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A 37-Year-Old Man With Pleuritic Chest Pain

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CASE PRESENTATION: A 37-year-old man with poorly controlled type 2 diabetes presented with severe right-sided pleuritic chest pain, respiratory splinting, and cough. Two weeks earlier, he had been evaluated at an urgent care for cough and was prescribed a 5-day course of azithromycin for bronchitis. He then presented to our ED reporting mild, right-sided pleuritic chest pain. Vital signs were normal, and his chest radiograph showed a trace right pleural effusion (Fig 1A). He was discharged with naproxen for pleurisy. Three days later, he returned, reporting a dramatic increase in the severity of his pleuritic chest pain and a cough that had become productive of yellow-brown sputum. He denied fever, but endorsed chills and night sweats. His medications included atorvastatin, lisinopril, metformin, and saxagliptin. His parents were from Guam, although he was born and raised in San Diego, CA. He was employed as a social worker and denied any history of cigarette smoking, alcohol, or drug use.

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Physical Examination Findings

On admission, the patient was afebrile and tachypneic, and his room air oxyhemoglobin saturation was 93%. He was in moderate distress, taking shallow breaths, and had diminished breath sounds, with dullness to percussion in the lower two-thirds of his right hemithorax. The remainder of the examination, including skin and neurologic evaluations, was normal.

Diagnostic Studies

The initial WBC count was 13,100 cells/μL (86% polymorphonuclear cells [PMNs], no eosinophils), and a chest radiograph (CXR) showed a large right-sided pleural effusion (Fig 1B). A CT scan of the thorax demonstrated a loculated pleural effusion with right middle and lower lobe compressive atelectasis (Fig 2).

Given the muted clinical presentation (eg, 10 days of symptoms, absence of fever, mild leukocytosis) and failure of outpatient antibiotic therapy, community-acquired pneumonia complicated by parapneumonic effusion seemed unlikely. In this regard, the differential diagnosis focused on empyema due to oral anaerobes or, less likely, macrolide-resistant organisms (eg, methicillin-resistant *Staphylococcus*

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Drs Galant-Swafford and Light are co-first authors.

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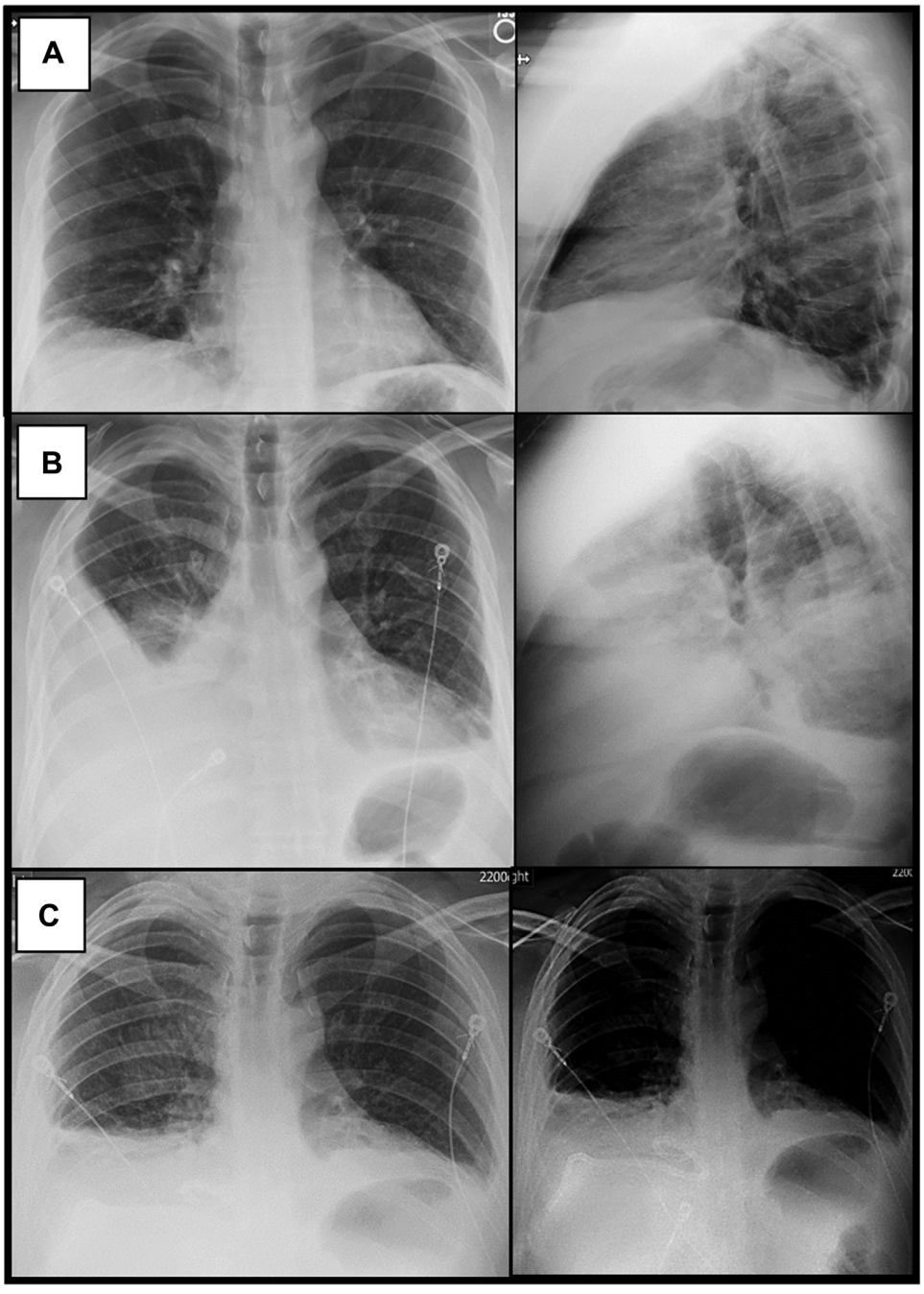

