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Clinical Case Seminar CCS 1(1-7)

An unusual association in a patient with COVID-19-related ARDS and bilateral pleural effusion

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Abstract

We present the case of a 76-year-old female, previously diagnosed with pulmonary sarcoidosis, that was admitted to our Unit of Pulmonology for acute hypoxemic respiratory failure secondary to COVID-19-related acute respiratory distress syndrome (ARDS) and with bilateral pleural effusions. Despite the therapy the patient's conditions gradually deteriorated during the hospital stay with progressive hypoxemia and the patient died 36 days after the admission.

KeyWords: acute respiratory failure, sarcoidosis, pleural effusion, pneumonia

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Introduction

We present here the case of a patient with a previous diagnosis of pulmonary sarcoidosis who contracted severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and who developed acute respiratory distress syndrome (ARDS) and bilateral pleural effusions. Pleural effusion is a rare clinical presentation of both coronavirus 19 disease (COVID-19) and sarcoidosis.

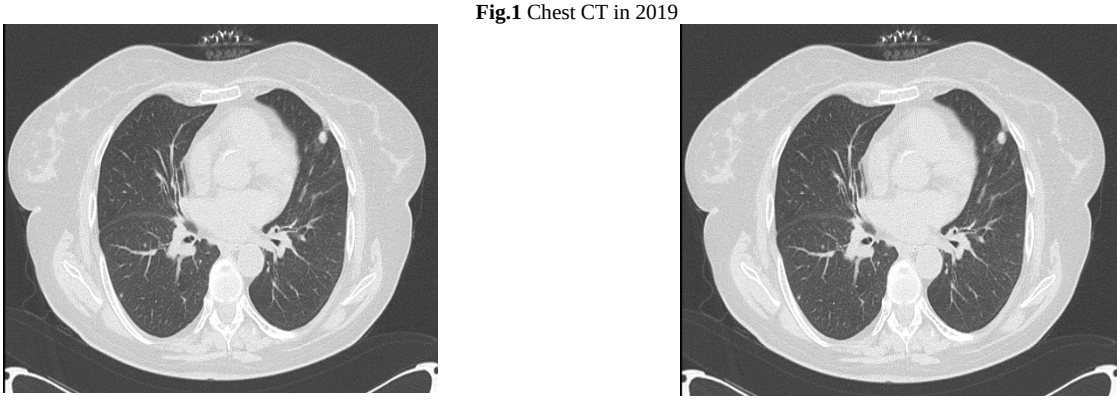
Case presentation

A 76-year-old female, housewife, lifelong non-smoking, with a medical history of systemic arterial hypertension (treated with nebivolol/hydrochlorothiazide 5/12.5 mg/daily and perindopril/amlodipine 4/10 mg/daily), diabetes mellitus (treated with metformin 500 mg/daily), hypothyroidism secondary to Hashimoto thyroiditis (treated with levothyroxine 25 µg/daily), hypercholesterolemia (treated with rosuvastatin 20 mg/daily), depressive disorder (treated with selegiline 10 mg/daily, paroxetine 20 mg/daily e mirtazapine 30 mg/daily).

The patient, in 2019, was diagnosed at the pulmonology unit of the University Hospital Gaspare Rodolico of Catania, Italy (www.policlinicorodolicosanmarco.it), with pulmonary sarcoidosis on a

