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Clinical and Imaging Characteristics of Imported and Domestic COVID-19 Cases: A Report from a Shanghai Screening Hospital

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Abstract

Background: Since the first case of unexplained pneumonia has been reported in December 2019, Wuhan, Hubei, China, the novel coronavirus disease (COVID-19) has been well controlled in China. But the increasingly serious overseas epidemic situation has led to an increasing number of imported cases abroad.

Objective: To investigate whether there are differences in clinical and imaging manifestations between domestic cases and imported cases, helping early identification of imported cases and preventing secondary outbreaks.

Methods: Cross-sectional, single-center analysis of domestic confirmed cases and imported cases abroad from Pudong New District Zhoupu Hospital, Shanghai, China, comparing the clinical manifestations, laboratory examination, imaging and other aspects of the two groups.

Results: Of the 23 COVID-19 patients, 12 were imported case (mean age 30.83±13.18 years, 8 males) and 11 were domestic case (mean age 40.73±11.32 years, 5 males). The general clinical manifestations of the two groups were similar, fever and cough still as the main clinical manifestations. No patients with dyspnea in the two groups. Among the overseas imported cases, the symptoms of fever (P=0.082) and systemic soreness (P=0.04) were lower, which may be related to the younger overseas imported cases. Imaging findings showed that both imported cases abroad and domestic cases were characterized by subpleural multiple ground-glass opacities, accompanied by halo nodules or "crazy-paving pattern", vascular bundle sign, and partial vascular thickening. But compared with domestic cases, more imported cases had no abnormalities in imaging findings.

Conclusion: The clinical and imaging manifestations of overseas imported cases are similar to domestic case, but most of the symptoms of overseas imported cases are atypical or asymptomatic, which is related to the domestic shift of epidemic prevention and control focus to prevent the spread of overseas imported cases, so that all immigrants can be diagnosed and treated at the first time. At present, the global epidemic situation is in the stage of rapid transmission, all countries should make measures to control the epidemic situation as soon as possible, and the China's experience may be used for reference.

Keywords: Clinical characteristics; Computed tomographic; COVID-19; Overseas

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Introduction

Since the first report of an unexplained pneumonia in Wuhan, Hubei, China. COVID-19 has been diagnosed more than 1 million cases in other countries including China, Asia, Europe, Africa and America just in 3 months, which posing a major threat to international health and economy. The World Health Organization (WHO) announced the severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) epidemic as a Public Health Emergency of International Concern (PHEIC) on January 30, 2020, and raised the risk assessment of COVID-19 from "high" to "very

Table 1: Demographic and baseline characteristics of COVID-19 domestic and imported patients.

	Number of case (n)	Imported case (n=12)	Domestic case (n=11)	X^2/t	P	95% CI
Gender: Male/Female	13/23	8/4	5/6	-1.000	0.329	-0.654~0.230
Age (years)	-	30.83±13.18	40.73±11.32	1.936	0.067	-0.738~20.525
Onset to treatment (days)	-	1.35±1.80	3.18±4.00	1.399	0.184	-0.986~4.658
Symptoms						
Fever n (%)	-	7(58%)	10(91%)	1.828	0.082	-0.045~0.696
Systemic soreness n (%)	-	1(8%)	7(64%)	3.263	0.004	0.201~0.905
Cough n (%)	-	7(58%)	6(55%)	-0.175	0.863	-0.489~0.453
Dyspnea n (%)	-	0(0%)	0(0%)	-	-	-
Sore throat n (%)	-	2(17%)	1(9%)	-0.524	0.606	-0.377~0.225
Runny nose n (%)	-	1(8%)	0(0%)	-0.956	0.350	-0.380~0.228
Laboratory inspection						
White blood cell count (×10mg/l)	-	5.13±1.57	6.13±1.60	1.514	0.145	-0.376~2.383
Lymphocyte count (×10mg/l)	-	1.33±0.58	1.41±0.60	0.327	0.747	-0.432~0.593
CRP (mg/l)	-	1.91±1.49	6.87±7.24	2.323	0.030	0.519~9.389

N (%), where N is the total number of patients with available data.

high" at the global level on February 28, 2020 [1].

A novel coronavirus disease (COVID-19) is mainly characterized by fever, cough (dry) and fatigue. A few patients are accompanied by nasal congestion, runny nose, sore throat, myalgia and diarrhea. Severe cases often develop dyspnea and/or hypoxemia one week after onset. Severe cases can rapidly develop into Acute Respiratory Distress Syndrome (ARDS), septic shock, difficult-to-correct metabolic acidosis, coagulation dysfunction and multiple organ failure [2].

