Saudi Journal of Medicine
Scholars Middle East Publishers
Dubai, United Arab Emirates
Website: https://saudijournals.com/

ISSN 2518-3389 (Print)
ISSN 2518-3397 (Online)

Cryptogenic Organizing Pneumonia (COP) in the Seventh Decade of Life Woman Yahya Al-FIFI's Diagnostic Criteria for Cryptogenic Organizing Pneumonia (COP) Without a Lung Tissue Histopathology. Is This the Truth of the Reality Or The Reality of the Truth?

Yahya Salim Yahya
Consultant Internal Medicine & Infectious Diseases, Department of Medicine, Infection Diseases Division, Prince Mohammad Bin Nasser Hospital, Jizan, Jazan, Saudi Arabia

***Corresponding author**
Yahya Salim Yahya

Article History
Received: 19.11.2017
Accepted: 24.11.2017
Published: 30.11.2017

DOI:
10.36348/sjm.2017.v02i07.004

Abstract: We describe the first and rare case report of a cryptogenic organizing pneumonia (COP) in a seventh decade diabetic and hypertensive women from low highlands, Jazan, Saudi Arabia. The evidence of the clinical scenario, laboratories testing , radiological images findings followed by treatment with steroid is quite enough to diagnose COP, irrespective of lung tissue biopsy procedures and processing accessibility for histopathology, in a timely manner as reveals in Yahya Al-FIFI's diagnostic criteria for cryptogenic organizing pneumonia (COP) without a lung tissue histopathology. We started a methylprednisolone forty milligram intravenously every eight hourly for seven days which is showing a dramatic clinical improvement within initial twenty-four hours of first seven days and complete recovery clinically and radiologically, at the end of the following fourteen days of tapering prednisolone doses without a relapse for seven months. Our successful experience approach in this case of COP has several advantages include that an early diagnosis and introduction of methylprednisolone may lead to preserve lung function, avoidance of biopsies procedure complications, may prevent relapses, early hospital discharge, improve the morbidity, mortality and the quality of life of the patient. So, we conclude these clinical, laboratories testing, and radiological findings are quite enough to diagnosing and treating with methylprednisolone to rescue patient life, when a lung biopsy performance accessibility or feasibility is obscured or delayed. We observe that beta-lactam; ceftriaxone and piperacillin/tazobactam, glycopeptide; vancomycin and macrolide; clarithromycin antibiotics are not effective in our patient COP case scenario. "Yahya Al-FIFI's diagnostic criteria for cryptogenic organizing pneumonia (COP) without a lung tissue histopathology is easy and sufficient enough to assess physician to diagnose COP in acceptable time frame and may have favorable outcome over all.

Keywords: cryptogenic organizing pneumonia (COP), prednisolone, Yahya Al-FIFI's diagnostic criteria

INTRODUCTION

Cryptogenic organizing pneumonia (formerly BOOP; bronchiolitis obliterating organizing pneumonia) is a description of a form of an idiopathic interstitial pneumonitis that describe it as a condition of unknown etiology to date where alveolar wall, ducts respiratory bronchioles and distal bronchioles that are widely affected and enrich with an inflammatory cells mainly lymphocytes in the lung peripherally but centrally may be involved similarly and frequently [1-4]. The radiological images of COP may reveals unilateral or bilateral extensive pneumonia in a form of consolidations, air bronchograms, nodular opacities and ground glass appearance in a plain chest x-rays images in addition to a form of a crazy paving radiological images appearance that may be reflected in a chest high resolution computerizes tomography (CT/HRCT) scan but not specific for acute or chronic COP [1-4]. COP may be postulated to be due to or associated with various factors including; connective tissue diseases, malignancies, hematological, solid tumors, drugs, chemical, toxins, allergens, and dusts [1-9].

The patient with COP may present with picture of acute clinical features of typical or atypical of community-acquired pneumonia or chronic longstanding pulmonary symptoms where empirical antimicrobial are initiated where the rest of work up process is in place including microbiology samples; bacterial, mycobacterial, fungal, parasitic and biopsy of the lung for histopathology to confirm the diagnosis of COP [5].

Acute or chronic COP is usually has an excellent outcome response to steroid treatment; however, relapses are a benign phenomenon that could be easily

managed with steroid treatment where a favorable outcome occurs [9, 10] COP may be suspected only by radiological solitary or diffused bilateral infiltrate that showed characteristics radiological features that may suggest a wide differential diagnosis where further evaluation is required including a lung biopsy to delineate the etiology [1-9]. A feasibility of biopsy may be obscured for several reasons including patient refusal to consent for the lung biopsy or an inaccessibility setting for the procedures. So, in the view of patient clinical respiratory status deterioration where further investigation is guarded or pending, it is a quite reasonable approach to start treatment with steroid mainly depending on clinical deterioration of the patient, the lack of response to empirical appropriate antimicrobial choices considering the duration in the view of the reflection of radiological imaging findings that suggestive of COP as reveals in this case report.

