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Secondary Organizing Pneumonia Following Influenza A in a Patient from Southern Khyber Pakhtunkhwa: A Case Report

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ABSTRACT

Influenza viruses are a frequent cause of seasonal respiratory illness and serious pulmonary complications. While both viral pneumonia and bacterial co-infection can be complications of influenza pneumonia, a rare but underrecognized complication is Secondary Organizing Pneumonia (SOP). Most cases of SOP due to influenza have been due to Influenza A. We report a case of a 56-year-old man from the Dera Ismail Khan region in Pakistan with severe influenza A pneumonia who, despite appropriate antiviral and broad-spectrum antibacterial therapy, clinically and radiologically deteriorated. A diagnosis of SOP was suspected based on characteristic imaging findings and confirmed after a workup showed there was no ongoing infection. Treatment with corticosteroids initiated, and there was rapid dramatic improvement. The case highlights the need to consider this diagnosis in patients with pneumonia who do not resolve following influenza.

Keywords: Organizing Pneumonia; Influenza A; Cryptogenic Organizing Pneumonia; Dera Ismail Khan; Pakistan

Introduction

Secondary organizing pneumonia (SOP) is a rare but known complication that can happen after viral infections like influenza A. It is an unusual healing response of the lung tissue, marked by the formation of granulation tissue inside the alveolar ducts and bronchioles. Clinically, SOP can look like unresolved pneumonia, which often creates diagnostic difficulties. Early recognition and corticosteroid treatment can greatly improve patient outcomes. This case report describes a case of secondary organizing pneumonia following an influenza A infection in a patient from southern Khyber Pakhtunkhwa, Pakistan.

Case Report

A 56-year-old male farmer from a rural area near Dera Ismail Khan, with a known history of hypertension on irregular medications, presented to the medical outpatient department with a 7-day history of high-grade fever, myalgia, and a non-productive cough. In the past 48 hours, he had developed worsening shortness of breath. He did not have a significant smoking history.

On examination, he was tachypneic (respiratory rate 28/min) and hypoxic with an oxygen saturation (SpO_2) of 88% on room air, which improved to 94% on 6 L/min of oxygen via nasal cannula. Blood pressure was 150/95 mmHg. The examination of the chest showed bilateral coarse crepitations. Initial lab investigations showed a leukocyte count of 11,200/mm^3 with neutrophilia (80%), and an elevated C-reactive protein (CRP) of 98 mg/L while the procalcitonin level was 0.08 ng/mL, which is within normal limits. A nasopharyngeal swab returned positive for Influenza A by RT-PCR, and negative for SARS-CoV-2. The initial chest X-ray showed bilateral, multifocal consolidations.

Upon his hospitalization, an initial regime of oseltamivir 75 mg twice daily, intravenous ceftriaxone and supportive care were started. Ultimately, after 5 days of treatment, he worsened from a respiratory standpoint, requiring an escalation in oxygen flow to 10 L/min via a non-rebreather mask to maintain SpO_2 > 92%. Repeat chest X-ray showed worsened opacity and HRCT thorax demonstrated extensive bilateral patchy consolidations with a predominance of bilateral peribronchovascular and subpleural distribution. Some of the consolidative areas demonstrated the "reverse halo sign" or "atoll sign" (Figure 1), which is characterized by central ground-glass opacity with consolidation surrounding it.

Due to clinical and radiological worsening, despite antiviral therapy, the differential diagnosis remained between secondary bacterial/fungal infection vs SOP. To exclude an infection, a fiberoptic bronchoscopy with bronchoalveolar lavage (BAL) was done. BAL fluid analysis was negative for bacterial culture, acid-fast bacilli, and fungal elements. BAL cytology reported mixed inflammatory cellularity with no malignant cells noted. Serologic evaluation for common autoimmune markers (ANA and ANCA) was also negative.

A diagnosis of Influenza A-associated Secondary Organizing Pneumonia was established. The patient was started on oral prednisolone at a dose of 40 mg per day (0.8 mg/kg/day). After 72 hours, the patient showed notable improvement in his dyspnea and oxygen requirements. Following 48 hours of steroid treatment, he was weaned to 2 L/min of oxygen. A chest X-ray taken after one week of steroid treatment showed substantial resolution of the pulmonary opacities. The prednisolone was tapered over a period of eight weeks. At a follow-up visit one month after discharge, the patient reported no symptoms on room air, and repeat HRCT chest showed nearly complete resolution of the consolidations and the reverse halo signs (Figure 2).

