Chest CT Findings of COVID-19 Delta Variant in A Hospital Cluster

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Abstract

The B.1.617.2 (Delta) variant of the SARS-CoV-2 virus has been the cause of surging COVID-19 cases in many countries in recent months. We present a review of the CT chest imaging findings of eight patients from a hospital cluster, where the SARS-CoV-2 virus was diagnosed with Real-Time Polymerase Chain Reaction (RT-PCR) testing and confirmed by whole genome sequencing to be of the same Delta (B.1.617) variant strain. This case series highlights CT findings considered atypical for COVID-19, but were observed in higher proportions than reported in the literature-specifically, upper lobe predominance, unilaterality and presence of pleural effusions. We recommend larger scale investigation into the CT imaging phenotype of Delta variant infection to sharpen our ability to diagnose COVID-19 as the pandemic evolves.

Keywords: COVID-19; CT findings; Delta variant; Epidemiology; Infectious diseases.

Introduction

The B.1.617.2 variant of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first identified in India in October 2020. It was assigned the Delta label following the World Health Organization's (WHO) effort to reduce potentially discriminatory names and misreporting [1]. Over the past few months, the Delta variant has risen to prominence, becoming the dominant strain in the United Kingdom (UK) [2,3] and rapidly displacing other known strains in the United States (US) [4]. WHO has designated the Delta variant as a Variant of Con-Cern (VOC) from May 2021 [5]. As of July 2021, the variant has been detected in at least 98 countries. Furthermore, recent studies show the Delta variant to be more transmissible [6] with potential reduction in neutralization by antibody treatments and vaccination [7].

Since the start of the Coronavirus Disease 2019 (COVID-19) pandemic, significant progress has been made in the understanding of the biology of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Testing for COVID-19 is now quicker and more accessible than before. Specific assays that detect viral nucleic acid from the upper respiratory tract are typically employed for diagnosis, but may miss infections involving only the lower airways. While the chest radiograph is commonly used to screen patients for positive radiographic findings, Computed Tomography (CT) is more sensitive and specific for depicting imaging features of COVID-19.

Established guidelines for CT diagnosis of COVID-19 pneumonia have been based upon literature in the earlier part of the pandemic [8,9]. We performed a more recent literature review but were unable to find reports specifying key imaging findings specific to COVID-19 Delta variant. Hence, we reviewed the CT chest findings in a recent local hospital cluster of SARS-CoV-2 Delta variant infection, which was confirmed by phylogenetic analysis. Given the in-creasing prevalence of the variant, radiologists should be cognizant of its potential for atypical imaging features. Prompt detection that can sometimes be alerted by imaging, coupled with infection control measures, can help to contain the spread of the virus and prevent a hospital-wide outbreak [10].

Case presentation

On 28 April 2021, COVID-19 was confirmed in a staff member working in an inpatient ward of a local hospital in Singapore. This subsequently led to the discovery of Singapore's first hospital COVID-19 cluster due to the Delta variant [11]. We conducted a review of the CT chest images of all patients who had undergone CT imaging from the same inpatient ward, blinded to their SARS-CoV-2 infection status. After the independent radiologic review, the relevant demographic and clinical data of patients with SARS-CoV-2 infection were collated and analyzed together with the imaging findings.

A total of 21 patients underwent CT imaging during the period of the outbreak for a variety of reasons. In the majority of cases, chest CT was done to investigate clinical deterioration such as development of breathlessness, oxygen desaturation and sinus tachycardia, or for specific clinical indications such as for exclusion of pulmonary embolism 10 out of these 21 patients tested positive for the SARS-CoV-2 virus on Polymerase Chain Reaction (PCR) test at various time-points. All 10 of them were confirmed to be of the same Delta variant strain via whole genome sequencing. Two of these patients underwent CT imaging prior to their first positive PCR test and were excluded. Thus, a total of eight patients were included in this case series. In the remaining 11 (of 21) patients, SARS-CoV-2 was not detected despite repeated PCR tests up to 14 days from the date of last exposure to the ward.