CASE PRESENTATION

A 61-year old woman, villager and farmer from the low highland of Jazan, Saudi Arabia, presented with shortness of breathing, dry cough which becomes slowly productive with greenish sputum and fever over seven days duration. She was brought to emergency department, with worsening of her shortness of breathing, fever, chills and shivering. Patient has no history of chest pain, orthopnea, paroxysmal nocturnal dyspnea or lower limbs swelling. There is no history of headache, dizziness, visual complains, weakness, seizures, gait instability or sphincters disturbances. She is non- alcoholic, non-smoker or drug abuser. She lives among her healthy three generations of her family in an environment where fifty days of sandstorms winds that blows annually in the summer. Her past medical history is significant for diabetic type II requiring insulin, hypertension on metoprolol 100 milligram daily, aspirin 81 mg orally once a day, amitriptyline 25 milligram for anxiety at night. She has no history of tuberculosis or brucellosis. The history of travel, family and social histories were unremarkable. The rest of systemic reviews were non-contributable.

On examination on her presentation to the emergency department, she reveals an overweight female in her estimated age. She is conscious, oriented to time place person. Vital signs reflect a temperature of 39.0° C, respiratory rate is 25 breaths per minute, pulse is 120 beats / minute, 130/75 mmHg, saturation is 88 % in room air and 96% on 2 L/minute (via nasal prongs). The jugular venous pressure is 4 centimeter above the sternal angle with normal hepato-jugular reflux. She is not pale or jaundiced and no lymphadenopathy enlargement. Chest showed symmetrical movement with expansion limitation bilaterally. She has a bronchial breathing with scattered rhonchi bilaterally. The cardiovascular system examination revealed first and second heart sounds are normal, no added sound murmurs or lower limb edema. The abdominal examination reveals an inverted umbilicus, with flanks bulging bilaterally, no scar, hepatomegaly, splenomegaly, masses or ascites. The neurological, the peripheral vascular and the locomotors examinations are normal. Skin examination revealed no rash, joint deformities or nodules. Genitourinary system examination was normal.

The initial Investigation showed WBC 5.70 with 78.7% neutrophil, hemoglobin is 12.7 gram/dl (normal 12-16 gram/dl) and platelets is 183 × 10^9 per liter.(Normal; 150–400 × 10^9 per liter.), liver function test showed aspartate transaminase (AST) 55 (normal up to 40 U/L), alanine transaminase (ALT) 49, (normal up to 40 U/L), alkaline phosphatase (ALP) 77 (normal 39-112 U/L), lactate dehydrogenase LDH) 250 (normal 72-182 U/L albumin 27 (normal up to 38-50g/L), calcium 2.04 (Normal 2.0-2.6 mmol/L) and total protein 71 (normal up to 66-87g/L) whereas renal profile , lipid profiles, phosphate, magnesium, prothromin time, Partial thromboplastin time, and bleeding time were within normal limits. Chest X-rays revealed bilateral patchy consolidations, air bronchogram, ground glass appearance and nodularity's shadow infiltrate (image I). Ultrasound shows a mild hepato-splenomegaly with normal kidneys sizes, no masses where the rest of the abdominal examination are normal. A sputum for gram stains, bacterial and fungal cultures, acid fast bacilli, tuberculosis polymerase chain reaction and cultures, viral studies and two sets of blood cultures are obtained prior the initiation of antibiotics; a ceftriaxone and clarithromycin are started empirically. Patient is admitted for further evaluation and management.

Our patient is admitted to hospital with diagnosis of community acquired pneumonia where ceftriaxone 2 grams intravenous every 24 hour and clarithromycin 500 milligram orally twice daily as an empirical treatment for a typical and atypical pneumonia organisms. The patient background indicated that she is known to have diabetes type II requiring insulin with hemoglobin A1C 7 (normal up to 6.4) and hypertension, which is well control on metoprolol without microvascular or macrovascular complications.

In spite of that the patient pulmonary status continued to deteriorate over following 48 hours of hospitalization where she requires oxygen up to 10 L/minute (via nasal prongs) to maintain her oxygen saturation above 94%. A bilateral patchy diffused consolidation, nodularity, air bronchogram and areas of ground glass appearance that become more evident in the repeated chest x-ray in the second day of hospitalization compare to initial chest x-rays on admission. Considering the clinical contest of this case scenario a wide differential diagnosis is entertained included infection; bacterial, fungal, mycobacterium tuberculosis and viral, connective tissue diseases; rheumatoid arthritis and mixed connective tissue diseases, malignancy, chemicals, toxins, environmental

factors; dust, pollens and cryptogenic organizing pneumonia.

