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Clinical Case Seminar

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An unusual non-resolving community-acquired pneumonia

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Abstract

We present the case of a 61-year-old male that was admitted to our Unit of Pulmonology for a suspected community-acquired pneumonia (CAP) with acute hypoxemic respiratory failure. However, despite many courses of empiric wide spectrum antibiotic treatment, the respiratory failure persisted and new bilateral migratory pulmonary opacities and serosal effusions appeared. The most common causes of non-resolving CAP were excluded and the combination of thrombocytopenia, autoimmune hemolysis, pleural and pericardial effusions in a patient with antinuclear antibodies ANA at a titer of 1:160 is diagnostic for systemic lupus erythematosus (SLE).

Key Words: non-resolving pneumonia, autoimmune pneumonia, organizing pneumonia, systemic lupus erythematosus, acute lupic pneumonitis.

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Introduction

Pneumonia is defined "non-resolving" when there is an inadequate clinical response despite antibiotic treatment (1,2). We present here an unusual cause of non-resolving community-acquired pneumonia.

Case presentation

A 61-year-old male, Caucasian, social worker, former smoker, by 4 years, of 90 pack-years, presented at the Emergency Room of the University Hospital G. Martino of Messina, Italy (www.polime.it), for the presence by 60 days of persistent dry cough, exercise-induced dyspnea and fatigue. In his past history there was a diabetes mellitus (controlled with gliclazide), systemic arterial hypertension (controlled with olmesartan), paroxysmal atrial fibrillation (controlled by 3 years with flecainide), depressive syndrome (under treatment by 15 days with paroxetine), long-lasting untreated thrombocytopenia and chronic normocytic normochromic anemia both of unknown cause. At the admission in our ward his vital signs were: systemic blood pressure 150/85 mmHg, pulse frequency 80/min rhythmic, breathing acts 22/min, body axillary temperature 36.5°C. An arterial blood gas analysis, performed with the patient breathing room air, showed an acute hypoxemic (PaO2 57 mmHg) respiratory failure. Physical examination of the chest revealed severe reduction of the vesicular murmur in the bilateral middle-basal lung fields and left basal crackles. A chest X-ray showed the presence of multiple bilateral

pulmonary opacities. The patient was admitted to our Unit of Pulmonology for a suspected community-acquired pneumonia (CAP) with acute hypoxemic respiratory failure.

Immediately it was started empiric wide spectrum antibiotic therapy (clarithromycin 500 mg IV twice daily and amoxicillin/clavulanic acid 1 g IV thrice daily for 10 days) according to community-acquired pneumonia guidelines (2).

During hospitalization, many investigations were made. Pathological laboratory data are shown in Table 1; in addition the urine sediment analysis showed traces of proteins and red blood cells.

Table 1. Pathological laboratory data during the hospitalization

	At the admission	After 5 days of hospitalization	After 15 days of hospitalization	After 20 days of hospitalization	After 30 days of hospitalization	After 40 days of hospitalization	After 45 days of hospitalization	After 48 days of hospitalization	After 52 days of hospitalization
Erythrocyts (cell/mm3)	**3530000**	**3620000**	**3480000**	**3400000**	**3010000**	**3390000**	**3160000**	**3220000**	**3690000**
Hemoglobin (g/dL)	**9.6**	**9.7**	**9.3**	**8.8**	**7.6**	**8.5**	**7.7**	**7.3**	**9.1**
Hematocrit (%)	**29.7**	**30.2**	**28.7**	**27.6**	**23.9**	**26.6**	**24.7**	**23.7**	**28.2**
Total leukocytes (cell/mm^3)	**9950**	**10700**	**9300**	**6600**	**6000**	**6700**	**9000**	**7400**	**8000**
Neutrophils (cell/mm^3)	**7326**	**8239**	**7161**	**4950**	**3960**	**5561**	**7110**	**6216**	**5840**
Lymphocytes (cell/mm^3)	**1683**	**1605**	**930**	**858**	**1680**	**670**	**1170**	**1178**	**1920**
Platelets (cell/mm^3)	**199000**	**140000**	**118000**	**110000**	**115000**	**100000**	**101000**	**122000**	**115000**
Serum CRP* (mg/dL)	**16.56**	**12.94**	**12.14**	**9.01**	**3.93**	**16.06**	**23.24**	**8.1**	**2.02**
Total plasma proteins (g/dL)		**6.8**			**5.9**	**4.9**			**5.3**

