

COVID 19 with false negative RT-PCR test in 4 patients: When Chest CT becomes a need.

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DOI: 10.29322/IJSRP.10.06.2020.p10284
<http://dx.doi.org/10.29322/IJSRP.10.06.2020.p10284>

Abstract- Objectives: To describe CT imaging features of 4 patients with initial negative RT-PCR results but high suspicion of COVID-19 infection.

Materiel and methods: Retrospective study including patients with COVID-19 pneumonia who underwent both CT and RT-PCR at initial presentation in our institution From March 31th, 2020 to april 27th.The results of both tests were compared. For patients with a final confirmed diagnosis ,clinical , laboratory data and CT imaging findings were evaluated.

Results: From 142 laboratory confirmed cases, a total of four patients had an initial negative RT PCR and positive CT findings . 3 patients were diagnosed in early stage (1-5days) and one in progressive stage (5-8 days).

The 4 patients had typical imaging findings, including ground-glass opacity (GGO) (2 patients) ,crazy paving (1 patient),mixed GGO and crazy paving (1 patient) .All the patients were isolated After for presumed 2019-nCoV pneumonia and they were eventually confirmed with 2019-nCoV infection by repeated swab tests.

Conclusion: rRT-PCR may produce false- negative results in the early stages of the disease mostly. We therefore suggest that CT features could be utilized as the immediate reference to screen the highly suspected cases and to take necessary actions, while rRT-PCR serves as a confirmation tool to decide the subsequent action of continuing isolated treatment or discharge.

Key points:

- Typical radiological presentation with high clinical suspicion of 2019-nCov infection should be considered even do negative RT-PCR results .
- In these cases,repeat swab testing and patient isolation should be applicable.

Index Terms- Pneumonia, Tomography ,Coronavirus,disease

I. INTRODUCTION

In December 2019, an outbreak of 2019-nCoV pneumonia began in Wuhan (Hubei, China) and spread rapidly(1). Definite diagnosis relies on real-time reverse-transcriptase- polymerase chain reaction (rRT-PCR) positivity for the presence of coronavirus [2,3]. Because of the strong infectivity of COVID-19, rapid and accurate diagnostic methods are urgently required to identify, isolate and treat the patients as soon as possible needed to reduce the risk of public contamination. However, the

sensitivity to detect COVID-19 of real time (RT)-PCR is reported to be lower than that of chest CT;We report here four false negative results of (rRT-PCR) with typical chest CT findings of covid 19 to discuss complementary of the two techniques .

II. RESEARCH ELABORATION

This study was approved by the Ethics Committee of our institution. Signed informed consent was obtained.

Type of study:

A retrospective study carried out in our institution From March 31th, 2020 to april 27th.

Participants:

Inclusion criteria were as follows:

- 1- Patients with a fever and COVID-19 pneumonia suspicion.
- 2-who underwent both thin-section CT of the chest and rRT-PCR examinations in our institution on the same day.

Exclusion criteria: Patients who had performed initial RT – PCR and /or chest CT in another institution, transferred to another hospital or lost to follow-up.

Laboratory confirmed 2019-n Cov patients in the database of the department of radiology of our institution were collected .Diagnosis of covid 19 was determined according to following three methods:isolation of 2019 ncov or at least 2 positive results by RT-PCR assay fo 2019-nCov or a genetic sequence that matches 2019 –nCov.

Available clinical history; laboratory and epidemic characteristic were collected. All patients underwent CT scanning on the same day when initial nasopharyngeal swab test was performed.

Image interpretation:

Examinations were performed on a 64-section scanner. Images were reconstructed with a 1,25 mm slice thickness, using a high frequency reconstruction algorithm. Acquisitions were performed during a deep inspiration breath-hold, without contrast administration.

Radiology Team, retrospectively reviewed all chest CT images and resolved discrepancies by consensus.

Both lung (width, 1500 HU; level, –700 HU) and mediastinal (width, 350 HU; level, 40 HU) settings were viewed for all images .

Different patterns were analyzed ground-glass opacities (GGO), consolidation, mixed GGO and consolidation, traction bronchiectasis, bronchial wall thickening, reticulation, subpleural bands, vascular enlargement and lesion distribution. The detailed definitions of the above features were as described in (6).