On the 3rd day of hospitalization (10th day of the illness) a clinical and radiological deterioration dictates discontinuation of ceftriaxone and osculating it to piperacillin/tazobactam 4.5 gram every 6 hourly intravenously. A vancomycin 1 gram intravenously every eight hourly for possibility of resistance pneumococcus or streptococcus pneumonia is added. A clarithromycin is continued to cover atypical bacterial pneumonias; legionella pneumophil, mycoplasma pneumoniae and, chlamydia pneumonia. A high resolution computerized tomography (CT/HRCT) images appearance that reveals bilateral diffused consolidations with air bronchograms, infiltrative nodularity's shadows, ground glasses appearance matching the chest-rays findings (Fig-1, 2, 3) in addition to a crazy paved pattern (Fig-4, 5) that are compatible with diagnosis of COP in this case reports.

On the 4th day of hospitalization (11th day of the illness) she becomes exhausted and her oxygen saturation dropped to 88 on 15 L/minute (via nasal prongs) where she requires an intubation and ventilation. The sputum gram stains and cultures for bacteria and fungal, acid-fast bacilli and polymerase chain reaction (PCR) for tuberculosis, blood culture and viral studies for influenza A and B and H1 N1 are negative.

However, in the view of this clinical deterioration of the patient and the evidence of absence of a pathogen recovery that may attribute to the declining in patient respiratory status, the lack of responding to appropriate antibiotics coverage, worsening of the radiology imaging findings pattern in the serial chest x-rays and CT/HRCT scan over five days duration, that suggestive of cryptogenic organizing pneumonia (COP), and infeasibility of a bronchoscopist or intervention radiology procedure to perform a biopsy in addition to a practical delay that may occur in obtaining the histopathology biopsy report to delineate the cause at the time. We concluded that the diagnosis, clinically and radiologically, is cryptogenic organizing pneumonia, irrespective of performing a lung tissue biopsy to prove COP diagnosis histopathologically.

We started on the fifth day of hospitalization; 12th day of the illness a methylprednisolone 40 milligram intravenously every 8 hourly, where we observe that the patient starts to show a significant clinical improvement in the initial twenty four hours of methylprednisolone treatment where within ninety six hours patient is extubated and transfers to the ward. The patient clinical improvement accompanies with radiological images that reveals a significant progressive

The patient is discharged from the hospital on tapering doses of prednisolone for two weeks to complete total course of three weeks of steroid. A CT/HRCT scan chest at the end of the three weeks of steroid tapering doses shows a very significant interval improvement radiologically as reflected in (Fig-4, 5), where the bilateral diffuse patchy opacities, nodularity's shadow infiltrate consolidation and air bronchograms with ground glasses appearances are resolved. Patient is able to return to her normal daily life style activities without any relapse up to seven months post discontinuation of prednisolone.

Table-1: Yahya Al-FIFI's diagnostic criteria for cryptogenic organizing pneumonia (COP) without a lung tissue biopsy for histopathology

Yahya Al-FIFI's diagnostic criteria for cryptogenic organizing pneumonia(COP) without a lung tissue histopathology All the 4 Clinical, 3 radiological, 2 laboratories testing and 2 treatment criteria are required for the diagnosis of COP
Clinical (4) (General and pulmonary symptoms, signs and management)
I-One general symptom: fever; decrease appetite, sweating , decreased weight
II-One pulmonary symptom: Cough, shortness of breathing, chest pain, etc.…
III-One pulmonary sign: Bronchial breathing, rhonchi, dullness, etc.
IV-One oxygen desaturation from a room air in 5 days
Radiology (3) (Chest x-rays and CT/HRTCT scan)
V- One chest x-rays and/or CT/HRCT scan image abnormality within 5 days.
VI- No chest x-rays and/or CT/HRCT scan image abnormality of specific pathogen or pathology i.e. TB, fungal, parasitic or tumor within 5 days.
VII-No evidence of pulmonary embolism; negative D-Dimer or pulmonary angiography.
Laboratories testing (2)

(Microbiology and pathology testing)
Microbiology
VIII- No evidence of pathogen that is recovered by any means in 5 days
Pathology
IX- No lung tissue biopsy for histopathology is done in 5 days
Management (2) (Empirical and specific treatments)
Empirical treatment
X- No evidence of response to appropriate antimicrobial coverage for 5days.
Specific treatment
XI- Excellent response to steroid (methylprednisolone) course of 5 days

