CT patterns and differential criteria for acute eosinophilic pneumonia and COVID-19 pneumonia

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1 INTRODUCTION

Laboratory data, computed tomography semiotics, and clinical currents in acute eosinophilic pneumonia and coronavirus disease pneumonia cases were examined. Disease dynamics, literature analyses, and differential signs were observed. Acute eosinophilic pneumonia should be suspected when coronavirus disease pneumonia patients experience recurrence or worsening symptoms; early glucocorticoid therapy prevents further complications. The coronavirus disease 2019 (COVID-19) outbreak began in Wuhan, China, in mid-December 2019, rapidly spreading worldwide to become a global pandemic.1,2 In particular, the disease’s main presentation is COVID-19 pneumonia, which is often described as bilateral interstitial pneumonia that is not amenable to standard treatment, with an increased risk for respiratory failure and development of acute respiratory distress syndrome (ARDS).3

On the contrary, acute eosinophilic pneumonia (AEP) presents as an acute respiratory illness that
appears within days or weeks and can develop into ARDS, with potential progression to death. Moreover, it can be idiopathic or secondary to inhalational toxic substances, drugs, or infections. Given the current pandemic situation, diagnosing AEP has become even more challenging, since its clinical picture might resemble that of COVID-19 pneumonia. As such, laboratory tests and anamnesis are crucial for ensuring a correct differential diagnosis. A CT scan is also particularly important in narrowing down the differential diagnosis and avoiding misdiagnosis. In some cases, patients recover quickly—within a few days after the initiation of steroidal treatment.

Currently, the standard diagnostic method for COVID-19 is reverse-transcription polymerase chain reaction (RT-PCR), with an estimated sensitivity of 60%–71%, which is probably due to sampling errors, specimen type, and viral load at the time of examination.

In addition, chest computed tomography (CCT) reveals pulmonary abnormalities in COVID-19 patients, even in those with a false-negative RT-PCR in the early stages of the disease. Furthermore, CCT can also identify features compatible with COVID-19 pneumonia in asymptomatic patients undergoing CCT for other reasons, in the setting of community transmission.

CCT has a sensitivity of approximately 94%–97% in detecting early signs of COVID-19 pneumonia, disease progression, complications, and possible alternative diagnoses, including heart failure or pulmonary embolism. However, it has a low specificity of approximately 37%, since many lung diseases can mimic the CCT findings of COVID-19 pneumonia.

Herein, two clinical cases of AEP and COVID-19 are presented, along with examination of their laboratory data, CCT semiotics, and clinical currents. In the course of therapy, disease dynamics, literature analyses, and differential signs of the two conditions were observed, including previously examined parameters and treatment approaches.

2 | CASE PRESENTATION

2.1 | Case report 1

A 46-year-old female patient was diagnosed with COVID-19, with a positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RT-PCR result, and was subsequently administered antibacterial and symptomatic therapies. On the 6th day of her illness, the patient was admitted to a hospital. Although her CT scan showed acute negative findings, clinical signs of respiratory failure had increased (Figure 1). On the 17th day of illness (July 10, 2020), her CT scan showed ground-glass opacities (GGO) (Figure 2), and on the 24th day of illness (July 17, 2020), more intense polysegmented sections in the subpleural regions were observed on CT (Figure 3). On the 65th day of illness, the patient recovered clinically; however, trace morphological changes in the left lung were observed in the form of parenchymal sclerosis (Figure 4). Furthermore, the pathological focus was redirected to GGO with the formation of gentle fibrous tissue (Figure 5). CT semiotics followed the order “GGO–consolidation–GGO–fibrosis,” and blood tests revealed no abnormalities. In addition, serological responses, particularly SARS-CoV-2 RT-PCR, were positive.

2.2 | Case report 2

A 35-year-old female patient with right breast cancer underwent lumpectomy and chemotherapy in July 2020. In December 2020, she presented with shortness of breath, cough, symptoms of intoxication, and progressive deterioration of her general condition. Bacterial cultures and bacilloscopy of bronchoalveolar lavage, bronchial aspirate, and biopsy specimens were all negative. Initially, the patient was suspected to have COVID-19, and despite her negative SARS-CoV-2 RT-PCR, she was treated for

**FIGURE 1** Minimal changes in the chest CT: the CT scan shows arrowed bilateral small ground-glass opacity (GGO) lesions
COVID-19. Measures taken did not yield positive results, and her serological reactions to SARS-CoV-2 were negative. Notably, eosinophilia (2640 mm$^3$) was observed on a blood test, and routine screening of the chest was conducted to prevent metastatic cancer spread.