Patient characteristics

Our eight COVID-19 cases were aged 52 to 91 years, with a mean of 70.5 years (Table 1). Half of them were female (n=4, 50%) and the majority (n=6, 75%) had significant comorbidities, with two of them having a history of malignancy.

Table 1: Patient demographics and Imaging features.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8
Age (years)	70	91	65	57	60	52	80	89
Gender	Male	Male	Female	Male	Female	Male	Female	Female
Significant Comorbidities*	√	√	√	-	√	√	√	-
Clinical Characteristics								
Time interval between date of last exposure to symptom onset^	0 days	1 day	1 day	0 days	2 days	8 days	1 day	1 day
Time interval between symptom onset and RT PCR^^	0 days	0 days	0 days	13 days	0 days	1 day	1 day	0 days
Time interval between symptom onset and CT scan+	1 day	4 days	3 days	11 days	6 days	30 days	11 days	1 day
Was CT imaging performed prior or after first positive RT-PCR	After	After	After	Prior	After	After	After	After
Time interval between first positive RT-PCR and CT scan++	10 day	1 day	17 days	2 days	70 days	29 days	11 days	3 days
First available cycle threshold value	22.3	14.9	12.4	20.7	31.73	23.2	40.4	12.9
Cycle threshold value (if available) on day of CT scan	NA	NA	15.2	NA	NA	NA	19.1	NA
Typical Imaging Features#	-	-	√	√	-	-	-	-
Atypical Imaging Features								
Unilaterality	√	-	-	-	-	√	√	-
Upper lobe predominance	-	√	√	-	-	-	-	√
Pleural effusion	√	√	√		√	√	√	√
Lymphadenopathy	-	-	√	-	-	-	-	-

*Examples include primary malignancies, end-stage renal disease, liver cirrhosis etc.

^Number of days that have elapsed from the date of last exposure to the affected ward to the onset of symptoms.

^^Number of days that have elapsed from date of symptom onset to the date of the first positive RT-PCR.

+Number of days that have elapsed between symptom onset and date CT scan was performed.

++Number of days that have elapsed between date when CT scan was performed and date of first positive RT-PCR, and vice versa, dependent on which occurred first.

#Multifocal, bilateral ground-glass opacities with or without consolidation in a peripheral distribution, more commonly in the lower lobes.

Of our eight patients, the duration from the time of last exposure to the affected ward, to the time of symptoms onset ranged between 0 to 8 days, with a mean duration of 1.8 days. These symptoms included acute respiratory symptoms such as fever (n=6) and cough (n=2), with the more clinically severe patients developing shortness of breath (n=3), desaturation (n=2) and hypotension (n=1). The duration from the time of symptom onset to the first positive RT-PCR ranged between 0 days (that is, symptom commencing on the day the patient tested positive for COVID-19) and 13 days, with a mean duration of 1.85 days. The cycle threshold levels, defined as the number of cycles required for the fluorescent signal to cross the threshold (i.e. exceeding background level), from the first positive RT-PCR for all six patients ranged between 12.40 to 40.40, with a mean value of 22.30.

Imaging features

All eight patients had CT scans reviewed. These patients had their scans performed typically at a point of clinical deterioration. Where available, the cycle threshold levels on the day of CT imaging were noted - 15.20 and 19.10 respectively, for two of the eight patients.

CT findings that were "typical" for COVID-19 included multifocal, bilateral ground glass opacities predominantly in a peripheral distribution, more commonly in the lower lobes (n=2), and bilaterality (n=5). "Atypical" features included upper lobe predominance (n=3), presence of pleural effusions (n=7) and presence of only unilateral findings (n=3).

Only one of our eight patients had a pre-existing history of cardiopulmonary comorbidities (Case 3). This patient, a 65 year-old female, had a significant past medical history of end-stage renal failure secondary to Type 2 Diabetes Mellitus and cryptogenic liver cirrhosis, and was electively admitted for insertion of a trans-jugular intra-hepatic portosystemic shunt to relieve her ascites. She developed fever 16 days following her first positive RT-PCR. CT imaging showed bilateral diffuse ground glass changes, with interlobular septal thickening and small bilateral pleural effusions. Her co-morbid disease likely contributed to her CT chest findings, and confounded her imaging diagnosis of COVID-19.