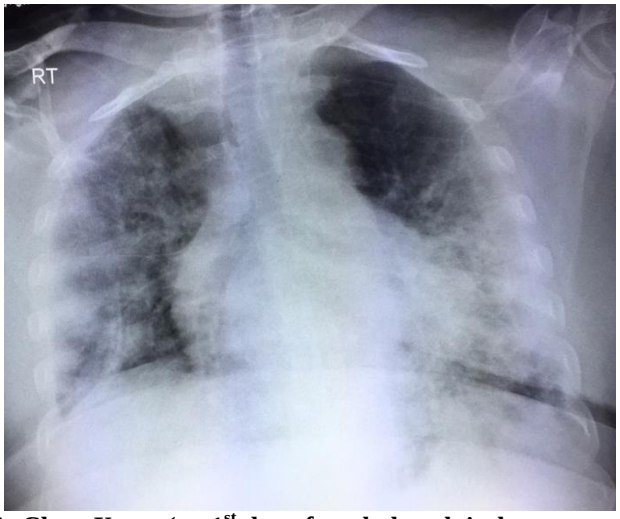

Fig-1: Chest X-ray (on 1st day of methylprednisolone treatment)

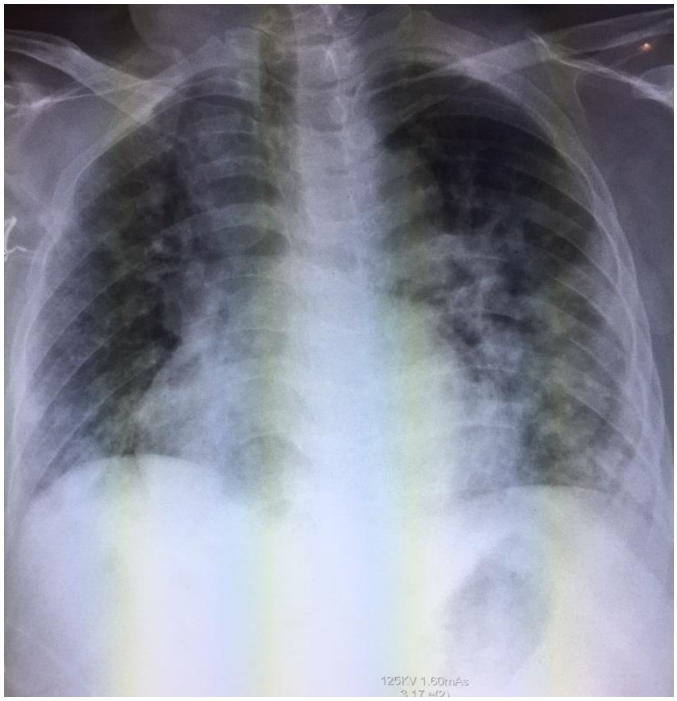

Fig-2: Chest X-ray (on the 2nd day of methylprednisolone treatment)

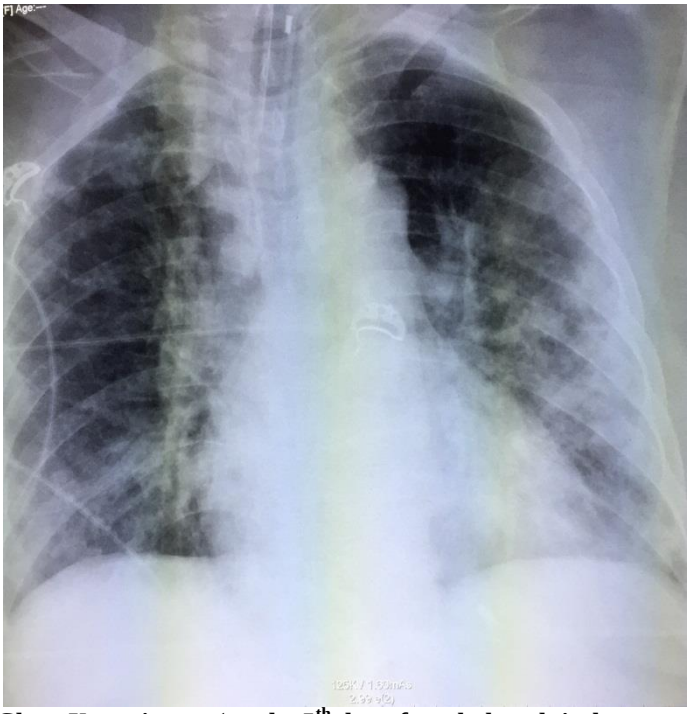

Fig-3: Chest X-ray image (on the 5th day of methylprednisolone treatment)