After homology analysis, it was confirmed that the novel coronavirus has 86.9% homology with the bat-SL-CoVZC45 (MG772933.1) coronavirus of Severe Acute Respiratory distress Syndrome (SARS), which belongs to the family member of the β coronavirus, like the 2003 SARS coronavirus (2003-CoV), both of them are belong to the Sarbeco virus family. Its genome including a 5′ untranslated region (UTR), replicase complex (orf1ab), S gene, E gene, M gene, N gene, 3′ UTR and several unknown unstructured open reading frames. So the novel coronavirus are quite different from the Middle East Respiratory Coronavirus (MERS-CoV) belonging to the Merbaco virus family [3].

As of April 4, 2020, There are 82,899 COVID-19 have been diagnosed in China, 76,992 cases have been cured and discharged, 3,335 cases have died, and the number of new diagnoses in China has been decreasing, which indicating that the prevention and control of the epidemic situation in China has made a periodic progress. On 11 March, however, the number of COVID-19 cases outside China increased 13 times, the number of countries involved has tripled, exceeded 118,000 in 114 countries and more than 4,000 people dead, so World Health Organization (WHO) declared COVID-19 a pandemic [4]. Until April 4, 1,040,772 cases had been diagnosed outside of China, among which, any of the cumulative number of diagnoses in the United States, Italy, and Spain exceeds 100,000, and the number of deaths has reached 55,698. As a result of the growing epidemic situation abroad and the movement of returnees, the number of imported COVID-19 abroad began to increase. As a result, it is particularly important to strengthen the management of overseas returnees and to curb the further spread of the COVID-19 epidemic.

Shanghai, China, is one of the most important cities for imported people. So, this article aims to study the clinical features and imaging findings of both domestic and overseas imported cases diagnosed in our hospital, in order to provide assistance for early diagnosis and prevention the control of epidemic situation.

Materials and Methods

Study design and inclusion population

By cross-sectional study, COVID-19 patients diagnosed in the fever clinic of Zhoupu Hospital, Pudong New District, Shanghai from January 23, 2020 to March 23, 2020. All patients were diagnosed in accordance with “China National Health Commission, Diagnosis and treatment of pneumonia caused by novel coronavirus infection (version 6 (February 18, 2020) and version 7 (March 3, 2020))”. According to the patient's epidemiology history, the patients were divided into domestic cases and imported cases.

The basic information of patients is counted by electronic medical record system, including the general clinical manifestation, the history of contact, the results of laboratory examination, the imaging (chest CT) performance, the time for came to Shanghai, the time of onset to visit the doctor and the place of origin of the imported personnel abroad, etc. All enrolled patients provided their informed consent.

Statistical analysis

The statistical software SPSS 25.0 was used for summary analysis. The data that met the normal distribution after normality test were expressed in means ± standard deviations, and t-test was used to compare differences between groups; the data with non-normal distribution were expressed in medians and interquartile range, and non-parametric tests were used for comparison; χ^2 test was used for paired count data. A two-tailed $P<0.05$ was considered statistically significant.

Results

We collected a total of 23 COVID-19 patients, including 11 domestic cases (47.8%) with an average age of 40.73±11.32 years; 12 overseas imported cases (52.2%) with an average age of 30.83±13.18 years. Overseas imported cases were younger but do not have statistically significance (P=0.067). Most of the domestic cases have the history of living in Wuhan (7/11), while 4 of the overseas