Of the remaining seven patients, 7 of them (87.5%) had pleural effusion on imaging. Of note, two of these patients had preexisting conditions, which may have accounted for the presence of pleural effusion. The first (Case 1), had left lung collapse secondary to known primary left upper lobe lung adenocarcinoma while the other (Case 6) had lymphangitis carcinomatosis due to metastatic breast cancer. The remaining 5 patients did not have predisposing medical conditions that could explain the presence of pleural effusions.

With regard to lymphadenopathy, one of the eight patients had calcified right hilar and mediastinal nodes (Case 3), deemed likely secondary to known prior pulmonary tuberculosis infection, and was unlikely to be from his current viral infection. None of the remaining seven patients demonstrated intra-thoracic lymphadenopathy.

Treatment and follow-up

Two of the eight patients underwent CT imaging at different time points, providing insight into the radiological manifestations of disease progression in Delta variant infection. The first patient (Case 1) was immunocompromised from dual metastatic malignancies, and had a second CT scan performed 10 days after the first CT. His repeat CT showed interval worsening of the pre-existing ground glass opacities, consistent with clinical deterioration. He subsequently demised, 3 weeks after testing positive for SARS-CoV-2. The second patient (Case 3) was admitted to the intensive care unit for mechanical ventilation support and prone therapy. Patchy ground glass opacification, which was observed on the initial CT, had progressed into extensive consolidation with an upper lobe predominance in both lungs. She was commenced on a 10-day regimen of IV Remdesivir and subsequently recovered uneventfully. Two other patients also tolerated IV Remdesivir (Case 2 and Case 8) well with a positive out-come but no follow-up CT was performed.

Discussion

This case series highlights imaging findings in a cohort of patients diagnosed definitely, on phylogenetic studies, to be infected with the Delta variant of SARS-CoV-2. The imaging findings are important to note because there remains paucity of published studies detailing CT imaging features of COVID-19 VOCs. The most commonly reported CT imaging features in COVID-19, prior to the discovery of VOCs, were: multifocal, bilateral ground-glass opacities with or without consolidation in a peripheral distribution, more commonly in the lower lobes [9,12-14]. While these findings were present in some of the cases we encountered, a significant proportion of our patients also exhibited radiological findings that are deemed un-common or atypical for COVID-19, specifically upper lobe predominance, presence of pleural effusions and presence of only unilateral findings.

Interestingly, we note that in our patients with unilateral CT findings, only the right lung was affected. This can be further corroborated with larger scale studies. The relatively higher prevalence of upper lobe and unilateral lung involvement in our series known to be atypical for COVID-19, but is consistent with a recent study that demonstrated the typical deposition of aerosolized SARS CoV-2 particles in the respiratory system via a complex 17-generation lung model [15] , alluding to an aerosol mode of transmission [16].

Bernheim et al., [17]. found that 56% of patients imaged 0-2 days after symptom onset (early phase) had a normal CT scan with complete absence of ground-glass opacities and consolidation, even though we found positive findings for all our patients despite early detection with PCR. Wang et al., [18]. Found that a higher proportion of unilateral lung involvement was observed in a retrospective cohort of 90 patients in the early phases of disease - 27-38% of patients 5 days or less, compared to 0% beyond 12 days after symptom onset. Thus, one could also argue that the higher prevalence of unilaterality in our cohort could lie in the fact that the majority (7/8) were had minimal or no

symptoms at the time of their first positive RT-PCR, due to active case finding through PCR tests as part of our institution's effort to contain the outbreak. It is noteworthy, therefore, that in all the cases for which disease was found to be unilateral, CT was performed as long as 30 days after a first positive PCR result. Furthermore, regardless of the presence of symptoms, all patients were found to have abnormal CT.

