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Case Report

Cryptogenic Organizing Pneumonia: A Misdiagnosis or Missed Diagnosis in Resource –Poor Settings: A Case Report and Literature Review.

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Abstract

Background: Cryptogenic organising pneumonia (COP) is a diagnosis made by a combination of clinical, radiological and histology features; after ruling out other causes of organizing pneumonia. There is no consensus on prevalence. COP is often missed or widely misdiagnosed and under-reported in resource-poor settings (like Nigeria); where diagnostic modalities such as Chest CT (computed tomography) scan and lung biopsy are not readily available. Most febrile patients who present with cough and have opacities or infiltrate on chest radiograph, are diagnosed as pneumonia (from infective causes) and treated with antimicrobial agent for prolonged periods, despite persistent of symptoms. **Case Presentation**: A 57-year-old male who was referred to the Pulmonologist for specialist evaluation for persistence of chronic cough, dyspnoea, weight loss and other constitutional symptoms despites prolong use of antibiotics. Chest examination revealed reduced breath sounds on the both lower lung zone and crackles on left mid and both lower lung zones posteriorly. Chest radiography showed consolidation. He was given several courses of antibiotic therapy with no resolution prior to referral. Chest CT scan done was highly suggestive of Cryptogenic Organising pneumonia (COP), which was confirmed by histology of a trans-bronchial biopsy. **Result:** Patient's symptoms abated within 72 hours of steroid administration. **Conclusion:** This case report demonstrates the delay in early diagnosis of COP, where confirmatory diagnostic procedures are limited. Furthermore, it shows the prolonged/inappropriate use of antibiotic in such cases without resolution.

Keywords: Cryptogenic organising pneumonia, misdiagnosis, trans-bronchial biopsy, steroids

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Background/Introduction

Organising pneumonia (OP) is a disease entity that result from the lung reaction to injury.[1] Most cases of Organising pneumonias are idiopathic, called Cryptogenic organising pneumonias (COP).[2]However, it is referred to as secondary organizing pneumonia (SOP) when it is associated with diseases from various systems of the body and other causes.[1] We present a case misdiagnosed as community acquired pneumonia who didn't respond to antibiotic but had rapid response to steroid when a confirmatory diagnosis of Cryptogenic organising pneumonia was made.

Case Presentation

A 57-year-old Ibo non-smoker being followed-up for dilated cardiomyopathy with his Cardiologist for a period of 2 years prior to his presentation on the 31st of February. 2023 with a 3-months history of weight loss, cough productive of blood-stained sputum and progressively worsening breathlessness. He also had hoarseness, fever, chest pain, and resolving bilateral lower limb oedema.

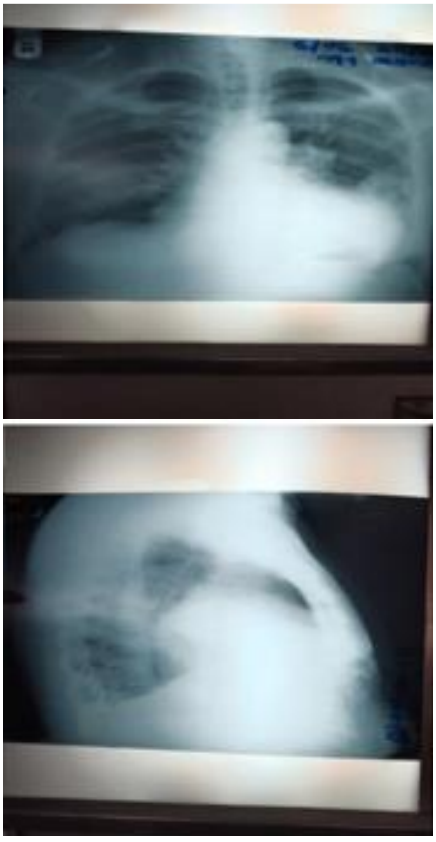

Fig.1. initial chest radiograph showing homogenous opacities in the right mid and both lower lung zones

There were no gastrointestinal, rheumatologic or neurological symptoms. He had several courses of antibiotic prior to presentation and was on his anti-heart failure regimen. Pertinent examination findings were reduced breath sounds on the both lower lung zone and crackles on left mid and both lower lung zones posteriorly. Complete blood count showed leucocytosis with neutrophilia, serum electrolyte urea and creatinine and lipid profile were essentially normal. Chest x-ray showed consolidation in the left mid and lower lung zone suggestive of a pneumonia.