***CRP: C-reactive protein**

Serum autoantibody panel [anti-double-stranded DNA (anti-dsDNA); anticardiolipin autoantibodies (aCL); lupus anticoagulant (LAC); anti-extractable nuclear antigen (anti-ENA)-Sm, Sm-RNP and SS-B; antiphospholipid antibodies (aPL); mitochondrial antibodies (AMA); anti-smooth muscle antibodies (ASMA); anti-centromere antibodies (ACA); antineutrophil cytoplasmic antibody (ANCA): c-ANCA and p-ANCA; complement C3 and C4] was normal, except for antinuclear antibodies (ANA) that were positive at a titer of 1:160 with a speckled pattern. Serum cancer markers [carcinoembryonic antigen (CEA); alpha-fetoprotein (AFP); carbohydrate antigen 19-9 (CA 19-9); prostate specific antigen (PSA); neuron-specific enolase (NSE)] were negative. The direct Coombs test was positive for IgG antibodies. Whereas the stool search for occult blood was negative.

Two fiberoptic bronchoscopies, performed at an interval of 10 days, were all negative for the cytopathological, microbiological and mycobacteriological analysis of the bronchoalveolar lavage fluid (BAL). Blood quantiferon TB as well as intradermal tuberculin (Mantoux) tests were positive, whereas other microbiological investigation [sputum culture, Mycoplasma pneumoniae, Chlamydophila pneumoniae and human immunodeficiency virus (HIV) serology, serum galactomannan, legionella and pneumococcal urinary antigens] were all negative.

Serial computed tomography (CT) scans of the chest, showed multiple bilateral pulmonary opacities, with areas both of ground glass and consolidations, crazy-paving pattern and serosal (left pleura and pericardium) effusions (Figure 1). Spirometry showed a restrictive (total lung capacity 65% of predicted) syndrome with a normal lung diffusing capacity for carbon monoxide (DLCO).

Despite many other courses of empiric wide spectrum antibiotics (piperacillin/tazobactam 4.5 g IV every 6 hours plus linezolid 600 mg IV every 24 hours for 14 days, then meropenem 1 g IV every 8 hours for 5 days), the severe respiratory failure requiring high oxygen flows persisted (Table 2) as well as the neutrophilic leukocytosis with increased serum levels of C-reactive protein (CRP) (Figure 2). Thirty days after the admission we started systemic glucocorticoid therapy for the suspicion of organizing pneumonia (OP), according to the protocol suggested by Cordier et al (3), in combination with isoniazid (plus pyridoxine) and rifampin, for the chemoprophylaxis of latent tuberculosis (4). After 7 days of this treatment, the respiratory symptoms, the chest imaging pattern (Figure 1) and the respiratory failure all sharply improved. A month later the patient was transferred to the Pulmonology Unit of the Hospital Morgagni-Pierantoni of Forlì, Italy, to perform a transbronchial cryobiopsy of the middle pulmonary lobe (5). The BAL performed in the middle lobe showed lymphocytosis (70% of all cells) and the absence of neoplastic cells. Histopathological examination of the lung cryobiopsy showed a pattern of organizing pneumonia (OP) and cellular nonspecific interstitial pneumonia (NSIP) (Figure 3).

After 2 months of follow-up post discharge at home, non-indurated psoriasiform lesions appeared on the lower limbs and on the elbows bilaterally.