Discussion

Secondary Organizing Pneumonia (SOP), once called Bronchiolitis Obliterans Organizing Pneumonia (BOOP), is a condition where granulation tissue grows in the alveolar ducts and alveoli, along with patchy inflammation.[1] SOP can occur on its own (cryptogenic organizing pneumonia, COP), but it more often follows a known trigger such as connective tissue disease, certain medications, radiation, or infections.[2] Here, we describe a classic yet often overlooked case of SOP after influenza infection in a patient from Southern Khyber Pakhtunkhwa, Pakistan.

Influenza A and B viruses cause seasonal outbreaks and can lead to illnesses ranging from mild upper respiratory infections to severe, sometimes fatal, viral pneumonia. The most serious lung complications are primary influenza pneumonia and secondary bacterial infections, often with Streptococcus pneumoniae or Staphylococcus aureus.[3] In contrast, SOP is a non-infectious, inflammatory problem that usually appears after the initial viral phase. It shows up as pneumonia that does not improve or gets worse, even after antibiotics. This is believed to result from an overactive immune response to the virus, leading to uncontrolled tissue repair, overgrowth of fibroblasts, and too much extracellular matrix in the lungs.[2]

We diagnosed SOP in our 56-year-old hypertensive farmer based on the constellation of clinical presentation, typical radiological features, and exclusion of other diseases. Clinically, what is pathognomonic is the worsening respiratory symptoms after the initial febrile illness has reached a peak. Worsening dyspnea and increasing oxygen needs after a full week into the illness, despite oseltamivir and broad-spectrum antibiotics, marked a turning point in our diagnosis for this patient. The timing of the illness progression is also a common finding in the literature on influenza-associated SOP

