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► **To cite this version:**

S. Neveu, I. Saab, S. Dangeard, S. Bennani, M. Tordjman, et al.. Incidental diagnosis of Covid-19 pneumonia on chest computed tomography. *Diagnostic and Interventional Imaging*, 2020, 101, pp.457 - 461. 10.1016/j.diii.2020.05.011 . hal-03491062

HAL Id: hal-03491062

<https://hal.science/hal-03491062v1>

Submitted on 22 Aug 2022

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Incidental diagnosis of Covid-19 pneumonia on chest computed tomography

Short title:

Incidental diagnosis of Covid-19 pneumonia

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Abstract

Purpose. The purpose of this study was to determine the prevalence and imaging characteristics of incidentally diagnosed COVID-19 pneumonia on computed tomography (CT).

Materials and methods. This retrospective study was conducted between March 20th and March 31st, 2020 at Cochin hospital, Paris France. Thoracic CT examinations of all patients referred for another reason than a suspicion of SARS-CoV-2 infection were reviewed. CT images were analyzed by a chest radiologist to confirm the presence of findings consistent with COVID-19 pneumonia and quantify disease extent. Clinical and biological data (C-reactive protein serum level [CRP] and white blood cell count) of patients with CT findings suggestive for COVID-19 pneumonia were retrieved from the electronic medical chart.

Results. During the study period, among 205 diagnostic CT examinations, six examinations (6/205, 3%) in 6 different patients (4 men, 2 women; median age, 57 years) revealed images highly suggestive of COVID-19 pneumonia. The final diagnosis was confirmed by RT-PCR. Three inpatients were suspected of extra thoracic infection whereas three outpatients were either fully asymptomatic or presented with fatigue only. All had increased CRP serum level and lymphopenia. Disease extent on CT was mild to moderate in 5/6 patients (83%) and severe in 1/6 patient (17%).

Conclusion. Cumulative incidence of fortuitous diagnosis of COVID-19 pneumonia did not exceed 3% during the highest pandemic phase and was predominantly associated with limited lung involvement.

Keywords: COVID-19 pneumonia; Multidetector, computed tomography; Incidental findings

List of abbreviations

CRP: C-reactive protein

CT: computed tomography

COVID-19: Coronavirus disease 2019

GGO: ground glass opacities

RT-PCR: reverse-transcriptase polymerase chain reaction

Introduction

The coronavirus disease (COVID)-19 pandemic led to a rapidly increasing number of patients with respiratory symptoms referred for computed tomography (CT) for a suspicion of coronavirus disease 2019 (COVID-19) pneumonia. In order to limit the risk of contamination of other patients, the radiology department of our institution decided to dedicate one CT unit for all suspicions of SARS-CoV-2 infection whereas two other CT units located in another building continued to evaluate other patients. While a severe course of SARS-CoV-2 occurs in about 4% of infected individuals who present a severe pneumonia, many patients may present with non-specific symptoms such as fever, asthenia or diarrhea, and some individuals may remain totally asymptomatic [1]. CT can reveal lung parenchyma abnormalities such as ground glass opacities (GGO) in asymptomatic patients with SARS-CoV-2 infection [2]. In a series of 24 asymptomatic patients, two-thirds had mild extension of the disease with involvement of a single lobe and only GGO on CT [3].

We hypothesized that in a high epidemic context, CT could reveal signs of infection in patients referred for CT for other reasons than a suspicion of SARS-CoV-2 infection. Several studies have reported CT findings during the early course of infection. Most of the time lung abnormalities consisted of bilateral GGO at the early stage of the disease, and band consolidations at a later stage, consistent with organizing pneumonia [1, 4–7].

The purpose of this study was to determine the prevalence and imaging characteristics of incidentally diagnosed COVID-19 pneumonia on chest CT.

Materials and methods

Study design

This retrospective study was conducted at Cochin Hospital, Paris, France, between March 20th and March 31st, 2020. We analyzed thoracic images of all diagnostic CT examinations which have been performed on the two CT units of our institution not dedicated to the evaluation of patients with suspected or confirmed COVID-19 pneumonia.

We included all in- and outpatients who presented images highly suggestive of COVID-19 pneumonia on their chest CT, and were later confirmed of having asymptomatic COVID-19 pneumonia by reverse transcription polymerase chain reaction (RT-PCR)

positivity. The requirement for informed patient consent was waived by the ethics committee of our institution (AAA-2020-08028).

CT image acquisition

All CT examinations were performed with the patient in the supine position, using two different 64-slice CT units: SOMATOM® Edge (Siemens Healthineers) or Revolution HD® (GE Healthcare).

The type of CT acquisition (thoracic or abdominal CT) and use of contrast depended on the reason for CT referral. However, all patients had an available thoracic CT acquisition with 1-mm slice reconstruction thickness and standard protocol [8], either performed at first or following the identification of abnormalities of the lung bases on abdominal CT. All reconstructed images were stored in our picture archiving and communication systems (PACS) (Carestream Version 12.1.6.0117).