After 5 months from the discharge, the dosage of prednisone has been reduced to 5 mg per day, with reappearance of dyspnea, hypoxemia and new parenchymal lung opacities bilaterally in the lower lobes, with both ground glass and consolidative areas without pericardial and pleural effusions (Fig 1). For this reason, the dosage of prednisone was increased to 20 mg daily.

Table 2. Arterial blood gas values during the hospitalization

DATE	pH	PaO2*	PaCO2**	SaO2***	OXYGEN THERAPY
At the admission	**7.48**	**57**	**37**	**89%**	**Room air**
After 3 days of hospitalization	**7.47**	**72**	**39**	**95%**	**Venturi mask FiO2**** 35%**
After 7 days of hospitalization	**7.53**	**81**	**34**	**95%**	**Venturi mask FiO2 35%**
After 15 days of hospitalization	**7.47**	**56**	**39**	**89%**	**Nasal cannula 3 L/min**
After 20 days of hospitalization	**7.46**	**80**	**39**	**97%**	**Venturi mask FiO2 40%**
After 24 days of hospitalization	**7.44**	**68**	**38**	**94%**	**Venturi mask FiO2 35%**
After 30 days of hospitalization	**7.47**	**70**	**39**	**95%**	**Venturi mask FiO2 35%**
After 35 days of hospitalization	**7.45**	**69**	**43**	**94%**	**Nasal cannula 3 L/min**
After 40 days of hospitalization	**7.49**	**60**	**39**	**91%**	**Nasal cannula 1 L/min**
After 45 days of hospitalization	**7.48**	**61**	**35**	**94%**	**Nasal cannula 1.5 L/min**
After 48 days of hospitalization	**7.44**	**65**	**39**	**94%**	**Nasal cannula 0.5 L/min**

aO2: partial pressure of oxygen
****PaCO2: partial pressure of carbon dioxide**
*****SaO2: oxygen saturation in the arterial blood**
******FiO2: inhaled fraction of oxygen**

Currently, after 19 months from the starting of the systemic glucocorticoid treatment, with a maintenance daily dose of 10 mg of prednisone per os, the patient is asymptomatic with a mild restrictive (last total lung capacity 71% of the predicted) syndrome, normal arterial blood gas data and a chest CT pattern almost normalized (Fig 1).