Corads system ,CT involvement score (CT severity score)and CT staging of the infection were also analyzed using”radiology assistant platform (11).

III. RESULTS AND FINDINGS

From 142 laboratory confirmed cases ,a total of four patients (All women; age range :48-60 years) had an initial negative RT PCR and positive CT findings. (Fig 1)

After positive CT findings ,all patients were isolated for presumed 2019-nCov pneumonia. Repeat rRT-PCR tests was performed in all patients.

In 8 patients, CT was initially negative while RT-PCR was positive. In 130 patients both Rt-PCR and CT were concordant for covid 19.

Of the four patients with negative RT-PCR and positive CT at initial presentation ,the highest CT involvement score was 26%-49% while the minimum was < 5% .

In our four patients both CT scan and initial RT-PCR were performed between 4 and 5days after symptom onset.

Ground glass opacities (GGO) were found in 2 patients, crazy paving (1 patient), mixed GGO and crazy paving in 1 patient.

3 patients were diagnosed in early stage(1-5days) and one in progressive stage (5-8 days).

Corads 4 was found in three patients and corads 5 in one case.

The description of 4 patients with positive CT and negative RT-PCR results are presented below (Table 1),figures 2,3,4,5.

IV. DISCUSSION

Reverse-transcription polymerase chain reaction (RT-PCR) is the gold standard diagnostic method. False-negative results could delay the prevention and control of the epidemic, especially when this test plays a key reference role in deciding the necessity for continued isolated medical observation or discharge(4).Regarding underlying reasons for false-negative rRT-PCR results, a previous published study supposed that insufficient viral specimens and laboratory error might be the cause (5).

We suggest from our study that infection phase might influence the rRT-PCR test accuracy .

Recent studies have shown that chest CT findings could be present even before the onset of symptoms with high sensitivity (98%) in COVID-19 patients with false negative RT-PCR results, and it shows a great importance in early diagnosis (9,10).

In our four patients, we found that the CT diagnosis was made in early(3patients) or progressive stage (1 patient) of the disease .

We have to notice that all patients have shown mild to moderate clinical manifestations concordant with CT severity score of all of them.

These findings support the fact that chest CT is performant for diagnosis of covid 19 in early phases (1-5days).

In our study the most common chest CT finding is GGO in 3 patients with lower lobe involvement in all of them.

Wich is compatible with most of the previous radiological studies (10,12).

False-negative rRT-PCR results were seen in many hospitals. By Collecting data at our hospital from march 21 to April 23, 2020, four out of 142 patients false negative cases shown by the rRT-PCR test were finally confirmed to be positive for COVID-19, yielding an approximately 2,8% false-negative rate of rRT-PCR.

A new diagnostic type called “Clinical diagnosis” was set according to the presence of pneumonia on chest CT, regardless of rRT-PCR results(5). To some extent, CT features and rRT-PCR results were complimentary in the diagnosis of COVID-19 (4).

In conclusion and according to this clinical perspective, CT features could be utilized as the first and immediate reference to screen the highly suspected cases and to take necessary actions while rRT-PCR serves as a confirmation tool, the results of which could be utilized later to decide the subsequent action of continuing isolated treatment or discharge.

This study had some limitations mainly the sample size of this study was small .Larger sample sizes are therefore required for further verification.

V. CONCLUSION

According to this clinical perspective, CT features could be utilized as the first and immediate reference to screen the highly suspected cases and to take necessary actions while rRT-PCR serves as a confirmation tool, the results of which could be utilized later to decide the subsequent action of continuing isolated treatment or discharge.

This study had some limitations mainly the sample size of this study was small .Larger sample sizes are therefore required for further verification.