An initial diagnosis of community acquired pneumonia to rule out pulmonary tuberculosis was made. Following which he was placed on tab (Tablet) Amoxicillin-clavulinic acid 625mg bd x 1/52, tab azithromycin 500mg daily x 5/7, tab. vitamin C 500mg daily and to continue his anti –failure regimen. Gene xpert done was negative, with persistent of symptoms, he was referred to the pulmonologist for further care. After the pulmonologist review, a chest CT (computed tomography) scan was done, which showed peripheral pulmonary consolidation of both lungs, one of the consolidations had reverse halo sign organising pneumonia. (The radiologist entertained differential diagnosis of fungal infection and broncho-alveolar cancer).

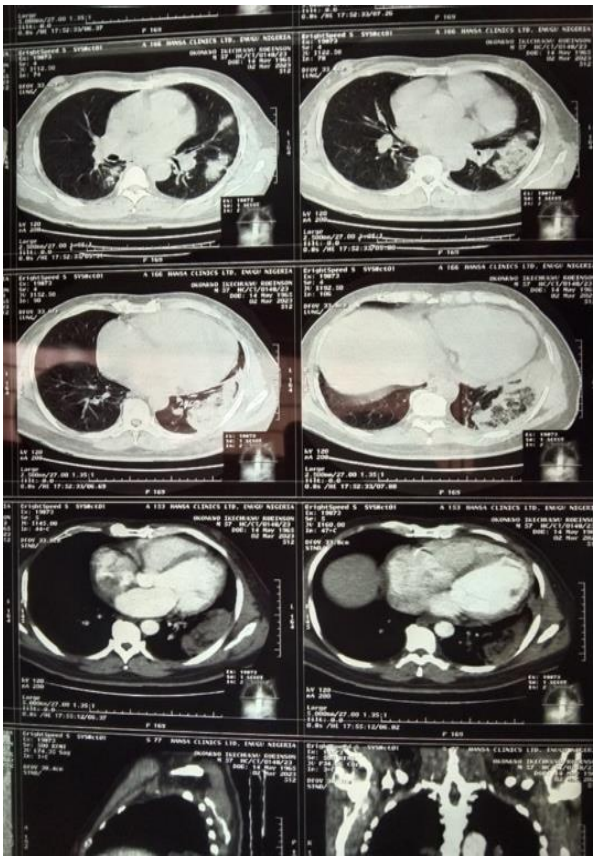

Figure 2: Chest CT scan showingconsolidations had reverse halo sign.

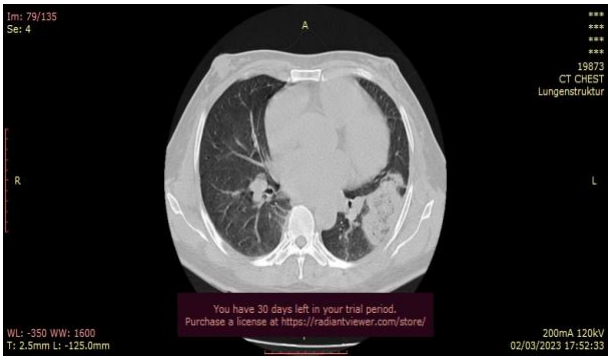

Figure 3: Chest CT scan demonstrating reverse halo sign.

A diagnosis of cryptogenic organizing pneumonia was made. This prompted a broncho-alveolar lavage and a trans-bronchial biopsy. The broncho-aveolar lavage demonstrated nil epithelial component, mixed lymphocytic and neutrophilic cellular patterns (Pulmonary alveolar macrophages-55%, Neutrophils-25%, Lymphocyte-20%, Eosinophils-0%, and Mast cells-0%), no malignant cells or granuloma was seen. The histology of the trans-bronchial biopsy sample showed preserved pulmonary architecture and a diffuse, uniform, mixed inflammatory infiltration of the alveolar wall, with admixed fibroblast and loose fibrosis. The inflammatory cells consisted of neutrophils, lymphocytes and plasma cells, no granulomatous lesion or atypical cells or structure were seen.

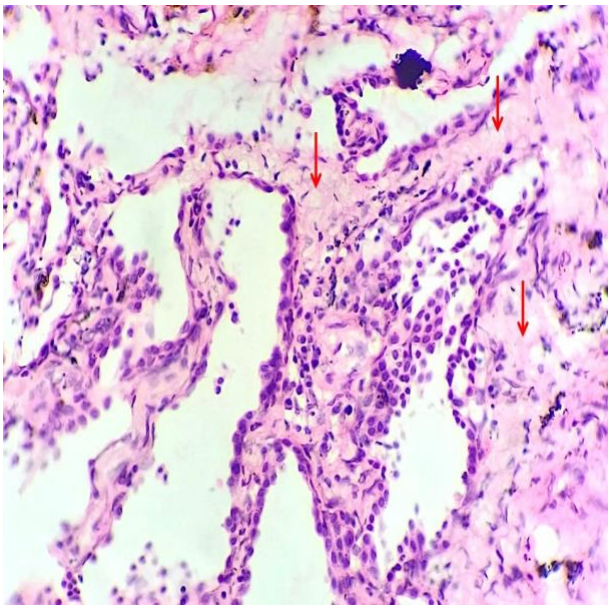
Figure 4:Overall preserved pulmonary architecture; loose interstitial fibrosis(red arrrows)[H&E400]