Figure 1 – *A, Posterior-anterior (PA) and lateral chest radiograph (CXR) from an ED visit for chest pain and cough 3 days prior to admission, showing a small right-sided pleural effusion and adjacent atelectasis. B, PA and lateral CXR on admission showing a large right-sided pleural effusion. Lateral film shows a large posterior ovoid mass-like opacity suspicious for loculation. C, Portable CXR following 14 French (F) chest tube placement (left) showing a reduction in the size of the effusion. An adjustment was made to the window contrast (panel on the right) to allow for clearer visualization of the chest tube position.*

aureus, pseudomonas). Tuberculous pleurisy was also considered, although the acuity of the presentation and the lack of exposure argued against it. The patient was empirically treated with vancomycin and piperacillin-tazobactam, and the effusion was drained via tube thoracostomy with a 14 French (F) catheter. Initial drainage yielded 1 L of cloudy yellow exudate (lactate dehydrogenase, 148 U/L; total protein, 4.9 g/dL) with a glucose level of 273 mg/dL. There were 2,719 leukocytes (54% PMNs, 40% lymphocytes, 1% eosinophils). Gram staining revealed PMNs without organisms. The immediate postprocedure CXR showed

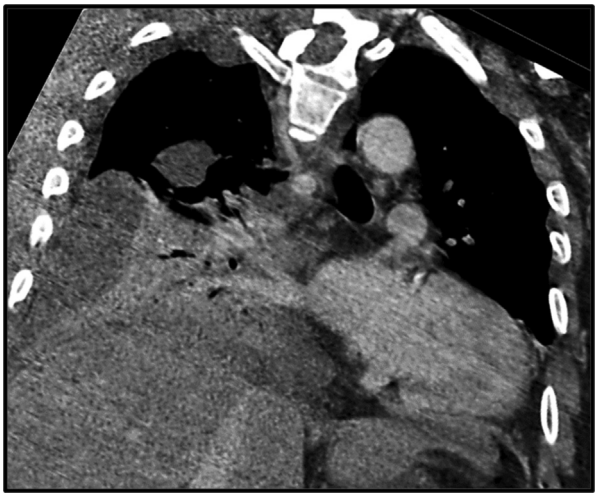

Figure 2 – *CT scan of the thorax in the coronal view on the day of admission shows a loculated effusion both inferiorly and in the horizontal fissure (ie, pseudotumor). There is associated compressive atelectasis of the right middle and lower lobes.*