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Patients	1	2	2	4
<u>AGE AND GENDER</u>	54 years old female	48 years old female	50 years old female	A 60-year-old female
<u>EXPOSURE HISTORY</u>	Recent Travel to Epidemic zone (FRANCE)	Direct contact with Infected Patient(sister)	Recent travel history to ITALY during the 2019-nCoV outbreak	Direct contact with Her husband who had been previously Diagnosed 2019-nCov.
<u>SYMPTOMS</u>	Fever with a body temperature of 38.5°C. Mild cough of 5 days duration.	Fever Dry throat and difficulty breathing during 4 days.	Dry cough with no fever of 5 days duration	Fever Loss of appetite for 5days
<u>RT-PCR TESTING</u>	A negative result for SARS-CoV-2 was found in the first rRT-PCR test. A second consecutive test was conducted 24h thereafter, and a positive result was obtained.	Initial RT-PCR for 2019-nCoV was negative. The patient was kept under observation and home isolation. 2 days after the swab test turned positive	The first swab test was negative and the patient was isolated. Over the next week, two more swab tests returned negative. On day 8, the swab test was positive.	The patient nasopharyngeal swab was initially negative she was diagnosed as "Presumed cases" based on early CT findings and she was immediately isolated. The second RT-PCR test was positive 24 hours after admission
<u>FINDINGS ON CHEST CT</u>	Unilateral GGO lesion in the left lower lobe traction bronchiectasies and vascular enlargement are also seen .	Bilateral peripheral ground-glass opacities with interlobular septal thickening (crazy-paving pattern) that affected right lower lobe.	slight reticular pattern in the left lower lobe (sub pleural area) resembling the sign of crazy paving	Ground-glass opacities in the bilateral lower lobes.
<u>CORADS</u>	4 High level of suspicion for pulmonary involvement by COVID-19	5 Very high level of suspicion for pulmonary involvement by COVID-19	4 High level of suspicion for pulmonary involvement by COVID-19	5 Very high level of suspicion for pulmonary involvement by COVID-19

CT INVOLVEMENT SCORE	< 5% involvement	26%-49% involvement	< 5% involvement	5%-25% involvement
CT STAGE OF INFECTION	Early	Progressive	Early	Early

Table 1: The demographic characteristics, initial symptoms, RT-PCR results and CT findings of our 4 patients.