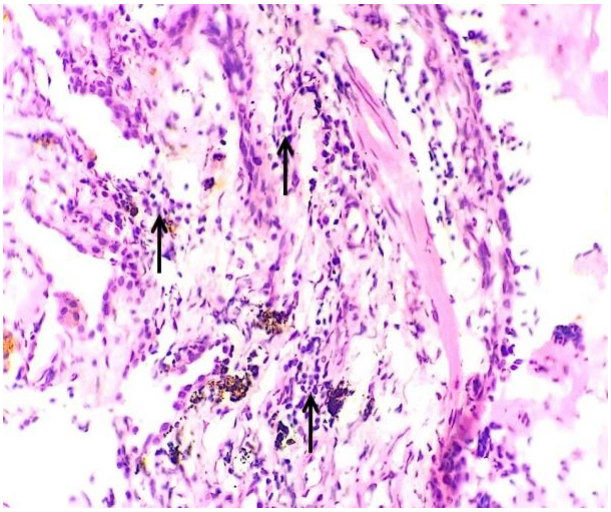
Figure 5: Diffuse interstitial mixed inflammatory infiltrates (black arrows) [H&Ex400]

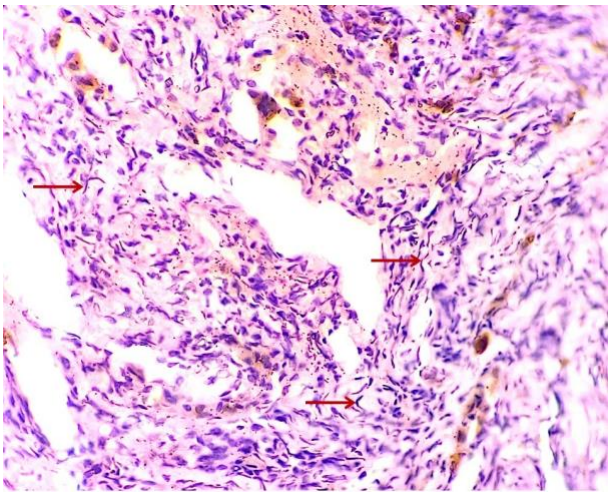
Figure 6: Dense proliferation of bland fibroblast (red arrows) [H&Ex 400]

The pathologist made a diagnosis of Non-specific interstitial pneumonia pattern, Anti-nuclear antibody (ANA), RF (Rheumatoid factor), Anti CCP (anti citrillunated peptide), ANCA (Anti-neutrophillic cytoplasmic antibody), Anti-Ro, and Anti ds-DNA (anti double stranded DNA) were requested but were not done. Considering the clinical, radiological and histological findings, the diagnosis of COP was sustained. He was commenced on steroid therapy for 6 months (initially with tab prednisolone at 30mg daily for 1 month then to taper off gradually) with regular serum glucose monitoring. Stool microscopy, culture and sensitivity done prior to commencement of steroid showed no ova or cyst of parasites. 3 days after commencement of steroid therapy, there was marked improvement in clinical symptoms. He was then discharging home to continue follow up on outpatient basics. A repeat chest x-ray done on follow up showed resolution of pulmonary consolidation.

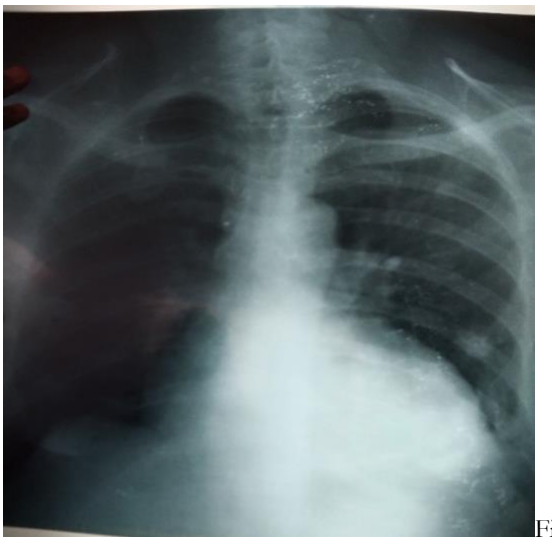
Figure 7: Repeat chest X-ray after 3 months of treatment.