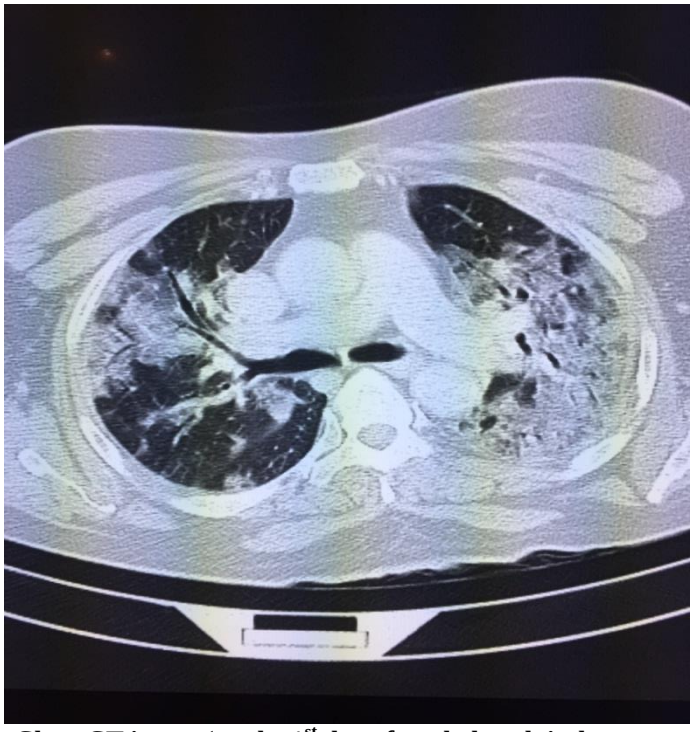

Fig-4: Chest CT image (on the 1st day of methylprednisolone treatment)

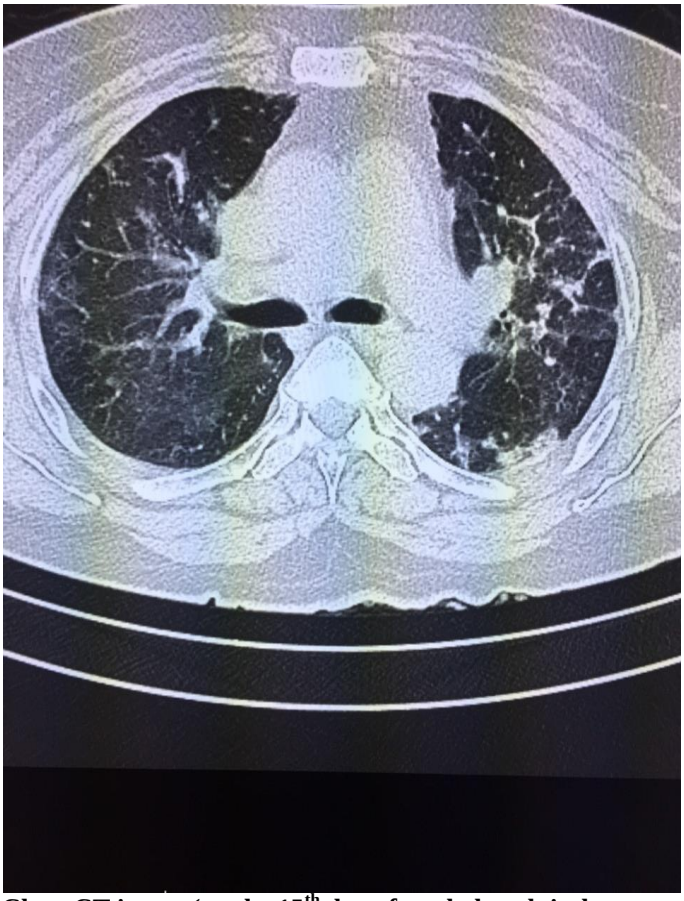

Fig-5: Chest CT image (on the 15th day of methylprednisolone treatment)

DISCUSSION

A cryptogenic organizing pneumonia is a quite rare disease and may mimic clinical manifestations and chest radiological images of several diseases categories including infectious diseases, connective tissue diseases and malignancies that require a lung biopsy to prove the diagnosis histopathologically. COP is a diagnosis that requires a low threshold of a clinical suspicion, in order to implement therapy to rescue the patient life with steroid, in the absence or existence of the means to perform lung biopsies for histopathological diagnosis confirmation [1-9]. However, lung biopsies procedures and histopathology processing accessibility, in a timely manner, is a quite challenging issue for the physician at the time of the clinical suspicion and may delay the therapy decision.