Pleural effusions are considered highly unusual for COVID-19, occurring in 5.2% of patients, based on a systematic review of 28 studies comprised of 3466 patients [19]. The relatively high incidence of pleural effusions (7/8; 87.5%) in our patient series is therefore remarkable, especially since pleural effusions in COVID-19 pneumonias are observed in patients with more advanced disease-more severe inflammatory responses that portend poorer clinical out-comes [20]. Patients with lower cycle threshold levels, corroborating with strong positive reactions indicative of abundant target nuclei in the sample and a higher viral load, predicted ad-verse outcomes independent of age, co-morbidities, and severity of illness at presentation [21]. Nevertheless, in our series, pleural effusions were present, irrespective of whether the patients were in the early or late phases of their infection, which were objectively determined by the cycle threshold results.

Our study has a few limitations. Firstly, this is a small case series with a sample size of eight patients. Nevertheless, we feel that it is important to report our preliminary observations given the higher prevalence of atypical CT chest findings observed, in the absence of published data on the imaging phenotype of the Delta variant. Large-scale cohort studies could be per-formed to validate our findings and to compare radiological findings across different VOCs. In addition, we are studying a hospital cluster for which underlying medical conditions could confound

analysis, in particular, the higher incidence of pleural effusions. However, 5 of 7 of the patients who had pleural effusions did not have co-morbid conditions that could explain its presence; and cardiopulmonary disease was only present in one out of seven patients with pleural effusions. We were also not able to identify confounding co-morbid conditions to ac-count for the unilateral predilection and predominant upper lobe involvement. Lastly, CT was performed at different stages of infection in each of the patients, and even though there were two patients with serial CT scans, we were not able to elucidate the temporal evolution of CT findings for the Delta variant.
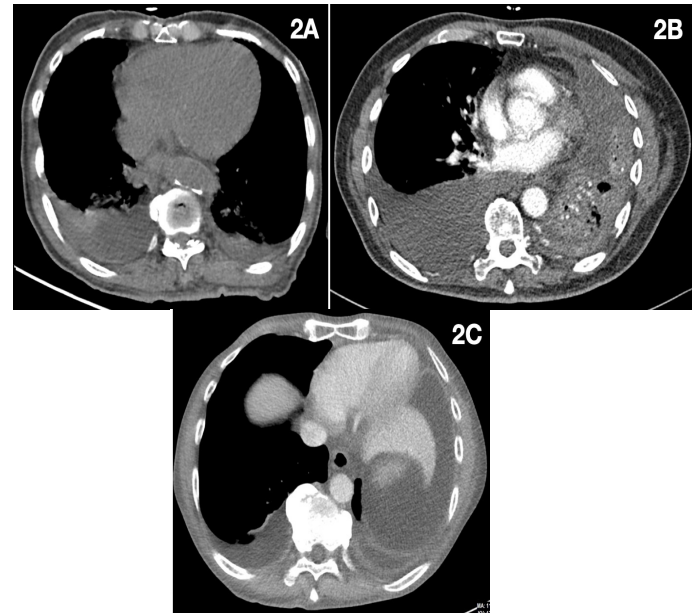

Figure 2A-C: Axial CT images were obtained from three different patients, aged between 70 and 91 years old, who tested positive for the Delta variant, as part of the ward's surveillance efforts. Their cycle threshold values ranged from 14.90 to 40.40, suggesting that they were at various stages of infection. Axial CT images from each of these three patients demonstrate consistent presence of bilateral pleural effusions, atypical for COVID-19 disease.
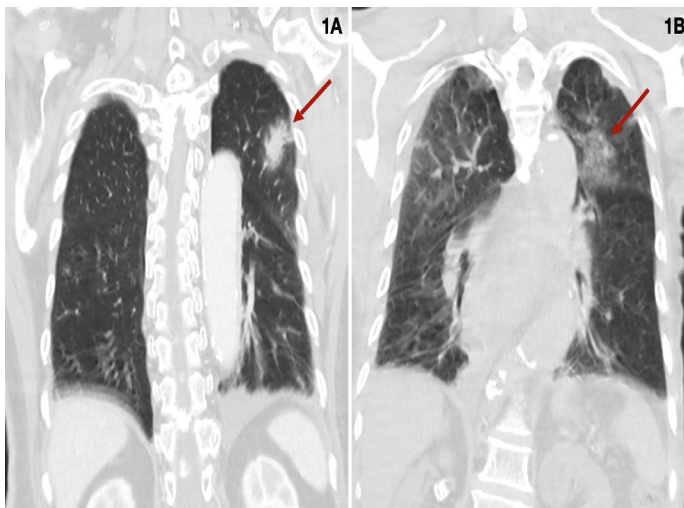