Image analysis

All chest CT images were reviewed by a board-certified radiologist (M.-P. R.) with 20 years of experience in thoracic imaging. CT features highly suggestive of COVID-19 pneumonia included peripheral ground glass opacities admixed with areas of consolidation, crazy paving pattern or band consolidation, as described in previous studies [4, 9]. Focal consolidation, centrilobular nodules and mucoid impactions were considered as sign of bacterial infection. The extent of CT abnormalities was visually quantified, and considered as mild, when affecting less than 10% of the lung, moderate when involving up to 25% of the lung and severe when affecting more than 50% of the lung.

Clinical and biological data

We analyzed the frequency and type of symptoms as well as the reason for CT referral. The oxygen saturation measurement was not available at the time of CT because the patients had no respiratory symptoms. The body mass index (BMI) of each patient was calculated. Regarding biological data, we analyzed white blood cell count (lymphocytes, platelets) and C-reactive protein (CRP) serum levels.

Results

Between March 20th and March 31st, 205 diagnostic CT examinations have been performed for routine indications at our Radiology Department, mainly for oncologic indications or suspicions of acute illness. Of these, six CT examinations (6/205, 3%) performed in six different patients, showed images highly suggestive of COVID-19 pneumonia. There were 4 men and 2 women with a median age of 57 years (IQR: 51, 78; range: 0 - 86 years). CT examinations were read first by the attending radiologist and then analyzed by the expert chest radiologist for confirmation. All patients were tested for SARS-CoV-2 infection following CT and had a positive RT-PCR result. The clinical characteristics of the 6 patients are summarized in **Table 1**. Three of them were inpatients, referred for CT because they had fever and were suspected of having extra thoracic infection. They had abdominal and pelvic CT examination but the presence of opacities in the lung bases had led to perform additional chest CT. Noteworthy, one of these febrile patients had been tested by RT-PCR with a first negative result, 5 days before CT.

Two totally asymptomatic outpatients were referred for CT for oncologic reasons. The last outpatient, an 85-year-old man was referred by the emergency department for suspicion of neoplasia because of recent alteration of the general status and repeated falls. None of the six patients had respiratory symptoms. The BMI of five patients was within the normal range (mean 24, range: 18 -25) and one had a BMI of 28.

All six patients had elevated level of C-reactive protein (mean value 45 mg/L, range: 29 - 91) and lymphopenia (mean value $0.95 \times 10^9/L$, range: 0.6×10^9 - $1.3 \times 10^9/L$). Platelet counts were in the range of normal values (mean value $175 \times 10^9/L$, range 155 - 230). CT showed presence of GGO in all patients, typically affecting the lower lobes with a peripheral, posterior and sub pleural distribution (Figures 1, 2). Four of the six patients had mild involvement, affecting less than 10% of the lung parenchyma. One of them had only unilateral involvement. One patient had a moderate disease extent (10 - 25%). Only one patient had a severe pneumonia extent (> 50%) with bilateral diffuse ground glass opacities associated with consolidations and a right pleural effusion. This patient secondarily developed respiratory failure, and the disease course had a fatal outcome. The other five patients were either not hospitalized or recovered and were discharged and followed-up through teleconsultation.

Discussion

In this retrospective evaluation, we found that 3% of the patients referred for CT for other reasons than a suspicion of COVID-19 pneumonia during the high epidemic study period were diagnosed with the condition. Half of them were febrile patients with suspicions of extra thoracic infection whereas the three others were either totally asymptomatic or only presented with fatigue. Even though this proportion is relatively low, it retrospectively justifies our decision to have our technologists provided with personal protective equipment, even when performing CT examinations on the non-COVID dedicated CT machines.

So far, only three studies and two case reports have reported incidental identification of SARS-CoV-2 related pneumonia on chest CT or PET/CT [3, 10-12]. These studies allowed the detection of SARS-CoV-2 infection at early stages, allowing prompt isolation of the patients.

Zhang *et al.* compared CT features between totally asymptomatic and common type symptomatic patients. This excluded severe type defined as breathing rate $\geq 30/\text{min}$, saturation $\leq 93\%$, mechanical ventilation shock or other organ failure. In this study, there were no significant differences in individual signs, patterns, zonal predominance or extent of CT abnormalities between common type symptomatic and asymptomatic patients [13]. We found that the majority of our patients had only minor lung involvement, in line with by An *et al.* [3]. Only one patient presented with more than 50% of lung involvement, but he had a metastatic cholangiocarcinoma with altered performance status, masking the symptoms of pneumonia.

Dane *et al.* reported COVID-19 pneumonia incidentally found on the lung bases in 23 patients referred for abdominal CT mainly for abdominal pain or diarrhea [12]. However, these researchers did not report the total number of CT examinations performed during the study period, thus it is not possible to evaluate the frequency of these incidental diagnosis [12].

The objective of our study was to obtain an prevalence analysis of COVID-19 pneumonia among patients referred for CT examination for other reasons than a suspicion of SARS-CoV-2 infection in a University Hospital in Paris, France, during the most intense phase of the pandemic. Our estimated cumulative incidence is only 3% (6/205), less than the recently derived estimate of 9% (6/65 patients) from data of department of nuclear medicine in Brescia, Italy between March 16th and March 24th [10]. However, Italy was about two weeks ahead of France regarding the spread of the virus.