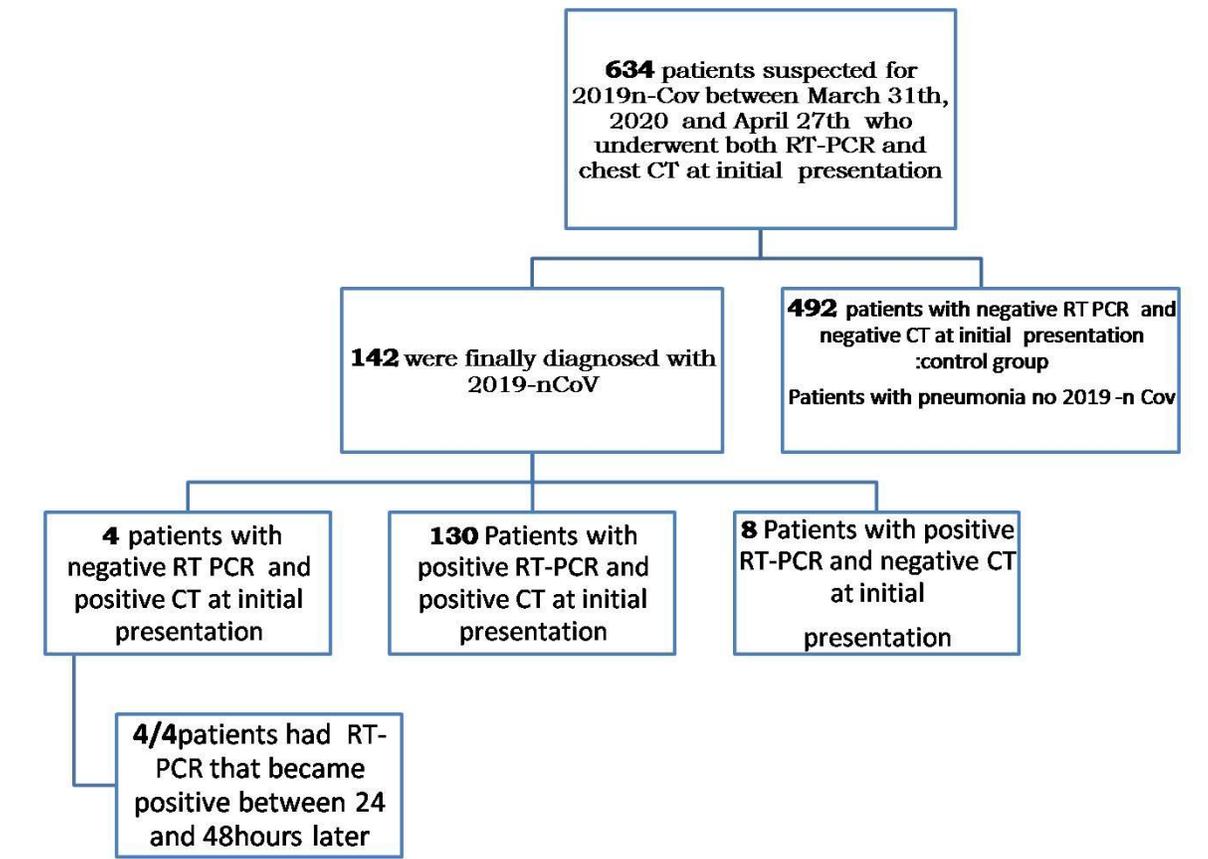


Fig1: Patient Flowchart: Of 142patients 4 (2,8%) had negative RT PCR and positive CT at initial presentation

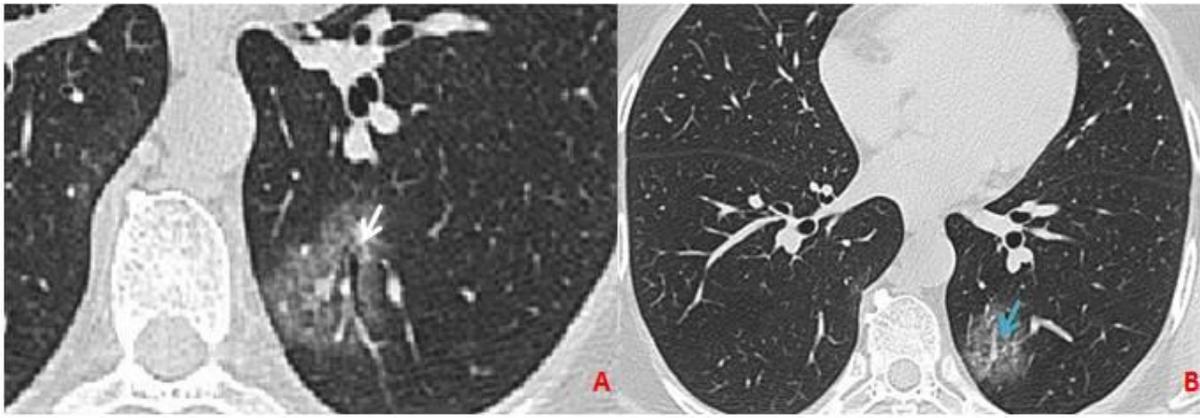


Fig 2: Chest CT imaging of patient 1. A-B, CT images show unilateral GGO lesion in the left lower lobe, traction bronchiectasies (white arrow) and vascular enlargement are also seen (blue arrow). CT score involvement < 5%; corad 4.

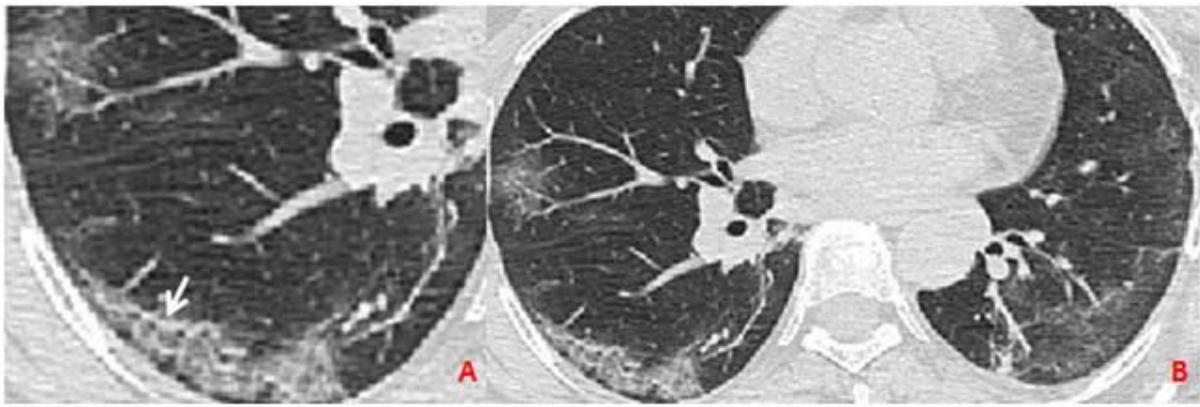


Fig 3: An axial CT images A-B obtained without intravenous contrast of Patient 2 Showed bilateral peripheral ground-glass opacities with interlobular septal thickening (white arrow) (crazy-paving pattern) that affected right lower lobe. CT score involvement 26%-49%; corads 5.