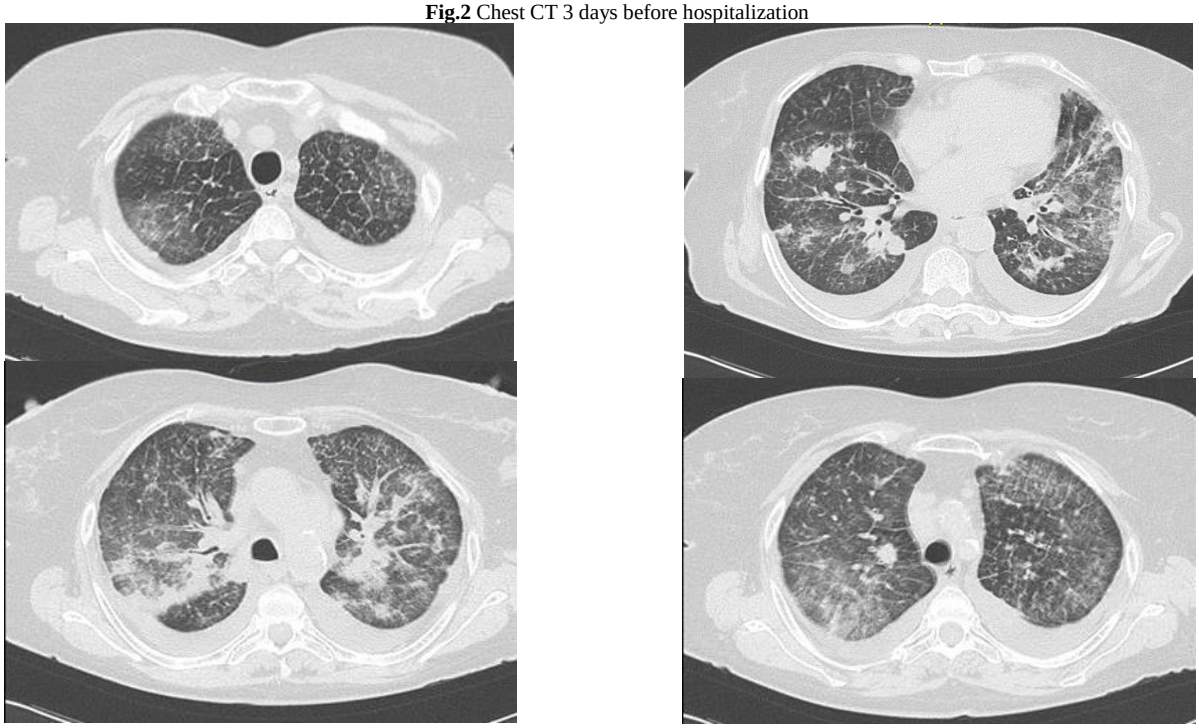
biopsy of a right lateral cervical lymph node performed for the presence of multiple pulmonary nodules on the chest computer tomography (CT) (Figure 1), but she was untreated and lost at the follow-up.

Fig.1 Chest CT in 2019



The patient has been vaccinated with 3 doses of SARS-CoV-2 mRNA vaccine (last dose in December 2021) and also reported SARS-CoV-2 infection in June 2021 with mild course without hospitalization. The 25th of June 2022 after the onset at home of dyspnea, she performed at the Hospital Villa Salus (www.casadicuravillasalus.it) of Messina, Italy, a total body (CT) that showed bilaterally, multifocal lung consolidative and ground glass opacities, multiple pulmonary nodules (largest 22 mm) and bilateral pleural effusions. Lymph nodes were enlarged, with contrast enhancement in the latero-cervical, sub-clavicular and hilar-mediastinal stations (Figure 2)

Fig.2 Chest CT 3 days before hospitalization

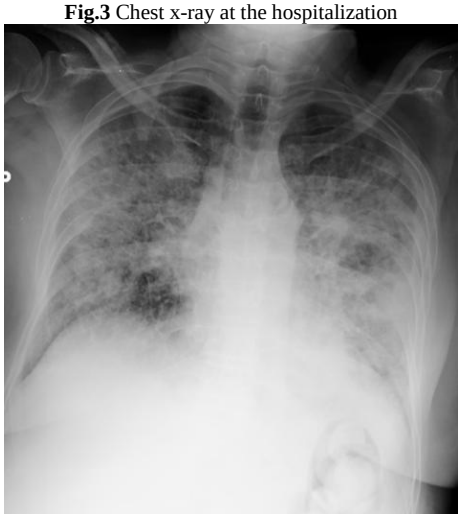


Three days later for the presence, at home, of oxygen desaturations she was admitted at the emergency room of the University Hospital Gaetano Martino of Messina, Italy (www.polime.it).

