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Case Report

Can Lung Ultrasound in Patients with Fever of Unknown Origin Detect Early Signs of COVID-19 Pneumonia?

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2. Key words

Lung Ultrasound (LUS); Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2); Coronavirus Disease 2019 (COVID-19); Pneumonia; Acute Respiratory Distress Syndrome (ARDS)

1. Abstract

The increasing interest in Lung Ultrasound (LUS) over the last years led to a great diffusion and better experience in using this technique, which became an essential tool for clinicians. During the current Coronavirus Disease 2019 (COVID-19) pandemic, LUS is being extensively applied to the evaluation and monitoring of lung damage in infected patients, improving their management in various clinical settings.

In this case report we describe the detection of very early ultrasonographic signs of lung involvement in a patient who presented no clinical signs of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) pneumonia, but who developed respiratory symptoms and tested positive for SARS-CoV-2 infection 22 days later.

This raises questions about the use of LUS to detect and monitor very early signs of lung disease in paucisymptomatic patients with low clinical suspicion of COVID-19.

Moreover, interesting questions are raised regarding the use of LUS as a means to consistently observe the timing of lung disease evolution, which to this day remains unknown.

3. Introduction

Over the last few years, Lung Ultrasound (LUS) has developed considerably as an important tool for clinical evaluation and monitoring in various clinical settings: from daily clinical practice in Emergency Departments and Internal Medicine Wards, with patients presenting pulmonary symptoms and clinical signs, to patients with Acute Respiratory Distress Syndrome (ARDS) in Intensive Care Units (ICU) [1,2].

Several studies have described the ultrasonographic patterns that reflect the alterations in lung parenchyma when it is affected by pathological conditions that change its constitutional air- predominant structure [3-6].

The recent outbreak of Severe acute respiratory syndrome coronavirus 2(SARS-CoV-2) epidemic – emerged in December 2019 in Wuhan, China [7], and rapidly spread throughout the world to become pandemic, with pneumonia and respiratory failure as its main clinical features, provoked a debate in the scientific community about the potential role of LUS in the management of patients with Coronavirus disease 2019 (COVID-19) [8,9].

Various authors have described how LUS can be even more informative than traditional Chest Radiography (CXR), and how this technique can provide important information about COVID-19 pneumonia [10, 11]. These patients present a wide range of ultrasonographic patterns, such as the thickening of the pleural line with pleural irregularity; the variation of B-lines patterns including focal, multifocal and confluent (white lung); and parenchymal consolidations. More complex and progressively worsening ultrasonographic findings are described in patients with severe and deteriorating lung involvement – suggesting a potential keyrole of LUS as a tool for close monitoring in these patients- with strong correlation with Chest CT findings [11].

4. Case Report

On March 15, 2020, while hospitalized, a 41-year-old woman was referred to theUltrasound Centre in the Medical Department of Maggiore Hospital, Bologna, for abdomen ultrasound.

She presented to our hospital's emergency department on March 10, 2020 having run a low-grade fever [37.8°C] for five days, accompanied by headache and two episodes of involuntary movement of her right extremities, followed by loss of contact with the environment.

She was an obese patient with a clinical history of childhood febrile convulsions, for which she had been treated pharmacologically.

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Entering adulthood, she suspended anti-epileptic therapy with no report of further seizures.

Brain CT and Magnetic Resonance Imaging (MRI) showed normal findings. The electroencephalogram (EEG) showed epileptiform abnormalities with generalised aspect. Laboratory tests showed slight microcytic anaemia(10.5 g/dl, MCV 77 fL, MCHC 25.7 pg/dl) and neutrophilic leucocytosis (12000/mmc, N 83%), with a serum C-reactive Protein (CRP) of 1.46 mg/dl and a negative value of serum procalcitonin. Anti-nuclear antigen (ANA) and Rheumatoid Factor test were negative; thyroid function was normal. Blood and urine cultures were negative. A CXR showed no abnormal findings. The abdomen ultrasound, aimed at identifying a possible source of infection, showed no abnormalities.

Considering the clinical history of fever with negative CXR as well as the recent COVID-19 outbreak in Italy, the ultrasonographic exam was then extended to the patient's lungs. The exam was performed by dividing each hemithorax into six regions (two anterior, two lateral, two posterior), as described in previous literature [12].

LUS documented slight/moderate B-lines in the left lung lower area, with a mild irregular thickening of the pleural line, associated with minimal pleural effusion (Figure 1).

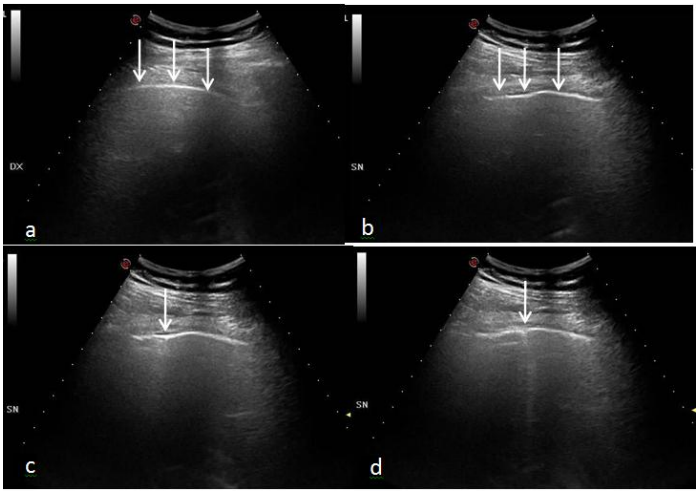

Figure 1: LUS a) regular pleural line in the right lung; b) thickening of the pleural line in the lower area of the left lung; c) irregular thickening of the pleural line in the lower area of the left lung d) irregular thickening of the pleural line in the lower area of the left lung associated with B-lines (white arrows)

In line with the criteria initially adopted to identify high-risk patients for SARS-CoV-2 infection, however, no nasopharyngeal swab SARS-CoV-2 PCR test was performed, due to the patient's lack of recent travel to or contact with people coming from high-risk areas. Chest CT was performed and showed no pathological findings (Figure 2).

