

Clinical findings in a patient with haemophilia A affected by COVID-19

To the Editor,

At the end of 2019, a cluster of pneumonia patients were confirmed to be infected with a novel coronavirus, known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), in Wuhan, Hubei Province, China. This infectious disease was designated as coronavirus disease 2019 (COVID-19). It rapidly spreads throughout the world. More than 80 000 cases have been reported in China and epidemics have grown in other countries.¹ However, minimal information is available regarding COVID-19 patients with haemophilia A. Herein, we retrospectively analysed the epidemiological, clinical, laboratory and radiological characteristics, treatment and clinical outcomes of an infected patient with haemophilia A in Wuhan. This case report may be a good example for the management of mild COVID-19 cases with haemophilia A.

1 | CASE REPORT

On 22 January 2020, a 35-year-old man with a history of haemophilia A presenting with 2-day fever came to an emergency department in Wuhan, China. He was diagnosed with severe haemophilia A at 1-year old with FVIII: C 0.7%. He had no history of inhibitors and received factor replacement therapy on demand with low dosage. Haemophilic arthropathy developed in his left knee joint with joint stiffness. The patient had no other underlying disease apart from a history of haemophilia A with his left knee as a target joint.

The patient described that before the onset of fever, aching pain developed in his limbs on 19 January 2020. Considering the underlying bleeding disorder, human coagulation FVIII (Conspin, 400 IU) was administered as usual at home, but his myalgia complaint remained unchanged. The next day (20 January 2020), he felt fatigue and presented with repeated low-grade fever with chills, recurrent vomiting and anorexia. The patient suspected that he might have infections with some bacteria, so he took oral amoxicillin and Chinese traditional medicines for 2 days on his own. However, his symptoms did not improve substantially. He disclosed that his mother developed fever and dry cough prior to his onset of symptoms and her condition had continued to worsen. The other family members also developed fever later except for his 3-year-old son. He decided to seek medical treatment because of suspicion of COVID-19.

The patient stated that he had never been out of Wuhan recently and denied a history of exposure to the Huanan Seafood Market. Given the history of his household members with fever

or history of fever, he was triaged to a fever clinic exclusively for patients with suspected SARS-CoV-2 infection. After waiting for approximately 5 hours, he was placed in a dedicated consultation room and underwent an examination by a physician. According to the records of physical examination, the vital sign of the patient revealed a body temperature of 38.2°C, pulse of 96 beats per minute, respiratory rate of 15 breaths per minute, blood pressure of 108/82 mm Hg and oxygen saturation of 96% breathing ambient air. Breath sounds were normal to auscultation. Chest computed tomography (CT) was performed and the CT images revealed ground glass opacities located in the right lower lobe of his lung. The laboratory results showed normal values of neutrophil count ($2.52 \times 10^9/L$), monocyte count ($0.23 \times 10^9/L$), haemoglobin (137 g/L) and platelet count ($214 \times 10^9/L$), but leukopenia (white blood cell count, $3.64 \times 10^9/L$), lymphopenia (lymphocyte count, $0.85 \times 10^9/L$), elevated plasma C-reactive protein (CRP, 12.6 mg/L) and serum amyloid A (SAA, 37 mg/L). Oropharyngeal swab samples were negative for influenza A and B viral antigens. Nucleic acid detection of SARS-CoV-2 was reported later as positive using his oropharyngeal swab by real-time reverse-transcriptase polymerase chain reaction (RT-PCR). At this time point, dyspnoea developed while he increased his physical activity. However, the patient was not admitted to the hospital because of limited wards where only critically ill cases were allowed. Uncomplicated COVID-19 patients are managed as outpatients.