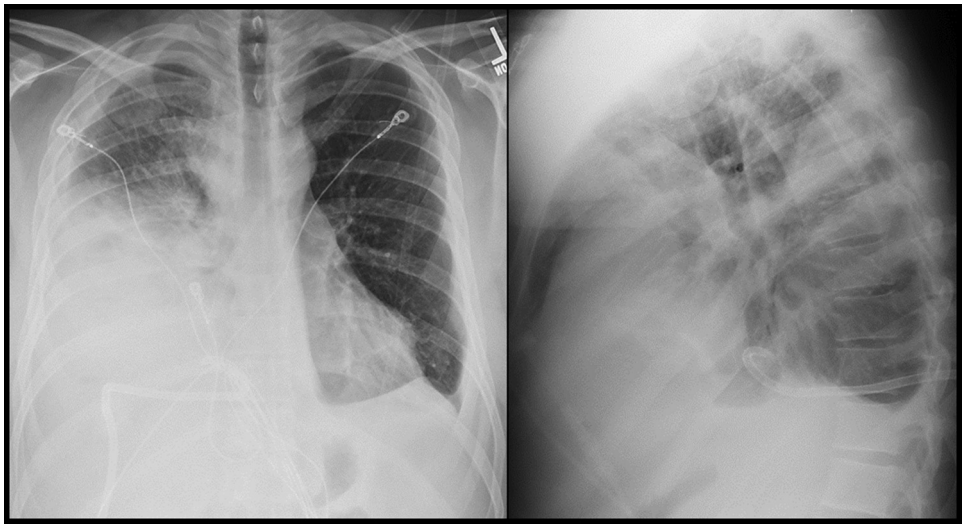

Figure 3 – *PA and lateral CXR showing expanding pleural effusion despite antibiotics, antifungal therapy, and 5 days of chest tube drainage with twice daily instillation of fibrinolytic and deoxyribonuclease. Lateral film continues to show an apical loculated fluid collection. See Figure 1 legend for expansion of abbreviations.*

appropriate tube position, decreased effusion size, and improved aeration of the right lung (Fig 1C).

Despite broad-spectrum antibiotics and continued drainage, the patient's WBC count increased. Pleural fluid and sputum cultures were negative for bacteria, and his TB interferon gamma release assay was negative. Three days following admission, the patient's initial sputum culture began growing white mold. The infectious disease service was consulted, and the patient was started on fluconazole. Despite 5 days of chest tube drainage with twice daily instillation of tissue plasminogen activator/and deoxyribonuclease, his effusion increased (Fig 3), and his chest pain, dyspnea, and hypoxemia persisted.

What is the diagnosis?

What is the next step in management?

Diagnosis: Coccidioides empyema.

Next step: The next step would be surgery for nonresolving *Coccidioides* empyema that has failed to improve with tube thoracostomy and antifungal therapy.

Discussion

Pulmonary coccidioidomycosis accounts for up to 30% of community-acquired pneumonia in endemic areas of the American Southwest. Pleural effusion develops in approximately 15% of cases, of which 22% are empyema and result from rupture of cavitary pneumonia into the pleural space. Patients with diabetes are at increased risk for severe coccidioidomycosis infection, specifically cavitary lung disease, and hyperglycemia also increases the likelihood of disseminated infection. Immunocompetent patients of African, Filipino, and Pacific Islander descent are also more vulnerable to disseminated disease.

Although this patient had *Coccidioides* pneumonia, his presenting symptoms and chest imaging were dominated by pleural infection. In fact, his CXR 3 days prior to admission lacked an obvious area of pneumonic consolidation. We speculate that the patient had a small focus of pneumonia adjacent to the visceral pleura, across which a pyogenic granuloma ruptured, releasing spherules into the pleural space and causing pleural infection with intense inflammation.