Case Discussion

Cryptogenic organising pneumonia is an uncommon condition often missed or widely misdiagnosed and under-reported in resource-poor settings (like Nigeria) as a result of limited or unavailability of some diagnostic investigations. There is no agreed prevalence. Authorship of this case from Nigeria is rare. There are no pathognomonic clinical features. Thus, most febrile patients who present with cough and have opacities or infiltrate on chest radiograph are treated for prolong periods with antibiotic for infective pneumonia without resolution. The clinical course can be acute, subacute and chronic.[3] Our patients symptoms started progressively which was similar to the report of Cordier et al.[4]This case presented with the commonly reported symptoms such as cough, dyspnoea, fever [5] and infrequent or rare symptoms of weight loss, chest pain , haemoptysis and hoarseness . Physical examination in this case was also nonspecific as it revealed only crackles as seen in 68% of the 94 patient studied by Epler et al.[6] Blood work up is of little significance in clinching on the diagnosis of COP. There may be leucocytosis, neutrophilia as seen in this case and raised markers of acute phase reaction like C reactive protein and ESR(erythrocyte sedimentation rate).[7]Chest radiograph which is widely available in developing nations is the initial diagnostic imaging and it usually shows consolidation.

There have been cases of nodules and tumour – like mass seen on chest x-ray.[8] The combination of the aforementioned clinical manifestation and chest radiograph are suggestive of pneumonia which could be from any cause. This usually prompt the commencement of antimicrobial agents in settings where further investigation is not doable. In addition, infectious causes can be associated with cryptogenic organising pneumonia as earlier mentioned leading to misdiagnosis. Nonetheless, the use of antibiotic does not result in resolution of symptoms in cases of COP as reported in this case. High resolution computed tomography of the chest when available, shows the disease's extent better than the chest radiograph. The most common pattern is either a unilateral or bilateral patchy consolidation (with or without air bronchogram) with predilection for the periphery and lower lung zones as in this case. Sometimes lesions may be peribronchiolar, linear or perilobular.

There may be ground glass opacities, reverse halo or atoll sign, mediastinal lymphadenopathy and pleural effusion. Migratory opacities have also been reported[9]as well as nodule or masses.[8] Some cases coexist with other types of interstitial pneumonia such as NSIP,[10]UIP and AIP.[11]Poletti and coworkers stated that bronchoalveolar lavage cytology performed among 34 cases has a negative predictive value in 29% with 57% specificity and 63% sensitivity.[12]The expected yield from a broncho-alveolar lavage cytology is a greater than 25% lymphocyte count with more CD8 cell than CD4 , greater than 20% foamy macrophages, with or without neutrophil more than 5% and with or without eosinophil more than 25 but less than 25% .[12]

The diagnosis of cryptogenic organizing pneumonia is a diagnosis of exclusion confirmed by histology of lung biopsy sample which is a relatively rare in Nigeria. Histologically, granulation tissue made up of fibroblast and myofibroblast obstructs the alveolar lumen up to the terminal bronchioles with a mixture of inflammatory cells as seen in this case. There is also a characteristic endoluminal buds of granulation tissue known as Masson bodies as reported by several Literatures[13]Radiological and Histological investigations of COP are best reported by radiologist and pathologist with interest in the lung to avoid missing the actual diagnosis, as the disease can coexist with other diseases as earlier mentioned. As a result of misdiagnosis or missed diagnosis, patient is usually placed on antibiotic until the appropriate diagnosis is made as seen in this patient. COP may resolve spontaneously in some instances .[14] The treatment of choice, corticosteroid[9] was used for this patient. Although, macrolides as well as steroid sparing agents such as cyclophosphamide, azathioprine and cyclosporine have being utilized in certain scenarios.[13] On commencement of corticosteroid therapy, clinical and radiological resolution may be apparent within a space of one week. The duration of treatment is still a subject of debate. The outcome of COP is good and better than that of SOP. Some poor prognostic factors are: lung parenchyma scarring and remodelling, absent lymphocytosis on Broncho-alveolar Lavage cytology, predominant interstitial involvement on imaging[15]

Conclusion

Summarily, COP is rare disease condition and even rarer in environment where diagnostic modalities are limited. It typically presents with feature of lower respiratory tract infection or disease. Thus, accurate diagnosis can be missed, judging by clinical presentation and chest radiography only. This results in delayed initiation of corticosteroid and prolonged inappropriate use of antibiotics. When exact diagnosis is made and appropriate treatment commenced promptly, the prognosis is usually favourable.

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