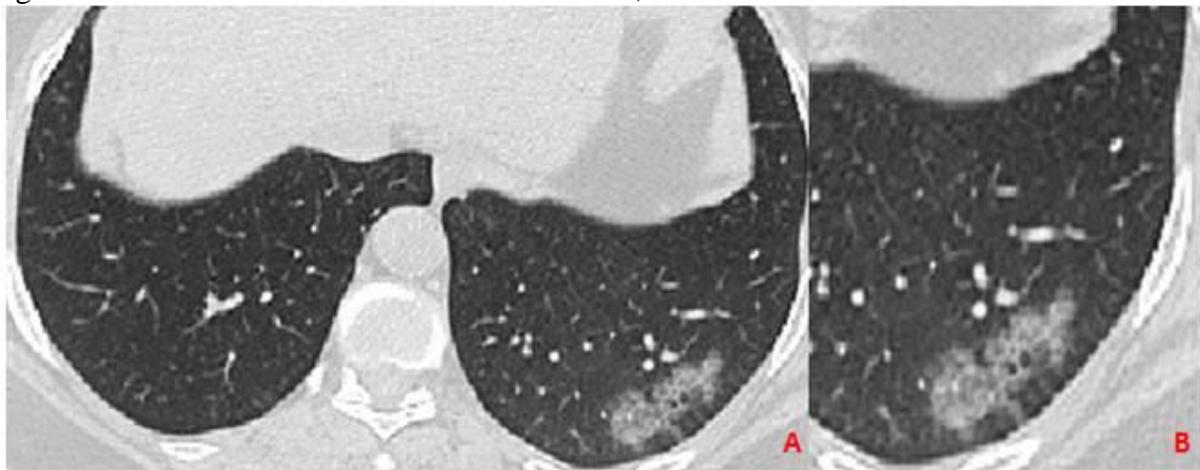


Fig 4: CT images (A-B) of patient 3 shows slight reticular pattern in the left lower lobe in subpleural area resembling the sign of crazy paving. CT score involvement < 5, corads 4.

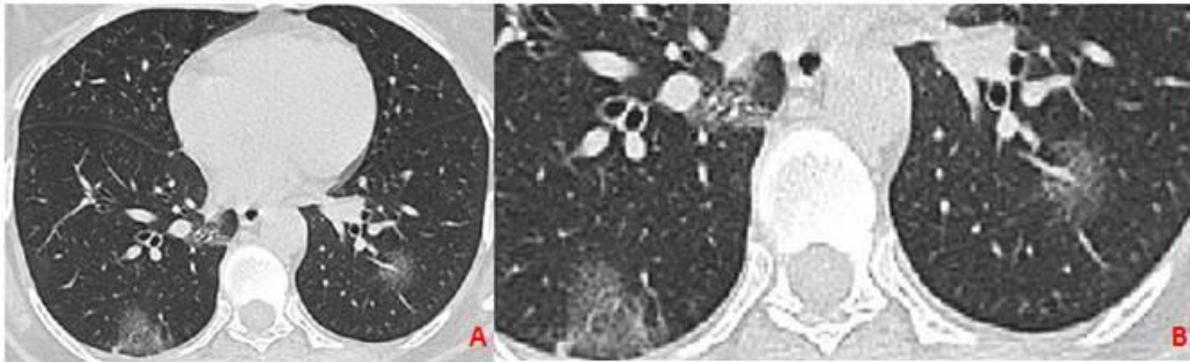


Fig 5: axial non contrast CT images (A-B) of patient 4 shows ground glass opacities in the bilateral lower lobes . CT score involvement 5%-25%, corads 5

Keywords:Pneumonia, Tomography ,Coronavirus.

Abbreviations:

CT:Computed tomography

rRT-PCR:Real time reverse –transcriptase –polymerase chain reaction

GGO:Ground glass opacities

Covid 19:Coronavirus disease 2019.