The neurologist interpreted it as a case as seizures during fever of unknown origin. The patient was treated with lamotrigine and benzodiazepine, and was discharged from the hospital eight days-later with a referral for a Positron Emission Tomography (PET).

Fifteen days after hospital discharge, the patient returned to the Emergency Department presenting persistent fever [38.2°C], occasional cough and asthenia. Laboratory tests showed a normal white blood cell count (WBC 4900/mmc) with slight lymphocytopenia (980/mmc) and low eosinophilic count (0.01/mmc), elevated serum CRP (8.4 mg/dl), serum Interleukin-6 (IL-6)(19 pg/ml - n.v< 5.9 pg/ml) and D-dimer (1.64 mcg/ml). Serum procalcitonin was normal. The search for urinary antigens of Legionella pneumophila and Streptococcus pneumoniae proved negative. The arterial blood hemogasanalysis revealed mild hypoxemia with P/F Ratio of 314. The Chest CT showed ground-glass opacities in the upper and medium areas of the right lung as well as consolidation in the lower area of the left lung (Figure 3). A nasopharyngeal swab SARS-CoV-2 PCR test was performed and resulted positive. The patient was then referred to the COVID-19 Unit to receive appropriate care and was discharged ten days later showing improvement in both her clinical picture and laboratory results.

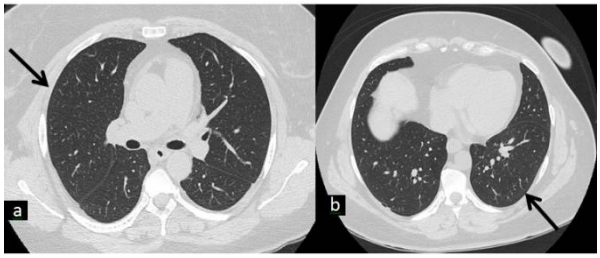

Figure 2: HRCT of the chest performed during the first hospitalization, which showed no abnormal findings both in the right (a) and in the left lung (b)

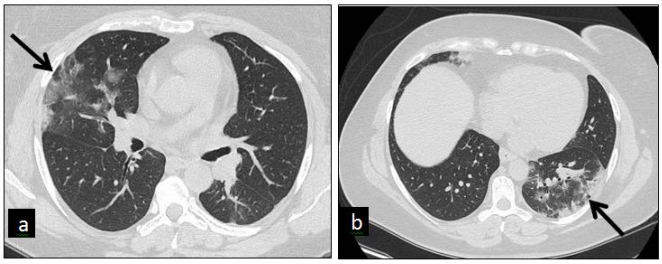

Figure 3: HRCT of the chest performed during the second hospitalization, which shows ground-glass opacities in the upper area of the right lung (a) and consolidation in the lower area of the left lung (b) (black arrows)

5. Discussion

SARS-CoV-2 is a new pathogenic virus for the human species. Thorough studies are needed to come to a better understanding of its natural history and the precise timing of its interaction with a human host. Important information, albeit not quite sufficient, is provided by the extensive studies conducted on its pathogenetic mechanism, which is related to some extent to cytokine release syndrome (CRS)-induced ARDS[13]. Whereas some infected people remain completely asymptomatic, others show mild and nonspecific symptomsonly [14, 15], while some patients develop a severe disease [16], which is mainly related to pneumonia and respiratory failure and sometimes leads to ARDS through CRS and diffuse alveolar damage [17].

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More data are needed on all levels - biological, anatomic-pathological and epidemiological. In the case in point, the Chest CT performed during the second hospitalization showed ground-glass opacities in the right lung and a parenchymal consolidation in the inferior area of the left lung.

Ground-glass opacities can be considered earlier findings of COVID-19 than parenchymal consolidations, that are likely to be a subsequent expression of lung damage [18].

A comparison between LUS and CT imaging showed a strict correspondence between the site of parenchymal consolidation shown by CT imaging and the site where the ultrasonographic examination had shown pleural thickening and significant interstitial involvement with B-lines.

What happened between the moment when LUS was performed and the second CT imaging that showed COVID-19 interstitial pneumonia? According to the literature, the SARS-CoV-2 infection could have evolved with different pathogenetic mechanisms and timing in lung parenchyma damage, leading to the clinical manifestations that we observed 22 days later. Finally, we suggest that LUS findings may have been an expression of early lung damage and we therefore assume that, in the case of patients with non-specific symptoms and with in the current epidemiological context, LUS could be used to detect very early features of lung damage .

6. Conclusion

The widespread use and knowledge of LUS in recent years has turned it into an essential tool for clinicians. Initially developed in emergency and critical care settings, its importance has increasingly grown within internal medicine wards. During the current COVID-19 pandemic, LUS is being extensively applied to the evaluation and monitoring of lung damage in infected patients, leading to a significant improvement in the management of patients when integrated into the clinical context.

Considering that clinical manifestations in SARS-CoV-2 infections can vary and that parenchymal damage in lung involvement can be incremental and progressive, we suggest that LUS could detect very early signs of lung disease in paucisymptomatic patients, and serve as an alert to increase the attention threshold and the clinical mon- itoring in such patients.

Furthermore, interesting questions are raised regarding the use of LUS as a means to consistently study the timing of lung disease evolution, which to this day remains unknown.

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