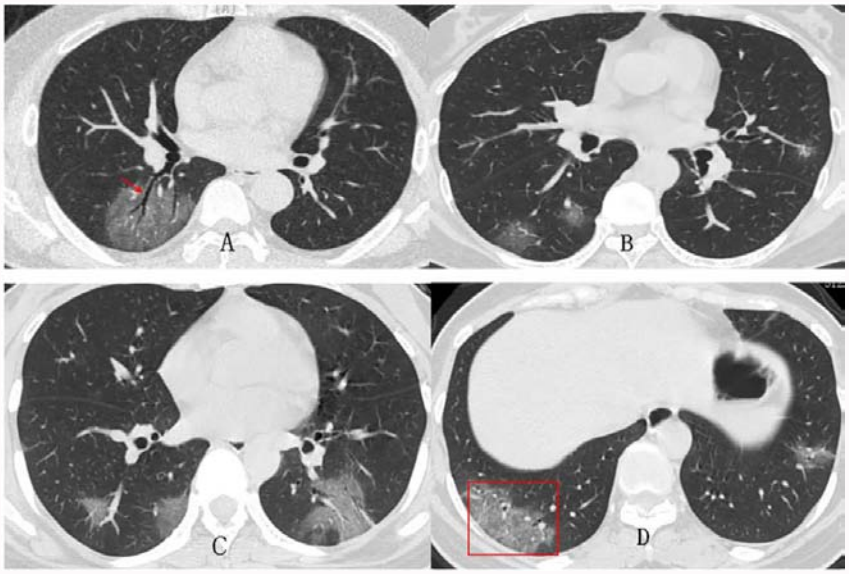

Figure 1: Domestic confirmed cases: 35-year-old male, fever, fatigue for 2 days, CT shows the right lower lobe Ground-Glass Opacity (GGO) (red arrow) under the pleura, with bronchial inflatable sign (**A**); 64-year-old female, fever for 1 day, CT shows double multiple Ground-Glass Opacity (GGO) with halo sign around (**B**); with air bronchioles sign and vessel thickening (**C**); 45-year-old female, with fever, fatigue and sore throat for 2 days, CT shows multiple Ground-Glass Opacity (GGO) with mesh-like changes, similar to the "crazy-paving pattern" (red box) (**D**).

imported cases came from the United States, 2 from the United Kingdom, 2 from Spain, 2 from Italy, 1 from Switzerland and 1 from Burkina Faso.

No clinical manifestations of dyspnea were found in the two groups of patients, and there is no obvious statistical significance in fever (*P*=0.08; 95% CI -0.045~0.696), cough (*P*=0.863; 95% CI -0.489~0.453), runny nose (*P*=0.350; 95% CI -0.380~0.228), Sore throat (*P*=0.606; 95% CI -0.377~0.225), no difference in blood white blood cell count (*P*=0.145) and lymphocyte count (*P*=0.747) between the two groups. However, there are fewer patients with fatigue symptoms (*P*=0.004; 95% CI 0.201~0.905) and lower plasma C-Reactive Protein (CRP) (*P*=0.030 95% CI 0.519~9.389) in imported cases than domestic cases (Table 1).

Imaging findings

We compared and analyzed the imaging features of both domestic and overseas imported cases, indicating that the chest CT findings were similar to each other. Both of the two groups were mainly shows patchy Ground-Glass Opacities (GGO) and consultation shadows, and they were mostly distributed along the broncho-vascular bundles, sub-pleural space, with the selected leaflet interval and the selected circular septum, showing "crazy-paving pattern" and vascal bundle sign; some patients shown isolated nodular lesions with halo signs in subpleural space (Figure 1 and 2).

The difference is that more cases (6/12) of overseas imported cases have no abnormalities in chest CT.

Discussion

At present, most studies show that most COVID-19 patients have fever with or without respiratory symptoms at the beginning of the onset, and a small number of patients' fever are not obvious on the onset. In addition, some patients only have cough (dry) or without any symptoms considered as asymptomatic infection. While severe cases develop into respiratory failure, even Acute Respiratory Distress Syndrome (ARDS) and/or shock [5,6].

As of 23 COVID-19 patients with fever, cough as the main clinical manifestations, none of them had dyspnea. Among the 12 imported case, 2 (16.7%) were asymptomatic infection, and imported case with lower C-Reactive Protein (CRP). Since the outbreak of a wide range of foreign outbreaks, all returnees in China have taken isolation observation at the first time and collected nasopharyngeal swabs for nucleic acid detection. So the patients are either in the incubation period or early mild stage. It has been reported that most patients have dyspnea during the advanced stage of the disease, and a few patients will have hemoptysis, diarrhea and other manifestations [7,8].

Comparing the imaging findings of the two groups of patients, whether imported cases or domestic cases, both characterized with subpleural multiple Ground-Glass Opacities (GGO) or solitary nodules. A few patients could be accompanied by halo nodules or "crazy-paving pattern", and some of the vascular thickening manifestations could be seen [9]. Some difference is that 6 (50%) of the 12 patients imported case showed negative imaging findings, which may because it is in the early stage of the disease. Domestic scholars followed and observed the transition process of chest CT in 25 patients with mild symptoms, confirmed that the chest CT generally began to be positive in the 5-6 days after the no set of clinical symptoms, showing patchy Ground-Glass Opacities (GGO) with unclear borders. With the progress of the lesion, after another 5-7 days, the lesion density gradually increased, and the infiltration developed from the center of the lesion to the periphery. The peak time of CT lesions will reached on the 10th to 13th days after the onset of symptoms. At this stage, chest CT shows a high-density solid transformation and maintained for a period of time before entering the stage of outcome repair [10].