A supine chest x-ray showed the presence, bilaterally, of multifocal lung consolidative and ground

glass opacities and bilateral pleural effusions, cardiomegaly and hilar enlargement (Figure 3).

Fig.3 Chest x-ray at the hospitalization



A nasopharyngeal swab was positive for the presence of SARS-CoV-2 genome, and she was admitted to our COVID-19 Pulmonology unit.

At the admission in our ward her vital signs were systemic blood pressure 140/70 mmHg, pulse frequency 80/min rhythmic, respiratory rate 30 acts/min, body axillary temperature 36.3°C.

An arterial blood gas analysis, performed with the patient breathing oxygen with a Venturi mask at a fraction of inhaled oxygen (FiO2 31%), showed the presence of acute hypoxemic respiratory failure (Table 1).

Table 1 Arterial blood gases data during the hospitalization

DATE	pH	PaO2*	PaCO2**	HCO3-***	SaO2****	PaO2/FiO2*****	OXYGEN THERAPY
Admission	**7.45**	**72**	**39**	**27**	**95%**	**234**	**Venturi mask FiO2 31%**
4 day after	**7.46**	**69**	**36**	**26**	**95%**	**287**	**Nasal cannula FiO2 24%**
15 days after	**7.45**	**64**	**42**	**28**	**92%**	**175**	**Nasal cannula FiO2 35%**
18 days after	**7.46**	**56**	**40**	**28**	**89%**	**140**	**Venturi mask FiO2 40%**
21 days after	**7.44**	**66**	**43**	**28**	**92%**	**132**	**HFNC FiO2 50%**
25 days after	**7.42**	**60**	**42**	**27**	**90%**	**158**	**HFNC FiO2 40%**
29 days after	**7.45**	**65**	**41**	**28**	**93%**	**130**	**HFNC FiO2 50%**
32 days after	**7.40**	**84**	**32**	**21**	**93%**	**121**	**HFNC FiO2 70%**

***PaO2: partial pressure of oxygen**
****PaCO2: partial pressure of carbon dioxide**
*****HCO3-: sodium bicarbonate**
******SaO2: oxygen saturation in the arterial blood**
*******FiO2: fraction of inhaled oxygen**
[§]HFNC: high-flow nasal cannula

Physical examination revealed in the chest a severe reduction of the vesicular sounds in the middle-basal lung fields bilaterally with the concomitant presence of crackles, in the same locations. Presence of bilateral palpable lymphadenomegaly in the lateral-cervical and supra-clavicular areas, mobile in the

superficial and deep planes, not painful. The remaining physical examination was normal. Laboratory data at the admission and during her hospital stay are shown in Table 2.

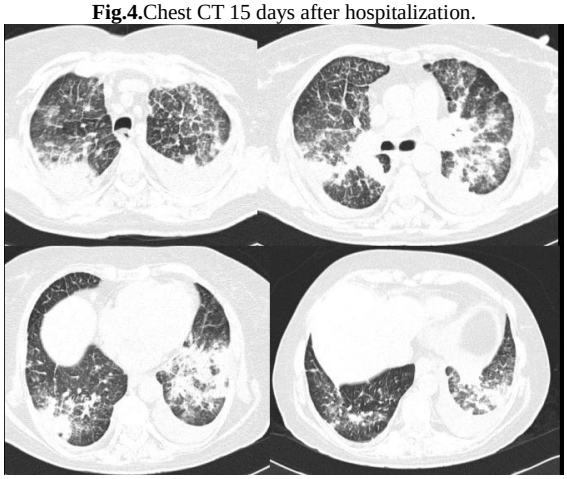
Table 2 Pathological laboratory data at the admission and during the hospital stay.

