asthmatic since 3 years old, with history of receiving high cumulative doses of systemic corticosteroid for asthma exacerbations, consulted the emergency room for a 3-day history of worsening dyspnea. The patient was managed as a case of asthma in acute exacerbation and was also screened for PTB due to identified risk factors. Her chest radiograph turned out normal, but sputum smear microscopy were twice positive for acid-fast bacilli (AFB). This atypical presentation of PTB could be due to the patient's immunosuppressed state, brought about by her history of systemic steroid use, which predisposed her to the absence of a parenchymal or nodal involvement in her chest x-ray. The patient was maintained on a combined beta$_2$-agonist and inhaled corticosteroid for her asthma, and she was also started on anti-Koch's medications. Repeat sputum smear microscopy after two months of anti-Koch's treatment were twice negative for AFB. There were also no recurrence of her asthma symptoms.

Asthma patients with history of systemic steroid use are considered immunocompromised. PTB screening in this population should include sputum smear microscopy aside from the usual chest x-ray, because imaging could be normal, as what this patient exhibited. Inhaled steroids may also be given safely to this group of patients.

**KEYWORDS:** Pulmonary Tuberculosis, Asthma, Adolescent, Chest X-ray Negative

*Selected for competition, Inter-hospital Interesting Case Contest, Philippine Academy of Family Physicians - Manila Chapter

**Resident Physician, Department of Family and Community Medicine, UP - PGH Medical Center

## INTRODUCTION

In screening for pulmonary tuberculosis (PTB), most physicians customarily request for a chest radiograph (CXR), wherein the disease would typically present with opacities, consolidations, cavities, and nodules (Kisembo, et al., 2012). Owing to its high sensitivity (at 97%) in detecting PTB (Piccazzo, et al., 2014), CXR-negative patients are deemed normal and further laboratory tests are seldom requested. However, there have been reports of false negative examinations, which amount to about 1% among the immunocompetent population, and increased to 7% to 15% in individuals seropositive for human immunodeficiency virus (HIV) (Piccazzo, et al., 2014). Further, among those who were immunocompetent, it was observed that CXR-negative PTB was commonly identified in those who were symptomatic or through contact tracing for PTB (Marciniuk et al., 1999).

Clinicians, therefore, must have a high index of suspicion in order to catch this group of patients who tend to present with CXR-negative PTB. Probing the patient's history is essential to identify the presence of co-morbid diseases, history of corticosteroid use, past medical history of PTB, and exposure to an active PTB case – factors that would increase the patient's risk for developing PTB and would therefore prompt the clinician to request for further laboratory tests in screening the patient.

This report looks into the case of an asthmatic adolescent who developed pulmonary tuberculosis presenting with a normal chest radiograph and positive sputum smear.

## CASE PRESENTATION

A 15-year-old female was seen at the emergency room on February 2015 for difficulty of breathing. She is a known asthmatic since 3 years old, with persistent symptoms, but with no maintenance medications, and relies only on daily Salbutamol nebulization. For the past 12 years, she had monthly emergency room visits for intravenous steroid administration if her symptoms were unrelieved by nebulization. Thus far, she has had six confinements, without having been intubated or put in intensive care.

Her symptoms were uncontrolled until three days prior to consult, she had worsening dyspnea, triggered by cigarette smoke exposure, and associated with chest tightness, shortness of breath, and productive cough, which were all not relieved by more than six Salbutamol nebulization at home nor by four doses of intravenous Hydrocortisone administered at the local district hospital. Persistence of symptoms thus prompted consult.

The patient has a history of Primary Complex at 10 years old, and she is allergic to *"Tulingan"* and to Cotrimoxazole. Her immunization status is complete only up to 9 months of age, and no booster doses have been given. Her father, who smokes at home, also has asthma and allergy to crabs. She has a close contact exposure to PTB through her paternal uncle. Please see Figure 1 for the family genogram.

The patient is an average year level eight student, who had to repeat levels two and five, because she had to stop in the middle of the school year due to her inability to tolerate climbing the stairs to attend her classes. The patient shares that she regrets having to repeat this two school years, because of the undue financial strain it caused their family, and she has also been feeling anxious that she might not be able to finish school because of her illness. Meanwhile, she reports that currently, she could exercise during her physical education classes without having an exacerbation.