The patient’s general condition deteriorated with worsening respiratory symptoms, including shortness of breath, cough, and symptoms of intoxication. Her CT scans showed normal pulmonary parenchyma (Figure 6), and one-sided lesions were localized in the upper and middle lobes of the right lung, which were characteristic of inflammatory spots (Figure 7). Moreover, lobar segments of the foci locations were noticeable. The patient’s laboratory results were within normal limits, except for eosinophilia and mild elevation in ferritin, interleukin-6, and C-reactive protein levels. Analysis of routine blood tests that she had undergone from August to December revealed linear increment in eosinophil levels (Graph 1). When symptoms of respiratory failure began, eosinophil growth was observed to have already reached very high values (28.78%). After the eosinophils reached their maximum value in the peripheral blood

**FIGURE 2**  The CT scans show multiple bilateral subpleural GGO fused into larger areas

**FIGURE 3**  The CT scans show that previously recorded foci had consolidated, decreased in size, and increased in density

**FIGURE 4**  The CT scans show a further regression in the symptoms: the inflammatory spots are limited, there are interstitial changes, and presence of intense, bright linear shadows (interlobular thickening)
and after comparing them with reference to clinical and CT semiotics, a decision was made to replace her management with glucocorticoids, since these changes were characteristic manifestations of eosinophilic pneumonia. After the change in treatment strategy, the response rate toward glucocorticosteroids was evaluated. Figure 8 suggests that morphological changes in the parenchyma had regressed, indicating that the steroids used were successful. Graph 2 also shows the same elevation in eosinophils, and their decline to normal levels after reaching a maximum number owing to the change in therapy. Laboratory data proved the effectiveness of glucocorticoid therapy and confirmed the diagnosis of eosinophilic pneumonia.

3 | DISCUSSION

Regarding the possible etiologies of AEP in the second case, SARS-CoV-2 was suggested as a first differential. During admission, the patient’s worsening pulmonary infiltrates resembled the inflammatory phase of COVID-19, but her RT-PCR results were negative. Previous histopathological studies of COVID-19 pneumonia have not reported the presence of eosinophils, and the role of pulmonary eosinophilia was not relevant in the physiopathology of COVID-19.\textsuperscript{18-20}

Therefore, we suggested that our second case was a rare AEP differentiated from typical COVID-19. Although parasites and fungi are the most frequently associated
infectious agents with AEP, other viruses, including influenza A H1N1, have been reported to be implicated. However, no such association has been made with respect to SARS-CoV-2.\textsuperscript{21,22}

Other potential causes of AEP may be related to the treatment that our patient had received. A few cases of drug-induced eosinophilic pneumonia associated with azithromycin and chloroquine intake have been reported.\textsuperscript{23,24}

Although the clinical manifestations of these two diseases are similar, based on the aforementioned observations and literature analysis, a number of differential features between the two conditions can be distinguished. They are comprise the following criteria: laboratory

**Figure 8** CT scans show that the inflammatory focus decreased markedly in size and increased in density

**Graph 1** The patient's blood tests showed a slight increase in eosinophils (percentage)

**Graph 2** The status of eosinophils before and after therapy
In order to diagnose COVID-19 accurately, models, such as a novel attention network for COVID-19 (ANC) and CCSHNet, are helpful. An assessment of both models revealed that the ANC model results were better than those of 9 state-of-the-art approaches and, similarly, CCSHNet showed the best performance when compared to 12 state-of-the-art approaches. Furthermore, CCSHNet could potentially aid radiologists in making more accurate, quicker COVID-19 diagnoses using CCTs. However, there are noticeable disadvantages to both models, including their utility with only small datasets, inability to handle heterogeneous data, and their lack of strict clinical verification. Therefore, datasets should be expanded together with strict clinical verification in both ANC and CCSHNet models to make more potential and accurate diagnostic models.

Generally, treatment tactics, dynamics, and outcomes of a disease depend directly on the differentiation of pneumonia, as each condition has unique etiological and pathological peculiarities. It should be noted, however, that the conclusions in this case report were drawn from only two clinical cases and from an analysis of existing literature. Thus, there is need for further larger studies to validate these findings. Nevertheless, AEP should be suspected when patients with COVID-19 pneumonia experience recurrence or worsening of symptoms; early administration of glucocorticoid therapy would avoid further complications.

**CONFLICTS OF INTEREST**
The authors declare no conflicts of interest.

**AUTHOR CONTRIBUTIONS**
Aliya Kadyrova involved in conception, design of the work, manuscript preparation, and data acquisition. Irina Antipina involved in design of the work, manuscript preparation, and data acquisition. Indira Kyrbasheva involved in conception, manuscript preparation, and data acquisition. Iliar Baudinov involved in design of the work, manuscript preparation, and data acquisition. Begaim Kulbaeva involved in design of the work, manuscript preparation, and data acquisition. Uuljan Aitieva involved in manuscript preparation and data acquisition. Cholponbek Zhunushaliev involved in manuscript preparation and data acquisition. Yethindra Vityala involved in manuscript preparation and data acquisition. Tugolbai Tagaev involved in manuscript preparation and data acquisition.

**ETHICAL APPROVAL**
The patient gave her informed consent prior to her inclusion in the study.

**CONSENT**
Published with written consent of the both patients.

**DATA AVAILABILITY STATEMENT**
Data are available from the corresponding author upon reasonable request.

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