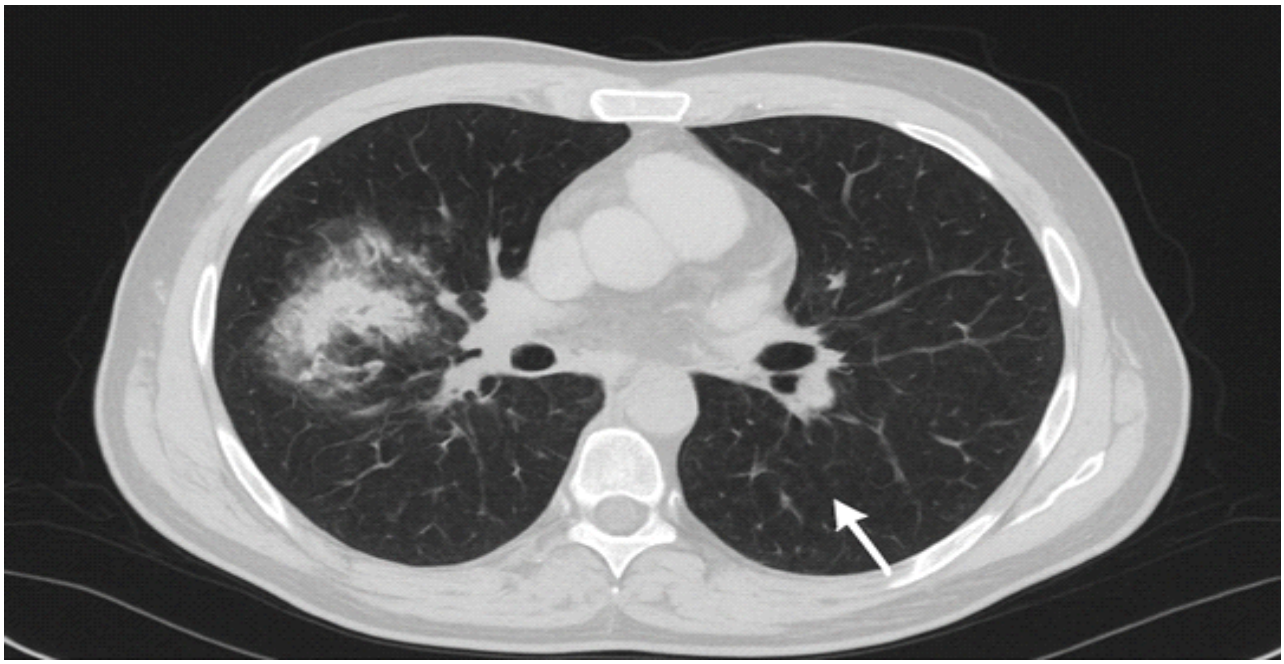

Figure 1. HRCT Chest (axial view) showing bilateral, subpleural consolidations with a prominent reverse halo sign (white arrow)

cases.[4] This causes the clinician to reconsider beyond simple treatment failure or superinfection in the differential diagnosis.

From a radiological perspective, High-Resolution Computed Tomography (HRCT) is the cornerstone of noninvasive diagnosis. SOP radiological findings are often very characteristic. The most common patterns are bilateral patchy consolidations with an impressive clinical predilection for peripheral (subpleural) and peribronchovascular distribution, as exquisitely shown in our patient. A less frequent but highly specific finding is the "reverse halo sign" (RHS), or "atoll sign," seen in ~20% of patients with COP/SOP.[6] The RHS can be described as a central ground-glass opacity surrounded by a crescent or ring of consolidation, and it was an important detail that led us away from the diagnosis of an infectious etiology. The RHS was initially applied to cryptogenic organizing pneumonia; it has been described as a secondary form, such as post-infectious SOP.[7] In the appropriate clinical context, the presence of an RHS sign should raise a high degree of clinical suspicion for organizing pneumonia after common infections such as tuberculosis and invasive fungal pneumonia are ruled out, as we did for our patient via bronchoalveolar lavage.

Diagnosing SOP often depends on lung biopsy results, but for many critically ill patients, including ours, the risks of procedures like transbronchial or surgical biopsy can delay this step. In our case, we relied on clinical and radiological findings after thoroughly ruling out other causes. Bronchoalveolar lavage (BAL) played a key role. No bacterial, fungal, or mycobacterial growth was found, and stains and antigen tests were negative, which helped exclude secondary infection.[8] The BAL cytology did not show a mixed neutrophilic and eosinophilic pattern, which would suggest other types of pneumonia or infection, further supporting inflammation as the cause. Serology also ruled out autoimmune rheumatic diseases, strengthening our diagnosis of post-infectious SOP.

Treating influenza-related SOP is a significant clinical challenge. Systemic corticosteroids are the standard first-line treatment for organizing pneumonia, and most patients improve within days.[1,2] However, using corticosteroids for acute influenza pneumonia is controversial and generally not advised. A meta-analysis by Lansbury et al. found that corticosteroids in influenza patients were linked to higher mortality (odds ratio 3.90) and more hospital-acquired infections.[9] Another review by Zhou et al. confirmed that corticosteroids increased mortality in influenza-related ARDS.[10] This highlights a critical point: while steroids help in SOP, they can be harmful during the acute viral phase. We must be certain that the main problem has shifted from active viral infection or bacterial co-infection to an abnormal inflammatory response. In our patient, negative microbiology results, typical HRCT findings, and the timing of symptoms gave us enough confidence to start prednisolone, which led to a rapid and life-saving recovery.

Most of the reported instances of influenza-associated SOP worldwide have been attributed to Influenza A, particularly the H1N1.[11] Cases of Influenza B have been reported as well, though they are less common and may be exaggerated in the literature.[12] Our case contributes to