LABORATORY DATA	VALUE 28/06	VALUE 28/07	NORMAL VALUES
Erythrocytes (cell/mm3)	**3920000**	**3980000**	**4500000-5500000**
Hemoglobin (g/dL)	**11.2**	**11.6**	**13.5 - 18**
Total leukocytes (cell/mm^3)	**10700**	**12500**	**4500 - 9000**
Neutrophils (cell/mm^3)	**9200**	**10050**	**1500 - 7700**
Lymphocytes (cell/mm^3)	**856**	**700**	**1500 - 3500**
Serum CRP[§] (mg/dL)	**0.89**	**12.50**	**0 - 0.50**
Serum D-dimer (µg/mL)	**1.038**	**1335**	**0 - 0.50**
Serum NT-proBNP (pg/mL)	**272**	**865**	**0 - 125**
Creatinine clearance (mL/min)	**53**	**53**	
Serum calcium (mg/dL)	**10.04**	**12.60**	**8.02 – 10.04**
Serum CA125 (U/mL)	**288**		**0 - 35**
Serum CA15.3 (U/mL)	**59.6**		**0 - 35**

***MCV: mean cell volume**
****MCH: mean cell hemoglobin concentration**
[§] CRP: C-reactive protein

Oxygen therapy was started with different modalities (Table 1), together with dexamethasone (6 mg/daily intravenous for 10 days), enoxaparin (4000 IU/daily subcutaneous) and pantoprazole (40 mg/daily per os). After 6 days of hospital stay has been started piperacillin/tazobactam (4.5 g IV every 6 hours) for an increase of the inflammatory indices and neutrophilic leukocytosis. After 25 days of hospital stay a rheumatological consultant added intravenous methylprednisolone 40 mg/daily. After 15 days from the admission, a chest CT was performed showing, compared to the previous one, increased number of the multi focal lung consolidative and ground glass opacities, especially in the lower left lung lobe, reabsorbed right pleural effusion whereas the left pleural effusion persisted (Figure 4)

Fig.4. Chest CT 15 days after hospitalization.