The Infectious Diseases Society of America recommends treatment of symptomatic *Coccidioides* pneumonia with oral azole therapy. In general, surgical management with video-assisted thoracoscopic surgery (VATS) should be considered when any exudate fails to resolve with tube thoracostomy. However, there are no randomized trials to definitively guide clinical practice in patients with *Coccidioides* empyema who fail to improve with antifungal therapy and tube thoracostomy. Retrospective studies and case series suggest that early surgical management of *Coccidioides* empyema, similar to empyema due to other organisms, reduces morbidity and mortality. In these studies, indications for surgery included persistent symptoms and clinical signs of infection despite appropriate antifungal therapy and progressive parenchymal disease such as cavitation complicated by pneumothorax.

In a retrospective study of 1,496 patients with coccidioidomycosis in Arizona, a chief complaint of chest pain was unusual (11%). In addition, nonresolving empyema was the indication for surgery in less than 5% of cases. More common indications for surgery included progressive cavitary disease and pneumothorax. Twenty-one percent of surgical patients developed complications, the most common of which was bronchopleural fistula (72%). Retrospective data show that VATS is as effective as thoracotomy in the treatment of empyema and is associated with reduced hospital length of stay and decreased rates of relapse. There are no randomized prospective data comparing these two interventions.

Our opinion, based on experience, is that *Coccidioides* infection elicits a uniquely intense inflammatory pleural reaction, compromising tissue integrity and increasing the risk of surgical complications, namely bronchopleural fistula. Our practice, therefore, is to attempt to avoid initial decortication, choosing instead to focus on sterilization of the pleural space. We then monitor for evidence of trapped lung and restrictive physiology, and pursue late decortication as an outpatient if symptomatic restriction develops.

Clinical Course

The patient underwent VATS with washout of the pleural space, lysis of adhesions, and placement of two 24F chest tubes. Upon visual inspection, the pleural space appeared inflamed and frankly hemorrhagic such that decortication, with the goal of maximum lung re-expansion, was not attempted (Fig 4A). Sputum and pleural fluid cultures ultimately grew *Coccidioides immitis*.

The patient's immediate post-VATS CXR showed a small decrease in effusion size and a small increase in aeration (Fig 4B). CXR 10 days following VATS continued to show only modest improvement (Fig 4C); however, the patient's leukocytosis improved, and his chest tubes were removed. He was discharged on a prolonged course of antifungal therapy with the plan to consider future decortication if symptomatic lung restriction developed. CXR at discharge showed persistent atelectasis and effusion (Fig 5A), mandating close follow-up.

One month later, the patient was free of chest pain and reported improvement in his exercise tolerance approaching baseline. At this time, however, his CXR still showed significant right lower lung zone opacity (Fig 5B). Five months following discharge, the patient's imaging significantly improved, revealing near-complete resolution (Fig 5C). Results of pulmonary function