In the view of our patient clinical status deterioration; where the patient oxygen demands requirements increases progressively, the respiratory exhaustion manifest in a form of excreting an accessory respiratory muscles, and the radiological evidence of chest images (bilateral patchy consolidations, air bronchogram, ground glass appearance and nodularity's shadow infiltrate) that is visualize in both the chest x-rays images (Fig-1, 2, 3) and a chest CT/HRCT images (Fig-4, 5) in addition to a crazy paved patterns images in (images IV and V) that worsening over the five days of admission where all findings are compatible with the diagnose of COP. In addition to the infeasibility of lung tissue biopsy and the expected delay in the processing time in order to obtain the histopathology report to confirm the diagnosis of COP. We depends on the clinical deterioration of the patient respiratory status, worsening of radiological findings, and absence of recovery of any pathogen by any means in five days of appropriate coverage of antibiotics, is convincing collective evidences and sufficient enough for us to diagnose our patient with COP. Hence we started a steroid in a form of methylprednisolone considering and admitting the clinical, laboratories and radiological supportive evidences in the view of the absence of lung biopsy.

We observe that the patient the fast initial improvement response to steroid (methylprednisolone) occurrence to confirm the diagnosis at the glance. However, the dramatic response of the patient occurs due to the short course of methylprednisolone 40 mg every eight hourly within the initial twenty –four hours, and continues to improve within the first seven days of treatment, where she is extubated, transfer to the ward and discharge home on tapered prednisolone for two weeks. We found this approach is enough diagnostically and effective therapeutically simultaneously for a cute form of COP. We believe that, in spite of her elderly age and diabetes mellitus type II requiring insulin without microvascular or macrovascular, however, we

observe important critical factors that have led to our patient excellent outcome. These factors are the early clinical suspicion and radiological images findings (chest x-rays and CT/HRCT scan) that highly suggestive of manifestation of COP, the initiation of methylprednisolone for seven days, within the first two weeks of her initial symptoms followed by rapid prednisolone tapering doses over two weeks, the absence of underlying pulmonary diseases and starting management with methylprednisolone without a delaying in order to perform a lung tissue biopsies histopathology in the view of our therapeutic approach that confirmed the diagnosis of COP.

This approach has several advantages; minimize the effect of the inflammatory process rapidly, preserve the patient lung physiology abruptly, avoidance of patient development of the acute adverse effects of methylprednisolone; "hypertension and bilateral pleural effusions" as describe in "Yahya Al-Fifi's Syndrome" and chronic adverse effects; include but not limited to mode changes, osteoporosis, risk of hip fractures, skin bleeding and capillaries fragilities s

We observe that the excellent outcome of our patient based on early diagnosis and introduction of a short course of methylprednisolone that associates with no relapse for seven months, which may remain forever. We believe the early and a short course of methylprednisolone cures an acute form of COP and prevents relapsing and the progression of the disease to a chronic form as manifests in our patient scenario. However, this requires a multicenter study to evaluate these clinical facts that base on our case report scenario.

Cryptogenic organizing pneumonia have been treated successfully with macrolide; clarithromycin, with less adverse effect and relapses compare to steroid, however, the duration was for three months where up to one-third of patient are cured [2]. However, we found our empirical treatment, macrolide; clarithromycin, beta-lactam; ceftriaxone that was osculates, to piperacillin-tazobactam and vancomycin are not effective. In fact, macrolide; clarithromycin is introduces on admission for seven days which associates with deterioration in the clinical pulmonary status where our patient is able to recover as short course of methylprednisolone introduces without adverse effect, which led us to discontinue antibiotics therapy [2, 10-12].

In searching for the cause of COP at this point we remain uncertain however, we entertain a hypothetical idea that the etiology may be environmental that may remain obscured for now probably forever in the absence of a lung biopsy that may be of a limited benefit at this time for patient management issue or need to confirm the diagnosis histopathologically. However, in case of relapse our hypothesis is remaining in the way of searching for the cause. We entertain that the patient lives in a habitat that is enriched of farms, rivers, sheep's pastures, landscapes, agricultures areas, and receives an annual rains that proceeded by up to fifty days of heavy red or black sandstorms that blows toward the province of Jazan, Saudi Arabia from African continent in the summer with various speeds ranging from 70 to 120 kilometer (Jazan, Saudi Arabia is located on the southwest of the country ;in the southwest corner of Asian southwest continent across the African horn countries in the south east corner of African continent facing each other across the red sea). These environment factors may play a role in her diagnosis that will probably remain a research question, which requires epidemiological studies to evaluate COP in the low highlands Jazan, Saudi Arabia in more depth of searching for the environmental etiology, and ask a critical question why and why now? [1-12].