In our cohort, a majority of patients had a current or a previous history of cancer. While several studies suggest a particular fragility in oncologic patients [14], our study shows that they can also present with moderate forms or even asymptomatic forms of the disease.

Our study has several limitations. First, it is a retrospective study involving a small number of patients with proven SARS-CoV-2 infection. The probability of selection bias is a concern. As mentioned, our radiology unit was supposed to receive only “non-infected patients”. Moreover, because of the current pandemic, only CT examinations for oncologic follow-up or suspicion of acute conditions were maintained. Our study population, selected on these two criteria, may be not representative of the usual patient population of a public general hospital in Paris, and our study does not allow estimating the true number of asymptomatic patients being infected.

In conclusion, even during the highest phase of the pandemic, incidental discovery of SARS-CoV-2 related pneumonia remained infrequent among patients referred for fever or oncological reasons, with asymptomatic patients having only minor disease extent on CT.

Authors' contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

Disclosure of interest

The authors declare that they have no competing interest.

Funding

The study received no funding.

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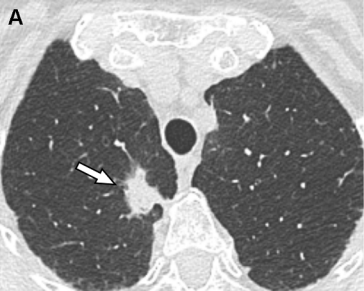
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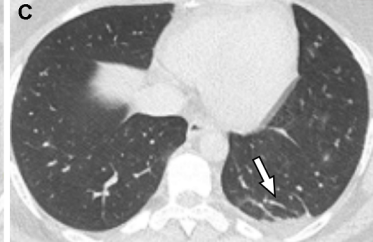
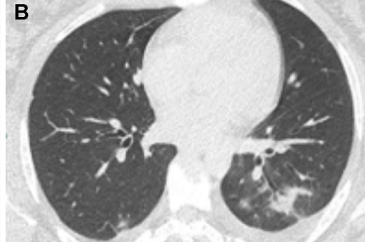
Figure legends

Figure 1. A 86-year-old asymptomatic woman with suspicion of lung cancer (Patient # 3). **A**, CT image of the thorax in the axial plane shows spiculated solid nodule (arrow) in right upper lobe. **B**, At a different level, sub pleural ground glass opacities are seen bilaterally, with superimposed intralobular thickening resulting in a crazy-paving pattern (arrowhead) in the right lower lobe.

Figure 2. A 30-year-old asymptomatic woman treated with antibiotics for post-partum endometritis who has unexplained persistent fever (Patient #5). **A, B**, Unenhanced CT images in the axial plane show focal ground glass opacities and consolidations. **C**, At a different level, CT image shows subpleural, curvilinear lines in left lower lobe (arrow).

Table 1. Clinical and imaging features.





Patient #	Age (years)	Sex	Clinical symptoms	Lymphocyte count ($\times 10^9/L$)	CRP (mg /L)	Indication for referral to CT	CT protocol	CT features	Lung extent on CT	Origin and number of days of hospitalization	Medical history
1	49	M	Fever	0.82	29	Suspicion of cholangitis	Contrast-enhanced CT of the thorax, abdomen and pelvis	Diffuse bilateral GGO with consolidations and right pleural effusion	Severe (> 50%)	Inpatient 5 days	Metastatic cholangiocarcinoma
2	85	M	Fatigue	0.6	91	Suspicion of neoplasia	Contrast-enhanced CT of the thorax, abdomen and pelvis	Bilateral GGO with few areas of consolidation in both lower lobes	Mild (< 10%)	Outpatient	Repeated falls and weight loss
3	86	F	Asymptomatic	0.8	40	Preoperative assessment of a lung nodule	Unenhanced chest CT	Patchy peripheral GGO with crazy paving in both lower lobes	Moderate (10 to 25%)	Outpatient	Chronic obstructive pulmonary disease Spiculated lung nodule
4	58	M	Asymptomatic	1.3	35	Routine oncologic follow-up	Contrast enhanced CT of the thorax, abdomen and pelvis, followed by an additional thoracic CT	Discrete areas of GGO in both lower lobes with unique image of atoll sign	Mild (< 10%)	Outpatient	Renal cell carcinoma surgically treated two years ago
5	30	F	Fever	1.2	46	Puerperal endometritis	Contrast-enhanced CT of the abdomen and pelvis, followed by an additional thoracic CT	Bilateral focal GGO and consolidations with linear consolidations in the left lower lobe	Mild (< 10%)	Inpatient 4 days	Vaginal delivery 3 days ago
6	55	M	Fever	1	32	Suspicion of postoperative abscess	Contrast-enhanced CT of the abdomen and pelvis followed by an additional thoracic CT	Subpleural GGO in the left lower lobe	Mild (< 10%)	Inpatient 60 days	Radical prostatectomy for prostate cancer 2 month ago

Note. CT = computed tomography; GGO i= ground glass opacities; CRP = C-reactive protein; M = male; F = female