On physical examination, the patient was conscious, coherent, spoke in sentences, with a blood pressure of 110/80 mm Hg, tachycardic at 101 beats per minute, tachypneic at 26 breaths per minute, with an $O_2$ saturation of 92%. Patient was underweight with a body mass index (BMI) of 15.52, with poor air entry and wheezing over all lung fields. The rest of the physical exam findings were unremarkable.

Assessment at this time was "Bronchial Asthma, in moderate acute exacerbation, rule out Pulmonary Tuberculosis." The patient was immediately nebulized with Salbutamol/Ipratropium for three doses every 20 minutes. There was decrease in dyspnea, though she still had wheezes, but no crackles. Her final $O_2$saturation was at 95%, which she was

able to maintain after three hours of observation. Patient was then sent home with requests for a chest radiograph and sputum smear microscopy, and with prescriptions for Budesonide/Formoterol 160/4.5 mcg, two puffs once a day; Montelukast 10 mg/tab, one tablet once a day; and Salbutamol/Ipratropium nebulization every six hours for three days then as needed for dyspnea.

The patient's chest radiograph revealed normal findings, while her sputum smear were positive for acid-fast bacilli (AFB) for days 1 and 2. The patient was then started on anti-Koch's treatment, Isoniazid-Rifampicin-Pyrazinamide-Ethambutol (HRZE) tablets, two tablets once a day for two months and HR tablets for four months through the Tuberculosis-Directly Observed Shortcourse (TB-DOTS) Program. Repeat sputum smear microscopy after two months of anti-Koch's treatment were twice negative for AFB. The patient had no adverse reaction to the medications. The patient then gained weight, with a BMI of 17.35.She also had no recurrence of dyspnea, chest tightness, shortness of breath, and cough.

## CASE DISCUSSION

Presented with a case of a 15-year-old female consulting for a 3-day history of dyspnea associated with chest tightness, shortness of breath, and productive cough, differential diagnoses for the patient's case include cardiovascular, psychogenic, and respiratory diseases. The cardiovascular causes include heart failure, anemia, and deconditioning. However, the patient does not have any history of congenital or acquired cardiac diseases, and she does not present with other heart failure signs and symptoms; she does not have physical exam findings indicative of anemia; and she is able to exercise without respiratory discomfort; so these conditions are unlikely in the patient's case.

Psychogenic causes of dyspnea like panic attacks and hyperventilation syndrome may also be ruled out, since the patient does not have any ongoing psychosocial stressor and does not complain of any anxiety or panic attacks.

The respiratory causes of dyspnea include disorders of the respiratory controller or the brainstem, the ventilatory pump, and the gas exchanger (Schwartzstein, 2012). Drugs, like aspirin or progesterone, and diabetic ketoacidosis can stimulate the brainstem and cause dyspnea; however, the patient is not taking these drugs, and she does not present with other symptoms of hyperglycemic crisis like nausea and vomiting, abdominal pain, or mental status changes. Similarly, the ventilatory pump, composed of the ventilatory muscles and bones of the chest wall, the pleura, and the airways could be affected by neuromuscular weakness as in Myasthenia Gravis or Guillain-Barre Syndrome. However, the patient did not present with the characteristic weakness and muscle fatigue of Myasthenia Gravis nor with the characteristic weakness and numbness of Guillain-Barre Syndrome.

There may also be dyspnea if there is reduced compliance of the chest wall as in kyphoscoliosis, or if there is reduced compliance of the lungs as in interstitial fibrosis; however, the patient also did not present with an abnormal curvature of the spine, likewise, the patient does not have any drug, radiation, or environmental exposure, nor does she have any comorbid autoimmune disease that may cause damage to her lungs; thus, these disease entities as the cause of her dyspnea are not considered. Pleural effusion as well as pneumothorax from any cause could result in dyspnea, but the patient's clinical picture does not fit with the usual presentation of these conditions. On the other hand, the patient does meet the criteria for bronchial asthma, and there are valid points to suspect pulmonary tuberculosis; thus, both diseases are considered in this patient.

The patient's asthma, previously diagnosed only by virtue of her dyspneic episodes being relieved by nebulization, could be validated using the criteria defined in the Global Initiative for Asthma (GINA) guideline (2014). This guideline states that asthma presents with "episodic wheezing, shortness of breath, chest tightness, and cough; symptoms often occur or worsen with viral infections; such occur variably over time; and they often occur or are worse at night or on waking;" which are all present in the patient's case.