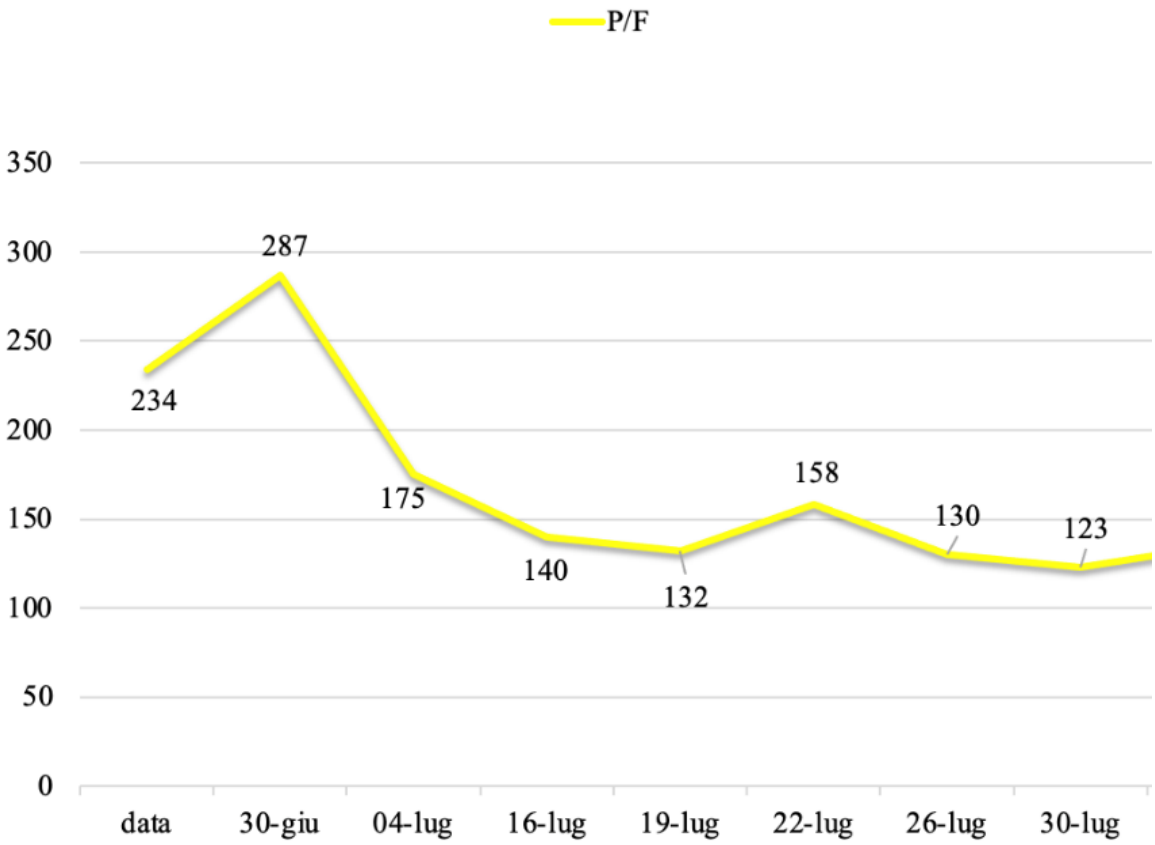


After 20 days from the admission the patient developed high-frequency paroxysmal atrial fibrillation treated with amiodarone.

After 30 days from the admission the patient performed an echocardiography that demonstrated the presence of pulmonary arterial hypertension (60 mmHg), hypertrophy of the left ventricle but with preserved left ejection fraction (60%).

The clinical course has been complicated by progressive worsening of the hypoxemia (Figure 5)

Fig.5 P/F trend.



The patient refused the non-invasive ventilation (NIV) and the transfer to the intensive care unit. After 36 days from the admission the patient deceased.

Discussion

This case report is unusual for many reasons. For example, the prognostic role of sarcoidosis and its different immunosuppressive therapies during COVID-19 is still unknown, however there is some evidence that these patients may have a significant burden of hospitalization with high lethality (1).

In addition, the onset of pleural effusion, particularly bilaterally, in both COVID-19 pneumonia and sarcoidosis is quite unusual in patients without co-morbidities, like heart failure and chronic renal failure, that by themselves may cause pleural effusions (2,3,4).

Our patient had biomarkers (increased serum NT-proBNP levels) of heart failure with preserved left ventricular (LV) ejection fraction, despite the decreased creatinine clearance (53 ml/min) may have

contributed to raise her serum NT-proBNP levels. Furthermore, in patients with sarcoidosis there is a high incidence of pulmonary arterial hypertension, which is linked with exercise limitation and a worse prognosis and there is a significant correlation between BNP level and pulmonary hypertension severity (5, 6). Myocardial lesions of cardiac sarcoidosis may be associated to both LV dysfunction and/or increased BNP level (7-9). Serum levels of carbohydrate antigen (CA) 125 and CA15-3 were increased at the admission, and both biomarkers may represent lung damage induced by COVID-19 and/or sarcoidosis (10-13).

Our patient at the admission had also hypercalcemia, that is sometimes observed in patients with sarcoidosis or other granulomatous lung diseases, including tuberculosis (14, 15).

In summary, it is difficult to understand the cause of the progressive clinical deterioration of our patient but there are likely several contributing diseases, including severe COVID-19, sarcoidosis and heart failure.

Conclusion

Although there are scarce data on the correlation between sarcoidosis and COVID-19 severity, our case report suggest that sarcoidosis can be associated with an increased risk of hospitalization with high lethality in COVID-19 patients. Moreover, pleural effusions, as in our unusual case, are a rare complication of both sarcoidosis and COVID-19.

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

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