



# Syndromic Differential Diagnosis—Lung–Brain Syndrome

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**Abstract:** The formulation of a rapid differential diagnosis can be aided by categorizing common clinical syndromes. Our review article presents a case of a lung/brain syndrome with a review of its most common causes. Cogent points for work up and treatment of each diagnosis will be presented as well.

**Keywords:** fever; lung infection; brain infection; Nocardia; Tuberculosis; Aspergillus; clinical syndrome

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## Introduction

Generating a Syndromic Differential Diagnosis (Syndromic D/D) is a mechanism to quickly develop a basic differential diagnosis at the bedside. This organizational structure provides a cogent way to touch on the major diagnostic categories so as to prioritize and implement the evaluation as quickly as possible.

The case below is representative of a patient that presents with lung and brain pathology. Four examples of infection follow with detailed clues to each diagnosis by history, physical exam, labs, or radiographic means.

## Case

A 56-year-old female presents with fever, chronic cough, headache, and memory loss. She has a history of mild Systemic Lupus Erythematosus for which she has taken intermittent Prednisone therapy.

Her exam is remarkable for a temperature of 101.5, a cachectic appearance, right upper lobe rhonchi, headache, and poor memory recall. A CXR reveals consolidation in multiple lobes of her lungs bilaterally.

## Differential Diagnosis

### Nocardia

Nocardia is reported in approximately 1000 cases per year in the US. It is an aerobic actinomycetes which is a filamentous Gram-positive rod and is distinguished from other Actinomyces species by its acid fast staining, and ability to grow aerobically [1]. The organism is found worldwide in decaying vegetable matter and aquatic environments. Inhalation is the usual method of contact with the organism. Seventy percent of infected individuals are immune compromised, and thirty percent can be normal hosts [2]. Dissemination occurs in up to one-third of patients, and can be found in any organ with a specific predilection for the central nervous system. Nocardia should be suspected with a pulmonary/brain process, with or without cutaneous lesions. Lung lesions can include endobronchial mass, localized or diffuse pneumonia, lung abscess, or empyema. CNS presentations include headache, and focal neurologic deficits, with or without meningitis. Lastly, Nocardia may relapse despite appropriate antibiotic therapy [2].

### Tuberculosis

Extrapulmonary tuberculosis may occur in up to 20% of patients infected with TB [3]. Miliary TB, prior to the HIV pandemic, occurred in approximately 1.3% of all TB cases. Factors contributing to CNS involvement include alcoholism, immunodeficiency syndromes, HIV, prolonged steroid use, and patients on tumor necrosis factor inhibitors. Symptoms of TB involvement of the CNS may include headache, confusion, nausea, seizures, and hemiparesis [4]. The CSF in such patients typically shows lymphocyte predominance, high protein, and hypoglycorrhachia [5]. Therapy for lung/brain TB should begin before the diagnosis is established, given the mortality of the syndrome.

### Aspergillus

Risk factors for Lung/Brain Syndrome with Aspergillus species include prolonged neutropenia, high-dose steroids, and immunosuppressive medications. Aspergillus cultured from the sputum of a patient with COPD may represent colonization, whereas a culture from a neutropenic patient would necessitate therapy [6]. Pulmonary invasion of Aspergillus can lead to tissue infarction resulting in fever, chest pain, and hemoptysis. Pulmonary lesions can manifest as ring-enhancing abscesses, multiple nodules, ground-glass infiltrates, and/or pleural effusions. Central Nervous System (CNS) Aspergillus typically occurs by extension from the paranasal sinuses. Case fatality rates of greater than 50% have been documented in immunosuppressed patients with CNS Aspergillus [7].

## Bacterial Infections

In addition to Nocardia, as discussed above, other bacterial infections can lead to Lung/Brain Syndromes. These abscesses usually originate from a contiguous site such as sinus, otic, or dental infections [8]. Hematogenous spread occurs in 20–35% of Lung/Brain Syndromes [9]. The most common organisms include Staphylococcal species (including MRSA), Streptococcal species (including Pneumococcus, Strep pyogenes, and Strep milleri), and anaerobic bacteria. Other less common bacterial etiologies include Listeria, Fusarium, and Actinomyces species [9,10].

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