On initial consult, a co-morbid pulmonary tuberculosis was considered because of the persistence of the patient's symptoms despite receiving systemic steroids, her history of Primary Complex during childhood, and her immunosuppression from receiving high cumulative doses of intravenous corticosteroids. In addition, the patient is a close contact of a pulmonary tuberculosis index case, and because of this, according to the 2013 Manual of Procedures for the National Tuberculosis Control Program, the patient should be investigated as part of the case finding process for contact investigation.

How common does PTB coexist with asthma? The association between bronchial asthma and PTB is rare, with a prevalence rate of 0.3% (Fekih et al., 2010). Pulmonary tuberculosis was found to be more commonly associated with Type 2 Diabetes Mellitus (DM) with 29.63% prevalence (Jimenez-Corona et al., 2013) and with HIV, having an 18.86% prevalence (Kamath, 2013). Common among DM and HIV patients is their immunosuppressed state, which could also be the reason for the development of PTB in this asthmatic adolescent, given that she has been receiving high cumulative doses of systemic corticosteroids.

This assertion is consistent with the findings in a case-control study by Jick, et al., (2006), that asthma is not necessarily a risk factor for the development of pulmonary tuberculosis. Asthma was found to be inconsistently associated with an increased risk for tuberculosis with an adjusted odds ratio of 1.4 and a 95% confidence interval of 1.0-2.0. The authors suggest that asthma appears to increase the risk for tuberculosis, particularly if the asthmatic patient would be dependent on systemic steroids for control of symptoms, as in this patient's case.

Moreover, the risk for tuberculosis appears to increase with cumulative doses of glucocorticoids (Jick, et al., 2006), which could be significant for this patient, since she has been having systemic corticosteroids for most years of her life, and though she does not use such medications continuously, she must have already accumulated a large concentration. According to the aforementioned case-control study, the adjusted odds ratios for current users with a cumulative dosage of <1,000 mg, 1,000-2,999 mg, and ≥3,000 mg, are 4.1 (95% CI 1.8-9.3), 8.3 (95% CI 2.1-33.5), and 3.9 (95%CI 1.5-9.7), respectively. This suggests that regardless of the dose, patients with cumulative steroid use are at in increased risk for developing pulmonary tuberculosis compared with patients who are unexposed.

Thus, the patient's immunosuppressed state, which is due to her cumulative systemic steroid use, predisposes her to the absence of a parenchymal or nodal involvement in her chest x-ray, because of her inability to mount an immune response to the pulmonary TB infection. Various authors thus agree that among immunocompromised patients, and particularly in those who are symptomatic and in those with tuberculosis exposure, a normal chest x-ray finding should not preclude further diagnostic evaluation in this population.

How should patients with coexisting asthma and PTB be managed? This adolescent patient was given combined $beta_2$-agonist and inhaled corticosteroid as maintenance medication for her asthma, since GINA guideline states that, "inhaled glucocorticosteroids are not contraindicated in patients with active tuberculosis."

Use of inhaled steroids for asthma among those with concomitant PTB infection is considered safe in clinical practice, as reported by Horton et al. (1977), since its use did not adversely affect the resolution of PTB in their cohort. Moreover, in the event of an asthma exacerbation, systemic steroids may also be safely given for those with concomitant PTB who are already receiving effective anti-Koch's treatment, as seen in the case series reported by Fekih et al. (2010), although they noted that a higher dose might be necessary, since rifampicin is a hepatic enzyme inducer, and thus would increase drug clearance.

Preventive measures imparted to this patient include avoidance of asthma triggers especially that of exposure to irritant smoke, which led to the motivation of the family to encourage the patient's father to stop smoking. Other measures consisted of putting emphasis on the patient's adherence to PTB and

asthma medication regimen, and updating of her immunization status. For the psychosocial intervention, Catharsis-Education-Action (CEA) was done to determine the impact of her illnesses on her quality of life, and to support her on the implementation of treatment and wellness plans.

## CONCLUSION

This case exemplifies the holistic approach in managing a patient with atypical presentation of pulmonary tuberculosis in an asthmatic adolescent.

The physician as a health care provider must be adept at obtaining the patient's medical history to determine the patient's immune status. Thus, when screening for PTB in an immunosuppressed patient, the physician could make a clinical decision to request for sputum smear microscopy in order to catch PTB patients who would present with a normal chest radiograph.