Figure 1A-B: Coronal reformatted contrast enhanced chest CT images of two different patients from the same cluster.
(1A): 89 year-old female admitted to the affected ward a week before the ward cluster. She tested positive for SARS-CoV-2 on surveillance but subsequently developed a fever during her admission. Coronal CECT image demonstrated consolidation and ground glass opacities in the left upper lobe (arrow). She was commenced on a course of IV Remdesivir for 10 days, remained clinically stable and discharged well subsequently.
(1B): 91 year-old male admitted for left little toe gangrene with fever. He tested positive for SARS-CoV-2 a day following the detection of the cluster. Coronal CECT showed ground glass opacities in both lungs, with upper lobe predominance, worse on the left (arrow). He was treated with a course of Remdesivir and was de-isolated on Day 48 when he tested negative.
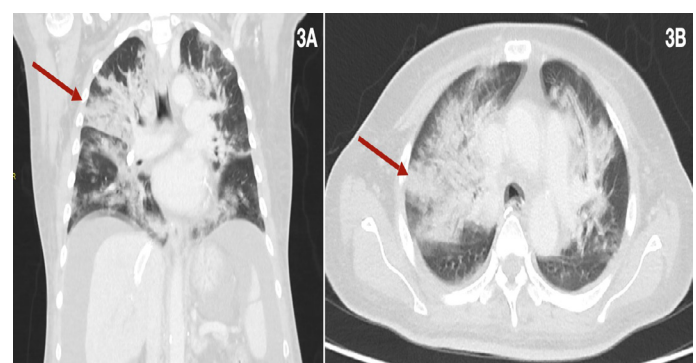

Figure 3A-B: A 65 year-old Chinese female with a history of decompensated cryptogenic liver cirrhosis and was electively admitted for insertion of a trans-jugular intra-hepatic portosystemic shunt to relieve her ascites. She tested positive for SARS-CoV-2 on surveillance but only developed a fever 16 days after first testing positive. She subsequently deteriorated clinically and was admitted to the intensive care unit for ventilatory support. (**A**) Coronal reformatted and (**B**) axial contrast-enhanced chest CT images then showed bilateral diffuse ground glass changes and consolidation with an upper lobe predominance (arrows). She was commenced on anti-viral therapy and improved clinically thereafter.

Conclusion

In conclusion, our case series highlights several key CT findings in a hospital cluster due to the B.1.617.2 (Delta) variant of SARS-CoV-2. We found a greater incidence of unilateral disease, upper lobe predominance and pleural effusions in our patients, which are considered atypical for COVID-19 pneumonia. If corroborated with larger studies, these "atypical" CT findings, together with RT-PCR findings can, in the future, aid the clinician in prompt diagnosis in unsuspected cases of the Delta variant.

References

1. WHO. WHO announces simple, easy-to-say labels for SARS-CoV-2 Variants of Interest and Concern. World Health Organisation. 2021.

2. Torjesen I. Covid-19: Delta variant is now UK's most dominant strain and spreading through schools. BMJ. 2021; 373: n1445.

3. Callaway E. Delta coronavirus variant: scientists brace for impact. Nature. 2021; 595: 7865.

4. Bolze A, Cirulli ET, Luo S, Simon White, Tyler Cassens, et al. Rapid displacement of SARS-CoV-2 variant B.1.1.7 by B.1.617.2 and P.1 in the United States. medRxiv. 2021: 21259195.