To sum up, the clinical and imaging manifestations are not typical weather in domestic case nor imported case in the early stage of COVID-19. In addition, there are more asymptomatic infections among imported case. Therefore, since February 26th,

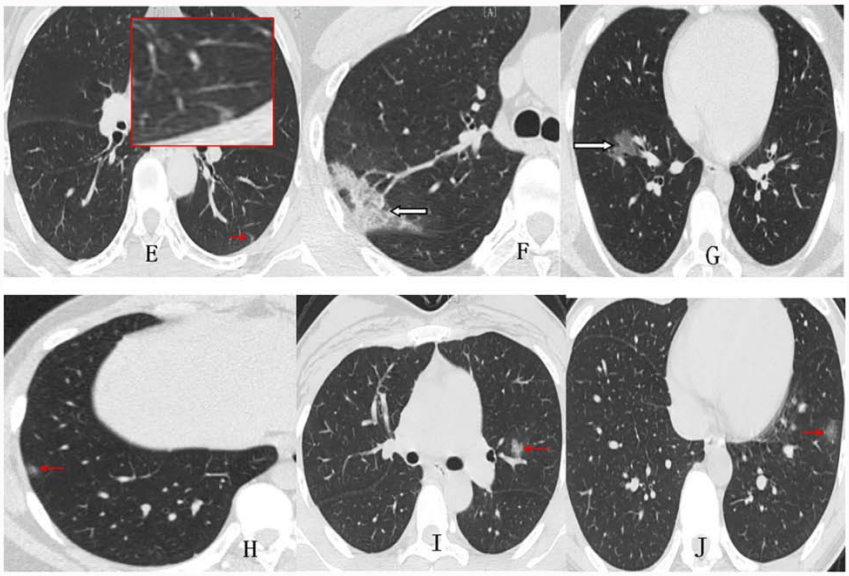

Figure 2: Imported cases: 50-year-old female, 2020.3.11 From Milan, Italy, *via* German transfer to Shanghai, China, fever for 1 day, CT shows subpleural Ground-Glass Opacity (GGO) with halo sign in the lower left lobe (**E**), subpleural Ground-Glass Opacity (GGO) in the posterior segment of the right upper lung with "crazy-paving pattern" and local vessel thickening (**F**); 18-year-old male, from Chicago, USA, *via* Taipei, to Shanghai, 2020.3.17, The patient was transferred from the isolation point by ambulance for cough 6 days, CT shows Ground-Glass Opacity (GGO) in the lower lobe of the right lung (**G**), subpleural nodule shadow with halo sign (**H**); 27-year-old female who came from London, UK to Shanghai, cough and fever for 1 day, from the self-isolation point transferred by the ambulance to see the doctor. The CT shows Ground-Glass Opacity (GGO) in the upper lobe of the left lung (**I**), the Ground-Glass Opacity (GGO) in the lower lobe of the left lung, with halo sign, and the "crazy-paving pattern "can be seen (**J**).

with the effective control of the epidemic in Shanghai, China, has issued relevant requirements for strengthening entry management and strict control measures to shift the focus of epidemic prevention and control to prevent the spread of imported cases (http://wsjkw.sh.gov.cn/xwfb/20200226/e06f8822ff8f45a79ce2b81cc6b60735.html). All immigrants conduct preliminary screening at the airport, including nasal and pharyngeal swab novel coronavirus nucleic acid testing for people from countries and regions with severe epidemics. All immigrants enter the designated isolation point for 14-day medical observation. During the designated isolation point, the immigration personnel are inspected by medical staff every day and the body temperature is monitored twice a day. For the immigration personnel with clinical symptoms (any symptoms of subjective discomfort), ambulance is arranged to transferred the COVID-19 to screening hospital for further medical examination. Strict COVID-19 prevention and control measures allow imported cases to be diagnosed and treated as soon as possible. This is also the main reason why the clinical and imaging performance of the 12 imported cases reported in this report is different from that of domestically diagnosed patients.

There are still some limitations in this study: (1) this paper is a single-center study with a small number of cases, which requires further big data or multi-center study under the premise of uniform norms; (2) failure to further track the correlation between clinical manifestations and chest CT manifestations of patients during the disease progression.

Conclusions

Both domestic or overseas imported cases, in the early stage of COVID-19 patients, its clinical manifestations and imaging manifestations are not typical. At present, China's domestic epidemic situation has made periodic progress, the main confirmed cases are imported cases from abroad, with the spread of the overseas epidemic, prevention and control work has entered a critical stage. We must resolutely block and prevent the repeated spread caused by imported cases. In addition, for the rapid spread phase of the global epidemic, all countries should establish early control of imported cases abroad, and the Chinese experience may provide some help.

Author Contribution

Ling Peng Yu-Zhong Zhou and Chao Zhou conceived and coordinated the study, designed, performed and analyzed the experiments, wrote the paper. Xiao-Ning Li, Fei Xue, Ya-Fang Miao carried out the data collection, data analysis, and revised the paper. All authors reviewed the results and approved the final version of the manuscript.

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