As an educator, the physician should ensure patient and family's understanding of the condition in terms of the risks, etiology, and pathophysiology, to empower them to adhere to the treatment and wellness plans.

As a counselor, the physician caring for an adolescent afflicted with comorbid illnesses should be able to empathize with the patient and his/her family, and to reassure them that specific measures can be taken to improve the patient's quality of life.

As a researcher, the physician should be able to apply evidenced-based information on clinical decision-making, and at the same time, to document his/her own experiences in caring for his/her patients.

Lastly, as a health manager, the physician should be able to coordinate patients with available resources in the community, such as the TB-DOTS program for PTB treatment, to minimize the financial burden put on the family and to further promote treatment adherence.

## References:


1. 2013 Manual of Procedures for the National Tuberculosis Control Program.
2. Fekih, L., Boussoffara, L., Jemaa, M., Fenniche, S., Hassene, H., Belhabib, D., & Megdiche, M. (2010). Asthme et tuberculose: Association bénéfique ou maléfique?. *Revue des Maladies Respiratoires*, 27: 679-684.
3. Global Initiative for Asthma, Guideline for Asthma Management and Prevention, 2014.
4. Horton, D., & Spector, S. (1977). Clinical pulmonary tuberculosis in an asthmatic patient using a steroid aerosol. *Chest*, 71:540-542.
5. Jick, S., Lieberman, E., Rahman, M., & Choi, H. (2006). Glucocorticoid use, other associated factors, and the risk of tuberculosis. *Arthritis & Rheumatism (Arthritis Care & Research)*, 55:19-26.
6. Jimenez-Corona, M., Cruz-Hervert, L., Garcia-Garcia, L., Ferreyra-Reyes, L., Delgado-Sanchez, G., Bobadilla-del-Valle, M., Canizales-Quintero, S., Ferreira -Guerrero-E., Baez-Saldana, R., et al. (2013). Association of diabetes and tuberculosis: impact on treatment and post-treatment outcomes. *Thorax*, 68(3): 214-220.
7. Kamath, R., Sharma, V., Pattanshetty, S., Hegde, M., & Chandrasekaran, V., (2013). HIV-TB coinfection: clinico-epidemiological determinants at an antiretroviral therapy center in Southern India. *Lung India*, 30 (4): 302-306.
8. Kisembo, H., den Boon, S., Davis, J., Okello, R., *Worodria, W.,* Cattamanchi, A., Huang, L., & Kawooya, M. (2012). Chest radiographic findings of pulmonary tuberculosis in severely immunocompromised patients with the human immunodeficiency virus. *The British Journal of Radiology*, 85:130-139.
9. Marciniuk, D., McNab, B., Martin, W., & Hoeppner, V. (1999). Detection of pulmonary tuberculosis in patients with a normal chest radiograph. *Chest*, 445-452.
10. Piccazzo, R., Paparo, F., & Garlaschi, G. (2014). Diagnostic accuracy of chest radiography for the diagnosis of tuberculosis (TB) and its role in the detection of latent TB infection: A systematic review. *The Journal of Rheumatology Supplement*, 32-40.
11. Schwartzstein, R. (2012). Approach to the patient with dyspnea (T. King, Ed.). Retrieved October 22, 2013, from UpToDate.

## TABLES

| Summary of Diagnostic Findings | | |
|---|---|---|
| **Date** | **Diagnostic Test** | **Results** |
| February 16, 2015 | Sputum AFB x 1 | +4, More than 10 AFB/visual field in at least 20 fields |
| February 17, 2015 | Sputum AFB x 2 | +2, 10-99 AFB/100 visual field |
| February 18, 2015 | Chest X-ray, PA | Normal chest |
| March 12, 2015 | Chest X-ray, PA | No significant chest findings |
| March 13, 2015 | AST | 19 – normal |
| March 13, 2015 | ALT | 13 – normal |
| March 13, 2015 | PPD Skin Test | 13mm |
| June 16, 2015 | Repeat Sputum AFB x 1 | Negative |
| June 17, 20915 | Repeat Sputum AFB x 2 | Negative |
| June 26, 2015 | Repeat ALT | 35.5 – Normal |
| June 26, 2015 | Repeat AST | 33.4 – Normal |

## ILLUSTRATION