5. WHO. Tracking SARS-CoV-2 variants. World Health Organisation. 2021.

6. Hester A, Vusirikala A, Flannagan J, Katherine A Twohig, Asad Zaidi, et al. Increased Household Transmission of COVID-19 Cases Associated with SARS-CoV-2 Variant of Concern B.1.617.2: A National Case-Control Study. 2022; 12: 100252.

7. Deng X, Garcia-Knight MA, Khalid MM, Venice Servellita, Candace Wang, et al. Transmission, infectivity, and antibody neutralization of an emerging SARS-CoV-2 variant in California carrying a L452R spike protein mutation. medRxiv Prepr Serv Heal Sci. March 2021: 21252647.

8. Revel MP, Parkar AP, Prosch H, Mario Silva, Nicola Sverzellati, et al. COVID-19 patients and the radiology department – advice from the European Society of Radiology (ESR) and the European Society of Thoracic Imaging (ESTI). Eur Radiol. 2020; 30: 4903-4909.

9. Prokop M, Van Everdingen W, Van Rees Vellinga T, Henriëtte Quarles van Ufford, Lauran Stöger, et al. CO-RADS: A Categorical CT Assessment Scheme for Patients Suspected of Having COVID-19-Definition and Evaluation. Radiology. 2020; 296: E97-E104.

10. Höring S, Fussen R, Neusser J, Michael Kleines, Thea Laurentius, et al. Management of a Hospital-Wide COVID-19 Outbreak Affecting Patients and Healthcare Workers. SN Compr Clin Med. 2020; 2: 2540-2545.

11. Mahmud AH, Ang HM. IN FOCUS: The rapid rise of the Delta variant and how it is shaping Singapore's COVID-19 fight - CNA. 2021.

12. Kwee TC, Kwee RM. Chest CT in covid-19: What the radiologist needs to know. Radiographic. 2020; 40: 1848-1865.

13. Chung M, Bernheim A, Mei X, Ning Zhang, Ming Qian Huang, et al. CT imaging features of 2019 Novel Coronavirus (2019-NCoV). Radiology. 2020; 295: 202-207.

14. Zhou S, Wang Y, Zhu T, Xia L. CT features of Coronavirus Disease 2019 (COVID-19) pneumonia in 62 patients in Wuhan, China. Am J Roentgen. 2020; 214: 1287-1294.

15. Islam MS, Larpruenrudee P, Paul AR, Gunther Paul, Tevfik Gemci, et al. SARS CoV-2 aerosol: How far it can travel to the lower airways? Phys Fluids. 2021; 33.

16. Greenhalgh T, Jimenez JL, Prather KA, Tufekci Z, Fisman D, et al. Ten scientific reasons in support of airborne transmission of SARS-CoV-2. The Lancet, 2021; 397: 1603-1605.

17. Bernheim A, Mei X, Huang M, Yang Yang, Zahi A Fayad, et al. Chest CT findings in Coronavirus Disease 2019 (COVID-19): Relationship to Duration of Infection. Radiology. 2020: 295.

18. Wang Y, Dong C, Hu Y, Li C, Ren Q, et al. Temporal Changes of CT Findings in 90 Patients with COVID-19 Pneumonia: A Longitudinal Study.2020; 296: E55-E64.

19. Adams HJA, Kwee TC, Yakar D, Hope MD, Kwee RM. Chest CT Imaging Signature of Coronavirus Disease 2019 Infection: In Pursuit of the Scientific Evidence. Chest. 2020.

20. Zhan N, Guo Y, Tian S, Binglu Huang, Xiaoli Tian, et al. Clinical characteristics of COVID-19 complicated with pleural effusion. BMC Infect Dis. 2021; 21: 1-10.

21. Zacharioudakis IM, Prasad PJ, Zervou FN, Basu A, Inglima K, et al. Association of SARS-CoV-2 Genomic Load with Outcomes in Patients with COVID-19. Annals of the American Thoracic Society. 2021; 18: 900-903.