The diagnosis of cryptogenic organizing pneumonia is proved in our patient by a clinical suspicion of COP, lack of response to appropriate broad spectrum of antibiotics, lack of recovering of any pathogen, worsening of the radiological imaging of chest x-rays and CT/HRCT scan findings and a dramatic therapeutic response to methylprednisolone in the first twenty four hours. We extubate and transfer the patient to the ward within two days to completing seven days course of methylprednisolone treatment. Then, the patient is discharged home on tapering steroid doses in a form of prednisolone for two weeks where the total course of the therapy of steroid is three weeks. The patient shows a significant improvement of the clinical status and the radiological images at the end of the tapering prednisolone therapy without relapse for seven months (Fig-1, 2, 3, 4, 5).

However, we observe that the diagnosis based on clinical, laboratories testing, radiological images findings evolvement reflections over time, treatment responses to steroid in absence of lung tissue biopsies for histopathology are enough to confirm COP diagnosis. This collective clinical, laboratories, chest radiology imaging finding (Fig-1, 2, 3, 4, 5), patient respiratory status deterioration in spite of appreciate broad spectrum antibiotics and absence of other diseases evidence approach to diagnose COP is acceptable and reasonable in order to safe patient life in the infeasibility of lung biopsies for histopathology as a gold standard diagnostic mean to confirm COP in the view of the absence of the existence of a laboratory diagnostic test to confirm COP to date.

Diagnostic criteria without a lung biopsy for COP is highly demanded, considering several factors including accessibility of procedure and possessing time of histopathology of lung biopsy that may delay the treatment and worsens the patient outcome. So, we decide to create criteria that should include clinical, laboratories testing; sputum for bacteria and fungal

gram stains and cultures, tuberculosis for acid fast bacilli and polymerase chain reaction, cytology), blood cultures, chest radiological evidences, and steroid treatment response collectively, that considers satisfactory to diagnose COP where a lung histopathology is not required. We believe these criteria will be quite enough, easy, fast and helpful in timely manner to diagnose COP and has an excellent outcome as a result.

We called these criteria "Yahya Al-FIFI's cryptogenic organizing pneumonia diagnostic criteria without lung tissue histopathology" (Table 1). The diagnostic criteria comprise of eleven criteria; clinical (4 criteria), radiological (3 criteria), laboratories testing (2 criteria) and treatment (2 criteria) where the patient requires to have all the eleven criteria in order to fulfills the diagnostic criteria of COP without a lung tissue histopathology. The eleventh criterion (Table1) is the cornerstone of the criteria, where the patient will receive a steroid (methylprednisolone 40 milligram intravenously three times daily for 5 days), if improvement is observed then the diagnosis of COP is confirmed. However, if the patient improvement is lacking, the performance of a lung biopsy to delineate the diagnosis etiology is mandatory.

In order to diagnose COP applying Yahya Al-Fifi's diagnostic criteria for cryptogenic organizing pneumonia (COP) without a lung tissue histopathology you required to have minimum of one item from each criterion within first 5 days of presentation to hospital ; I-one general symptom within 5 days, II-one respiratory symptom within 5 days , III-one respiratory sign within 5 days, IV-one oxygen desaturation within 5 days, V-one chest radiology finding in chest x-rays and CT/HRCT scan within 5 days, VI-no radiological abnormality of specific pathogen as mycobacterium tuberculosis, fungal or parasitic in 5 days, VII-no pulmonary embolism which confirm by negative D-dimer or pulmonary angiogram, VIII-no evidence of pathogen recovered by any means from sputum and blood including gram stains and bacterial and fungal cultures, mycobacterium tuberculosis acid fast bacilli, culture and polymerase chain reaction and blood culture in 5 days IX- no lung biopsy histopathology X-No response to appropriate broad spectrum antibiotics for 5 days, XI- Response to steroid (methylprednisolone) within 5 days.

We report our patient scenario to show our successful diagnostic and therapeutic approach for COP, that is depends on the fact that it is enough to have a low threshold of a high clinical suspicion, laboratories testing, radiological images findings and steroid induce clinical improvement without any need for lung tissue biopsy to confirm COP in order to start methylprednisolone. We may say even at the best scenario of accessibility to histopathological diagnosis this approach is faster, quite reasonable and acceptable. Yahya Al-FIFI's diagnostic criteria for COP (Table1) are very practical to diagnose and manage simultaneously. We believe our approach is very safe and facilitate an early discharge of the patient from the hospital and improve morbidity, mortality and the quality of life. It leads to excellent outcome and without relapse for seven month as our patient case scenario expresses.