Since he was confirmed to be infected with SARS-CoV-2, he was treated with intravenous immunoglobulin (5 g/d) for 2 days in the outpatient clinic. After the infusion ended, he was discharged to home isolation with active monitoring for clinical condition online by the local community health workers. He further received oral administration of antiviral agents (oseltamivir), empiric antibiotic (cef-dinir) and Chinese traditional medicines (Lianhua Qingwen capsules) for 6 days at home. On the 3rd day of treatment (day 7 of illness, 25 January 2020), the patient's appetite remarkably improved and other encountered symptoms resolved, including myalgia, vomiting and chills. On the 5th day of treatment (day 9 of illness, 27 January 2020), his body temperature returned to normal, but he reported that dry cough remained unchanged and chest pain developed in his right lung when breathing deeply. Dry cough, dyspnoea and chest pain alleviated gradually and vanished 2 weeks later. This patient never reported any hemoptysis. As of 10 March 2020, this case was asymptomatic and bleeding events did not increase more than usual during the follow-up period.

Unfortunately, owing to the isolation measures and inconvenience of traffic in Wuhan city, the patient has been isolated in his home since 23 January 2020 and from then on, no additional follow-up was available regarding his respiratory signs, the change of his chest imaging characteristics and the alteration of laboratory results, especially coagulation function and viral load.

2 | DISCUSSION

More recently, the rate of new cases outside of China has outpaced than inside of China, which can be characterized as a pandemic. Since the first report of these cases, more than 375 000 cases have been reported throughout the world and up to one-seventh of them came from Wuhan, a city of Hubei Province in China.² The epidemic in China peaked between late January and late February 2020. The infection for this patient's case occurred in this period and despite the special feature of his underlying severe haemophilia A, his clinical course is typical among the susceptible populations in Wuhan.

This patient's clinical history supports that the mode of transmission was likely person-to-person transmission. Adults of middle age and older are most likely to be affected while symptomatic infection in children appears to be relatively uncommon.³ Clinical features of this family conformed to the above characteristics. The most common features at the onset of COVID-19 were fever, fatigue, myalgia, anorexia, dry cough and dyspnoea. Pneumonia appeared to be the most frequent manifestation of infection, characterized by different degrees of lung involvement on chest imaging.⁴ Additionally, gastrointestinal symptoms including nausea, vomiting and diarrhoea were relatively uncommon.⁵ In terms of laboratory results of infection, lymphopenia appeared to be most common, although the white blood cell count could vary.⁶ Some inflammatory markers were affected by complicated factors. Moreover, SARS-CoV-2 infection was associated with coagulation activation with prolonged prothrombin time.⁷ Oropharyngeal swab was suitable as samples for patients with haemophilia A rather than nasal swabs. Fortunately, the case herein presented with mild pneumonia and no bleeding events occurred.

This case report showed a recovery course of mild COVID-19 with no bleeding events under active treatment at home with antiviral agents, empirical antibiotics and supportive therapies, which may be a good example in home management. According to the product information for oseltamivir and cefdinir, adverse events of bleeding are not described. It seems that his haemophilia may not impact his ability to receive antimicrobial treatment. Haemophilia affects individuals lifelong. In patients with haemophilia with bleeding or suspected bleeding, the immediate goal is to raise the factor activity to a level sufficient to achieve haemostasis.⁸ They do know when they have to receive administration of replacement factor. Moreover, when other health risks emerge, early replacement therapy is often thought to be beneficial. In China, many have access to potent prescription drugs at home, resulting in a different regime at home than in the hospital. For example, as for discomfort with myalgia in limbs at the onset of COVID-19 in this case, it would be more likely the

occurrence of bleeding events because of the underlying bleeding disorder rather than infection of unknown cause. This case may benefit from the administration of FVIII at the onset of COVID-19 that results in zero bleeding events. Moreover, home management with active monitoring is appropriate for mild infected cases with haemophilia when they are adequately isolated at home. Importantly, if clinical conditions deteriorate, the patient should promptly be hospitalized.

In conclusion, clinical manifestations and outcomes of this mild COVID-19 patient with haemophilia were similar to that in non-haemophilic individuals. Mild infection of SARS-CoV-2 may not increase the occurrence of bleeding events in haemophilic cases. And such cases may benefit from administration of replacement factors at the onset of COVID-19. Despite the insufficient clinical investigation of these cases, the success of this case reveals that home management may be possible for them.

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