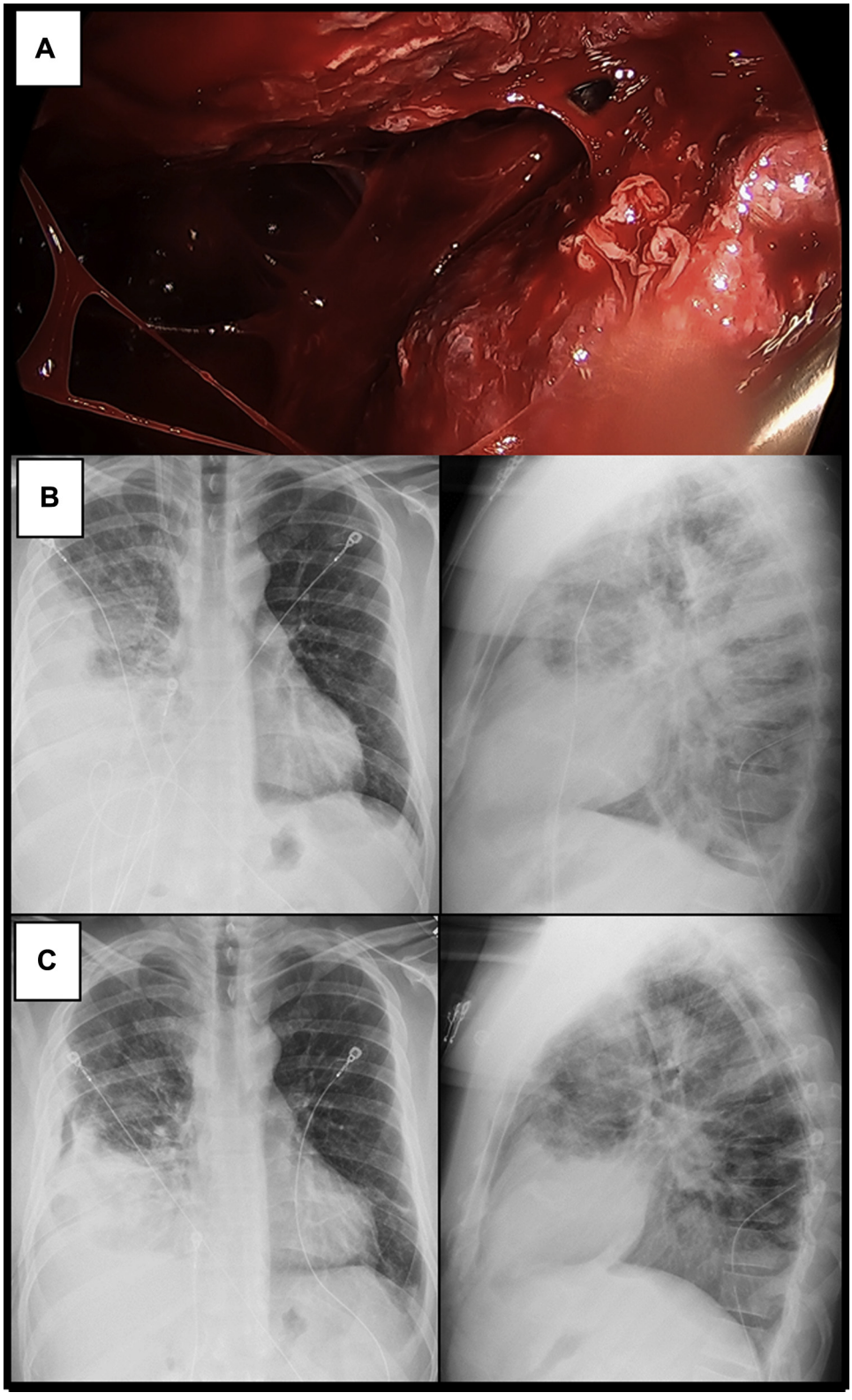

Figure 4 – *A, Image from video-assisted thoracoscopic surgery (VATS) showing an inflamed, frankly hemorrhagic-appearing parietal (top) and visceral (bottom right) pleural surface. B, PA and lateral CXR immediately post-VATS revealing persistent atelectasis and effusion with both anterior apical and posterior basal 24F chest tubes in place. C, PA and lateral CXRs 10 days following VATS showing decreased density of the abnormality in the right lung base, suggesting improved aeration. See Figure 1 legend for expansion of other abbreviations.*