Fig.1. Evolution of the computed tomography (CT) scans of the chest

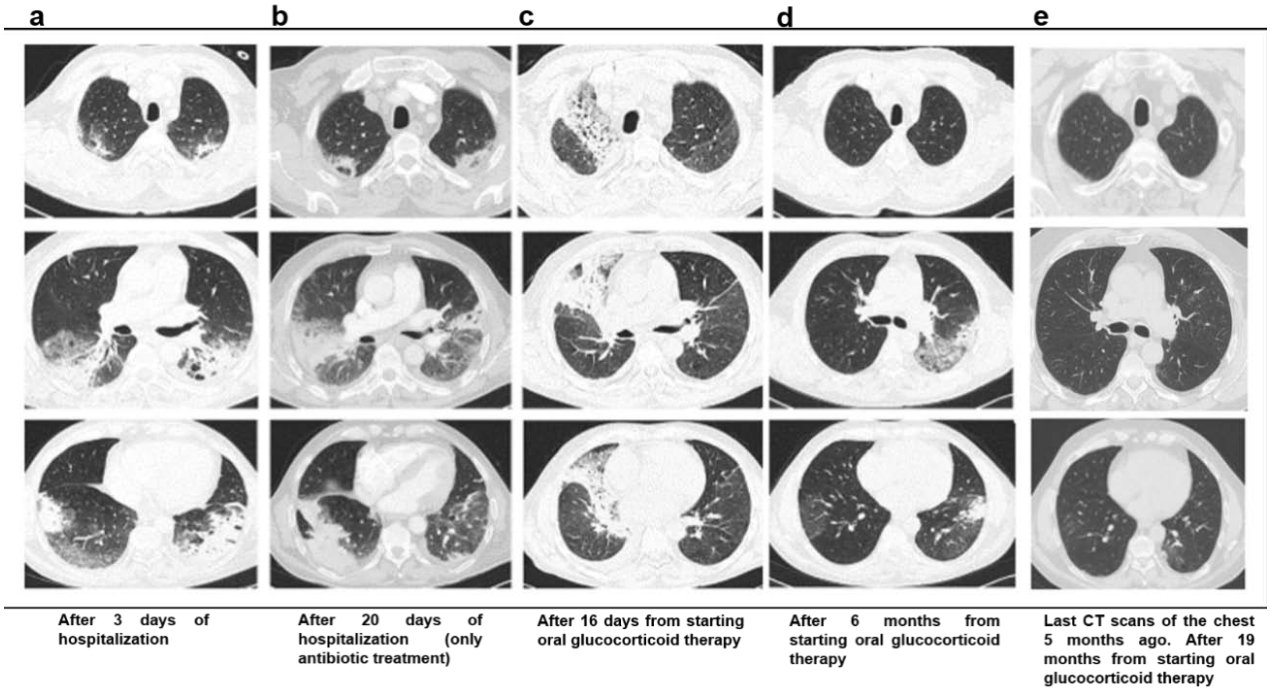
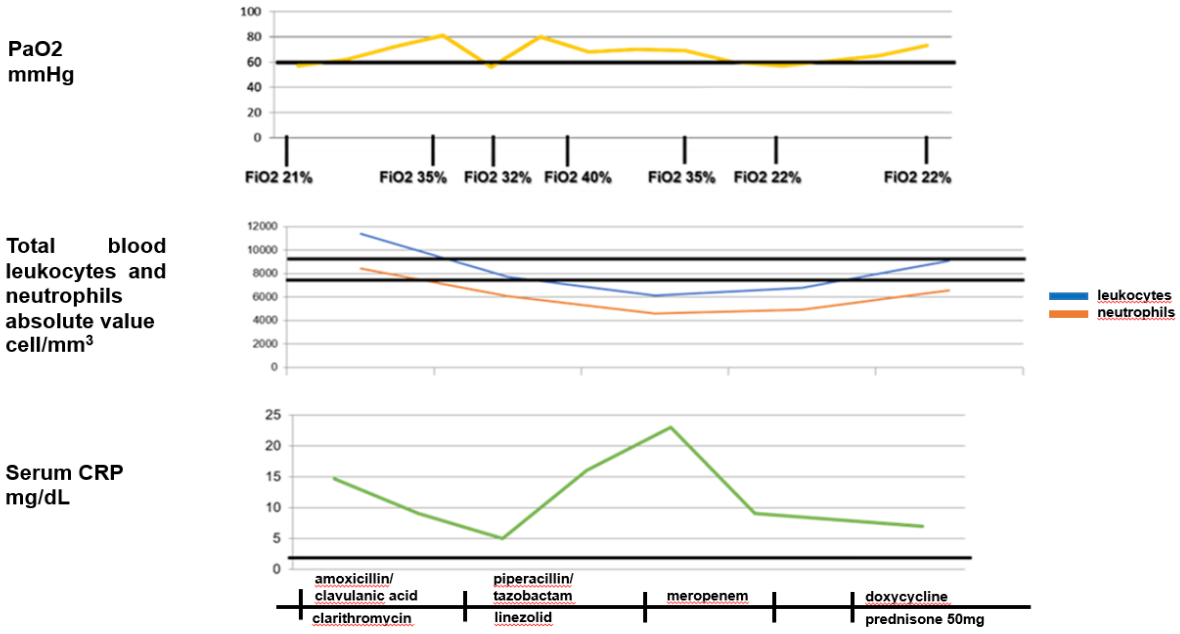


Fig.2. Trends during the hospitalization of the arterial pressure of the oxygen (PaO2), total blood leukocytes, neutrophils absolute value and serum C-reactive protein (CRP)