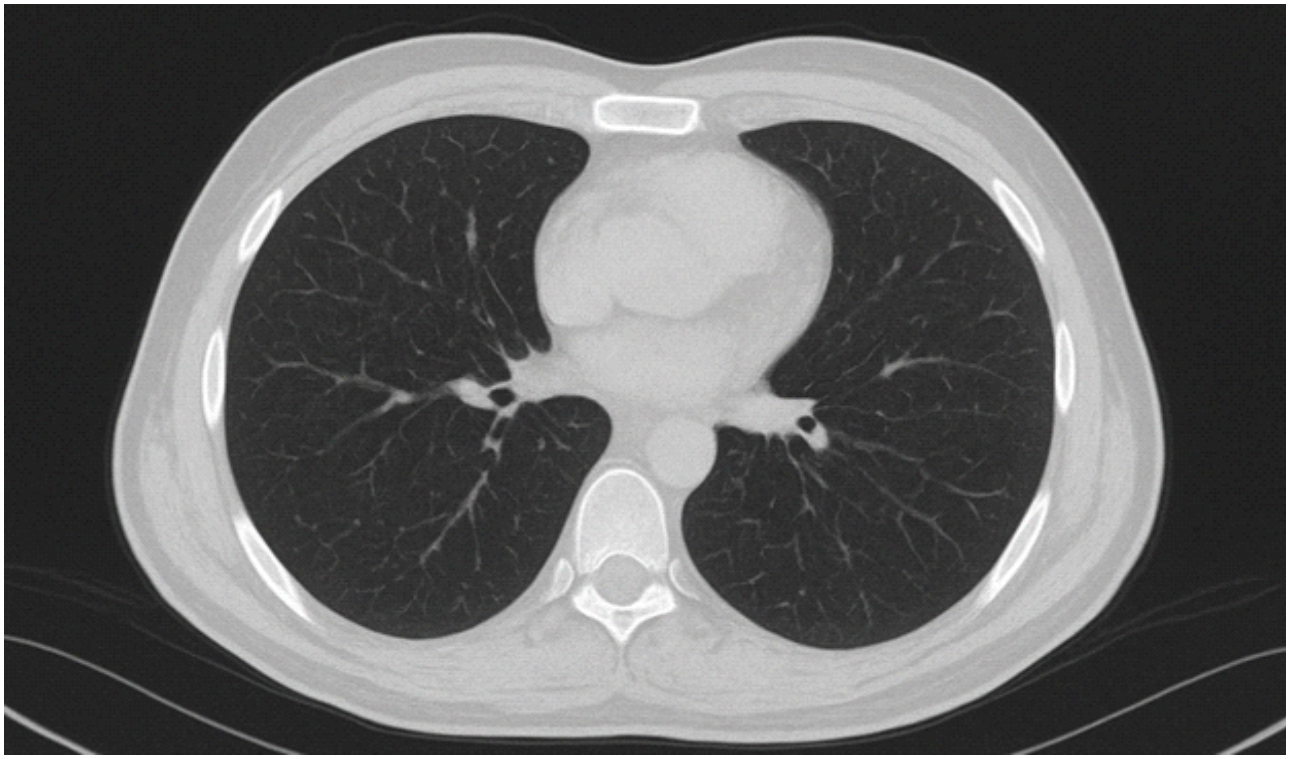

Figure 2. Follow-up HRCT chest after 4 weeks of corticosteroid therapy, demonstrating near-complete resolution of the prior consolidations

the growing body of literature on this topic and is, to our knowledge, one of the earliest detailed reports from the Dera Ismail Khan region of Pakistan. This is noteworthy and important because it increases awareness of this complication among local clinicians. In an area such as this with a high burden of respiratory infections, particularly tuberculosis, initial presentations can be misleading. Understanding the different clinical and radiological appearance of SOP may save patients from prolonged, ineffective doses of anti-tuberculosis or broad-spectrum antibiotics and allow for the initiation of targeted, effective treatment with high-dose corticosteroids.

Conclusion

To conclude, this case highlights several important educational points. First, in a patient with influenza pneumonia, if the patient experiences clinical and radiological worsening despite appropriate antiviral and antibacterial therapy, it is important to entertain the possibility of SOP. Second, HRCT findings, specifically the peripheral distribution of consolidations and the reverse halo sign, are both useful diagnostic clues. Third, a careful workup is important and should include bronchoscopy and BAL (ideally) to exclude an infection before starting corticosteroid therapy, as corticosteroids can have undesirable effects with active infection. Last, once the diagnosis is made, corticosteroid therapy is effective and can be curative, as seen by how quickly our patient recovered and how he was completely restored to baseline. Continued vigilance for this complication can assist in timely diagnosis and prevent unnecessary mortality from a treatable condition.

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