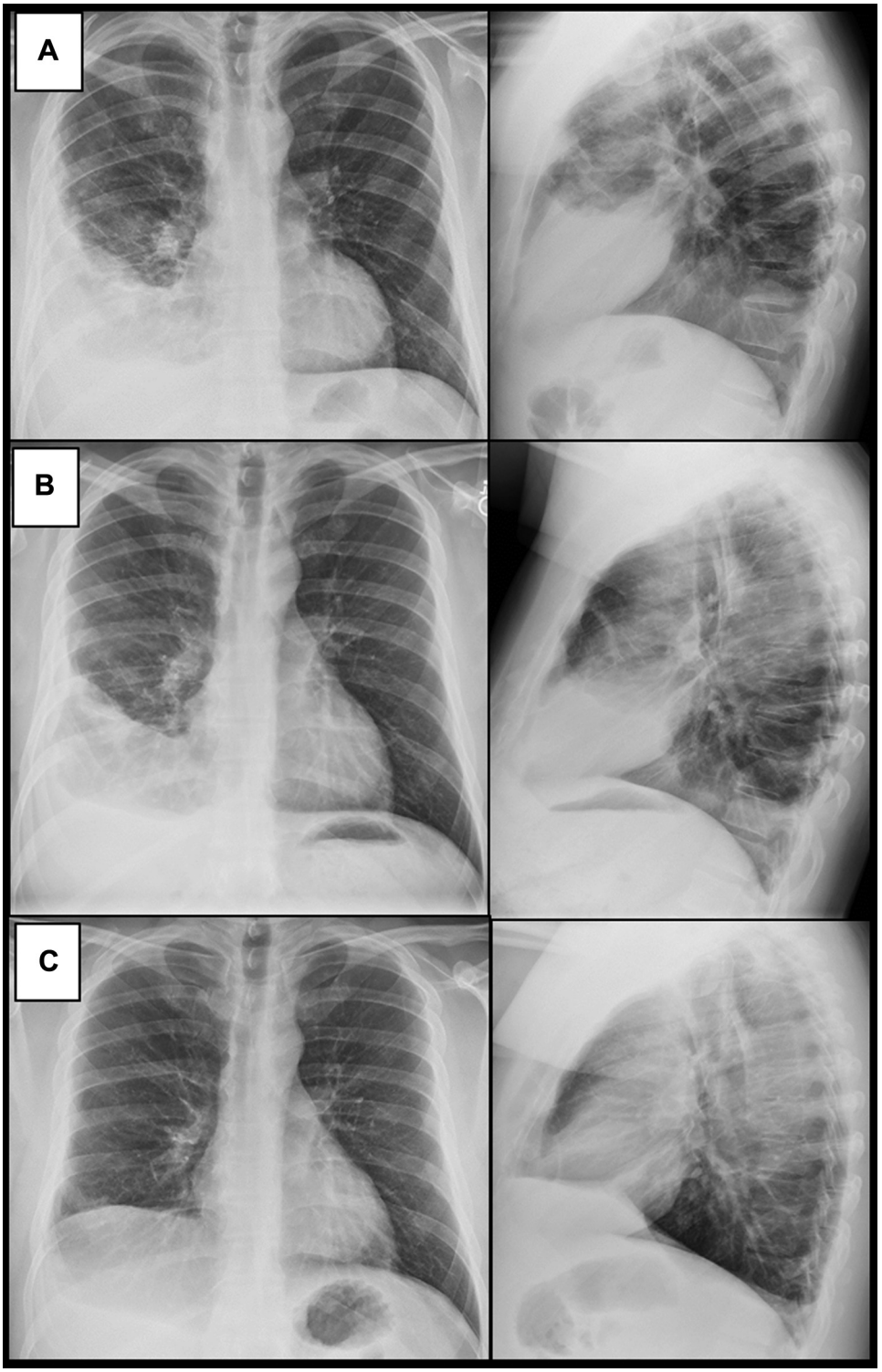

Figure 5 – *PA and lateral CXRs at (A) discharge and (B) 1-month follow-up showing modest interval improvement. C, CXRs 5 months following discharge showing near-complete resolution of the effusion and atelectasis, although a small amount of residual pleural scarring is evident along the lateral aspect of the right hemidiaphragm. See Figure 1 legend for expansion of abbreviations.*

testing revealed mildly reduced diffusing capacity of the lungs for carbon monoxide with normal total lung capacity, likely related to residual pleural scarring and associated atelectasis. The admission *C immitis* complement fixation was < 1:2, which may be expected as these antibodies take weeks to develop. Results of

repeat serologic testing 2 months later was positive with a peak titer of 1:32, which subsequently became negative following 6 months of antifungal therapy.

Clinical Pearls

1. *Coccidioidomycosis should be considered in patients presenting with empyema in endemic areas who do not have classic bacterial pathogens recovered from their pleural fluid or sputum and who fail to respond to empiric antibiotics.*
2. *Coccidioidomycosis may cause pneumonia and pleural infection with relatively small foci of consolidation such that it may not be obvious on chest radiograph.*
3. *If tube thoracostomy does not result in clinical improvement, VATS with washout, lysis of adhesions, and placement of large-bore chest tubes should then be pursued.*
4. *In the setting of Coccidioides empyema, initial decortication with the goal of maximum lung re-expansion may increase the risk of persistent bronchopleural fistula formation such that it may be deferred to the outpatient setting and reserved for individuals who are left with symptomatic restriction.*

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Suggested Readings

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