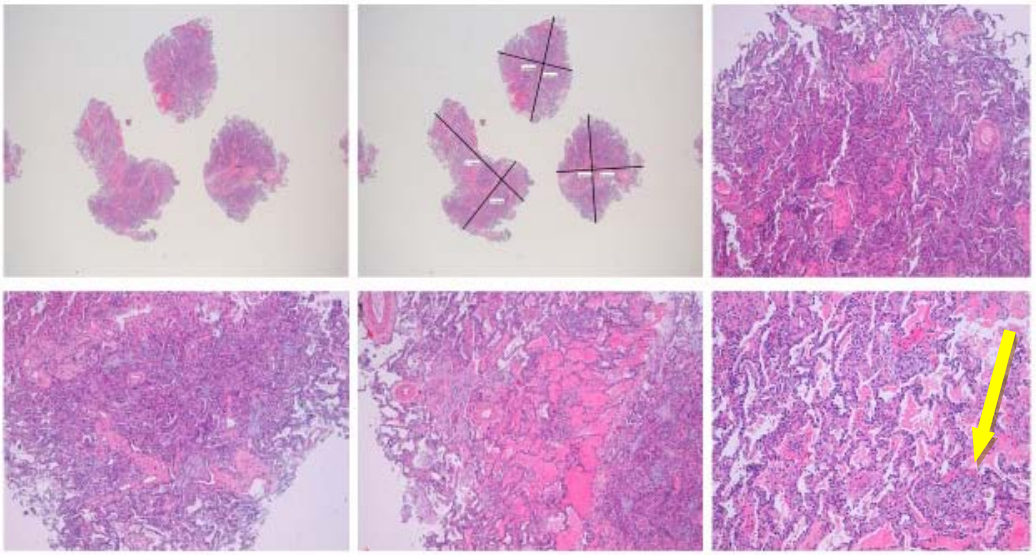
Discussion

The patient presented with non-resolving CAP despite many courses of different empiric wide spectrum antibiotic treatment and many investigations. The main causes of non-resolving pneumonia were excluded according to Infectious Disease Society of America (IDSA) guidelines (1) except OP.

The combination of autoimmune hemolysis, pleural/pericardial effusions and psychosis in a patient with ANA at a titer of 1:160 is diagnostic for systemic lupus erythematosus (SLE) according to the most recent European

League Against Rheumatism/American College of Rheumatology Classification Criteria for SLE (the total score is 12 and the value that must be reached for the diagnosis is 10) (6).

Fig.3. Transbronchial lung cryobiopsy. Images show a pattern of organizing pneumonia (arrow) and non specific interstitial pneumonia, with very rare eosinophilic granulocytes.



Acute lupic pneumonitis is a rare complication of SLE and is more common in women but in males has usually a more aggressive clinical course (7). Serum anti-dsDNA antibodies are not specific for SLE (8) and are not always present in the patients with acute lupus pneumonitis.

The lung involvement in patients with acute lupic pneumonitis is usually associated with a histopathological pattern of a combination of NSIP and OP (9,10).

Acute lupus pneumonitis is a rare SLE manifestation, reported in 1–4% of patients, often misdiagnosed, with poor prognosis. Mortality has been described as being up to 50%. Pathologic findings are neither diagnostic nor pathognomonic. Being a diagnosis of exclusion, investigations must first focus on ruling out infection, pulmonary embolism, drug-induced lung toxicity, organizing pneumonia, heart failure and malignancy. Treatment mainly consists, depending upon the type of involvement and its severity, of systemic glucocorticoid therapy, which may be combined with immunosuppressants, such as cyclophosphamide or azathioprine (11-14).

Conclusion

We presented here a case of an unusual non-resolving community-acquired pneumonia caused by an acute lupuc pneumonitis.

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Conflicts of interest: The authors declare no conflict of interest.

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