CONCLUSIONS

Cryptogenic organizing pneumonia (COP) is a rare manifestation of unknown etiologies to date. COP has wide differential diagnoses where it may be usually mimicking chronic obstructive pulmonary diseases exacerbation or community acquired pneumonia presentation. The recognition of COP requires meticulous, close and frequent reevaluation, if the patient response to appreciate initial antimicrobial therapy is lacking. The clinical, laboratories testing, radiological findings and management with steroid reach our patient diagnosis that is shows in Yahya Al-FIFI's diagnostic criteria for cryptogenic organizing pneumonia (COP) without a lung tissue histopathology (Table1). Steroid therapies introduce in a form of a methylprednisolone and prednisolone, for seven days and fourteen days respectively, which induces a complete recovery of our patient COP clinical and radiological manifestation without a relapse for seven months.

This case reports scenario support starting therapy with steroid depending on the clinical, laboratories testing and radiological images findings that compatible with COP without a need for a lung biopsy to confirm the diagnosis. This approach is very safe, facilitates early hospital discharge, and improves morbidity, mortality and the quality of life.

"Yahya Al-FIFI's diagnostic criteria for cryptogenic organizing pneumonia (COP) without a lung tissue histopathology (Table1)" is easy and sufficient enough to diagnose COP in acceptable time frame and may have rapid and favorable outcome over all.

REFERENCES

1. Epler, G. R., Colby, T. V., McLoud, T. C., Carrington, C. B., & Gaensler, E. A. (1985). Bronchiolitis obliterans organizing pneumonia. *New England Journal of Medicine*, *312*(3), 152-158.
2. Sara, A. G., Hamdan, A. J., Hanaa, B., & Nawaz, K. A. (2008). Bronchiolitis obliterans organizing pneumonia: pathogenesis, clinical features, imaging and therapy review. *Annals of thoracic medicine*, *3*(2), 67.
3. Lee, K. S., Kullnig, P., Hartman, T. E., & Müller, N. L. (1994). Cryptogenic organizing pneumonia: CT findings in 43 patients. *AJR. American journal of roentgenology*, *162*(3), 543-546.

4. Johkoh, T., Itoh, H., Müller, N. L., Ichikado, K., Nakamura, H., Ikezoe, J., ... & Nagareda, T. (1999). Crazy-paving appearance at thin-section CT: spectrum of disease and pathologic findings. *Radiology*, *211*(1), 155-160.
5. Cornelissen, R., Senan, S., Antonisse, I. E., Liem, H., Tan, Y. K., Rudolphus, A., & Aerts, J. G. (2007). Bronchiolitis obliterans organizing pneumonia (BOOP) after thoracic radiotherapy for breast carcinoma. *Radiation Oncology*, *2*(1), 2.
6. Yamanda, S., Kobayashi, S., Hanagama, M., Sato, H., Suzuki, S., Ueda, S., ... & Yanai, M. (2016). Two cases of tsunami dust pneumonia: organizing pneumonia caused by the inhalation of dried tsunami sludge after the 2011 Great East Japan earthquake. *Internal Medicine*, *55*(24), 3645-3653.
7. Kahraman, H., Tokur, M., Sayar, H., & Inci, M. F. (2013). Cryptogenic organising pneumonia presenting with bilateral hilar and mediastinal lymphadenopathy. *BMJ case reports*, *2013*, bcr2013009712.
8. Alasaly, K., Müller, N., Ostrow, D. N., Champion, P., & Fitzgerald, M. J. (1995). Cryptogenic Organizing Pneumonia A Report of 25 Cases and a Review of the Literature. *Medicine*, *74*(4), 201-211.
9. Cordier, J. F. (2004). Cryptogenic organizing pneumonia. *Clinics in chest medicine*, *25*(4), 727-738.
10. Radzikowska, E., Wiatr, E., Langfort, R., Bestry, I., Skoczylas, A., Szczepulska-Wójcik, E., ... & Roszkowski-Śliż, K. (2017). Cryptogenic organizing pneumonia—Results of treatment with clarithromycin versus corticosteroids—Observational study. *PloS one*, *12*(9), e0184739.
11. Ding, Q. L., Lv, D., Wang, B. J., Zhang, Q. L., Yu, Y. M., Sun, S. F., ... & Deng, Z. C. (2015). Macrolide therapy in cryptogenic organizing pneumonia: A case report and literature review. *Experimental and therapeutic medicine*, *9*(3), 829-834.
12. Al-Fifi, Y. S. Y. (2017). A methylprednisolone induced hypertension and bilateral pleural effusions as acute adverse effects in a young woman "Yahya Al-Fifi's Syndrome". Saudi Journal of Medical and Pharmaceutical Sciences, 3(7), 653-657.