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Letter to the editor

SARS-CoV-2 infection presenting with hematochezia

Infection à SARS CoV 2 et hématochézie

ARTICLE INFO

Keywords:
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1. Introduction

The newly emergent coronavirus (2019-nCoV, now known as SARS-CoV-2) was first identified in Wuhan in December 2019 and spread rapidly to all provinces and cities in China [1]. Current research suggests that efficient transmission of SARS-CoV-2 from infected individuals (both symptomatic and asymptomatic) to uninfected contacts can result from respiratory droplets, aerosols, and direct contact. Other routes, including the fecal-oral and mother-to-child vertical transmission, have not been confirmed. The main clinical symptoms of SARS-CoV-2 infection (known as COVID-19) are fever, fatigue, and cough leading to pneumonia that can develop into acute respiratory distress syndrome [2,3]. There are currently several documented cases of patients diagnosed with COVID-19 that had digestive findings as the first sign of disease [4]. We present a case of COVID-19 that presented to our hospital with a chief complaint of hematochezia.

2. Case report

An 83-year-old man presented with chief complaint of dark-red bloody stools. He reported stool volume of approximately 200 mL 2–3 times per day, fatigue, and poor appetite beginning one day prior to presentation. He was admitted to the Gastrointestinal Ward 1 of Luoyang Central Hospital on January 27, 2020 for evaluation and follow-up. At admission the patient was oriented but in low spirits. He was eating and sleeping poorly and was oliguric although no significant weight loss was observed.

On the second day of admission, the patient excreted bloody stools several times during the day. He received initial symptomatic treatment with oral pantoprazole enteric-coated capsule, once a day. Abdominal computerized tomography (CT) scan performed on the third day of admission suggested the presence of a space-occupying lesion at the right adrenal gland; the diagnosis of adrenal tumor was considered. As the patient was elderly and not specifically symptomatic, follow-up observation was recommended. A magnetic resonance imaging (MRI) examination revealed abnormal signals within the seminal vesicle, suggesting the possibility of internal hemorrhage; follow-up prostate MRI was recommended.

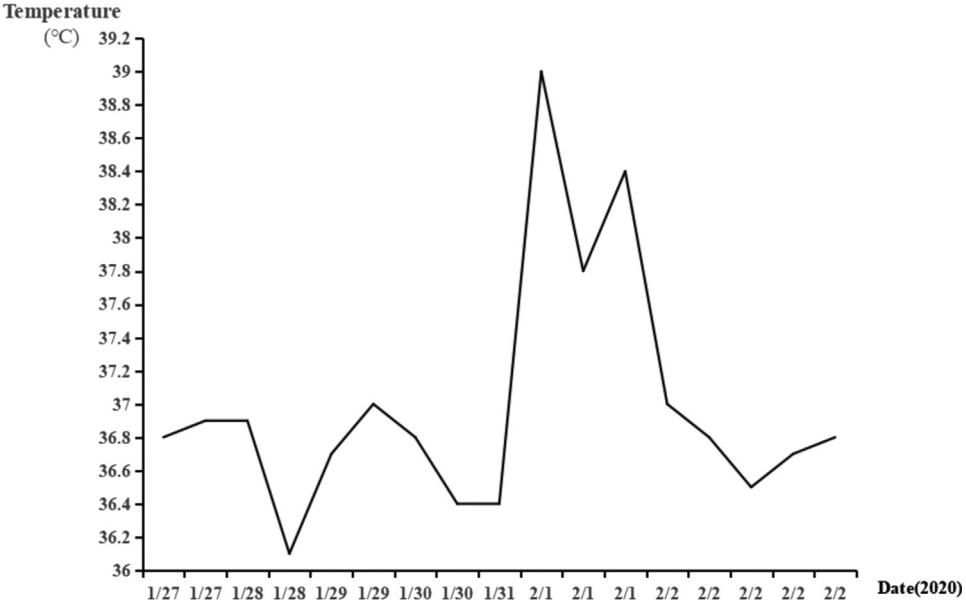

Fig. 1. Body temperature during hospital admission.

Table 1
Laboratory data including complete blood count (CBC).

Measure	Reference range	Hospital day 1	Hospital day 6
White blood cell count (109/L)	3.5–9.5	6.62	5.15
Red blood cell count (10^{12}/L)	10–12	3.77[a]	3.66[a]
Absolute neutrophil count (10^9/L)	1.8–6.3	5.61	4.42
Absolute lymphocyte count (10^9/L)	1.1–3.2	0.73[a]	0.36[a]
Platelet count (10^9/L)	125–350	122[a]	81[a]
Hemoglobin (g/L)	130–175	115[a]	110[a]
Hematocrit (%)	40–50	34.6[a]	32.4[a]
C-reactive protein (mg/L)	0–10	/	21.78[b]
Procalcitonin (ng/mL)	0–0.5	/	0.53[b]
Type B natriuretic peptide (pg/mL)	0–100	49.44	108.7[b]
Fibrinogen (g/L)	2–4	1.83[a]	2.89
Prothrombin time (s)	9–13	13.7[b]	10.8
International normalized ratio	0.76–1.24	1.21	0.96
Activated partial prothrombin time (s)	20–40	26.7	32.7
Thrombin time (s)	14–21	15.5	14.7
D-Dimers (ng/mL)	0–550	220	1.100[b]

[a] Values below normal range.
[b] Values above normal range.

Colonoscopy was also recommended to clarify the acute colorectal findings and to identify the source of bleeding.

On the fifth day of admission, the patient's condition remained stable. Colonoscopy revealed three polyps in the colon, but no tumors or hemorrhagic sites were identified. Therefore, hematochezia secondary to infection was considered. On this same day, the bloody stools disappeared, but the patient suddenly developed a fever, with peak body temperature measured at 39 °C (Fig. 1). The patient denied any symptoms including chest tightness, cough, expectoration, or dyspnea. The physical examination on this day was notable for bilateral rough breath sounds and moist rales in the lower right lung. He was treated with dexamethasone injection, and the fever disappeared.

Laboratory tests on and during admission revealed a white blood cell count within the normal range, but the number of lymphocytes and platelets as well as red blood cell count, hemoglobin, and hematocrit levels all decreased gradually during the hospital stay (Table 1). The rapid antigen test was negative for both influenza A and B and blood cultures were negative. On hospital days six and seven, throat swabs obtained from the patient tested positive for SARS-CoV-2 by real-time RT-PCR. CT scan images on admission showed no abnormality (Fig. 2), but when repeated on the fifth day after admission, the CT scan revealed infiltrates in the lower right lung (Fig. 3).

Upon questioning, the patient disclosed his granddaughter had contact with people who had returned from Wuhan. This contact took place on January 23, 2020 and lasted for approximately 30 minutes. At that time, his granddaughter had no symptom, although his daughter had developed a fever but did not have any sign or symptom of pneumonia.

Based on the epidemiological history, detection of SARS-CoV-2 by real-time RT-PCR, and the chest CT scan findings, the patient was diagnosed with COVID-19. On his seventh day of admission, he was transferred to the first affiliated hospital of Henan University of Science and Technology for further evaluation and treatment.

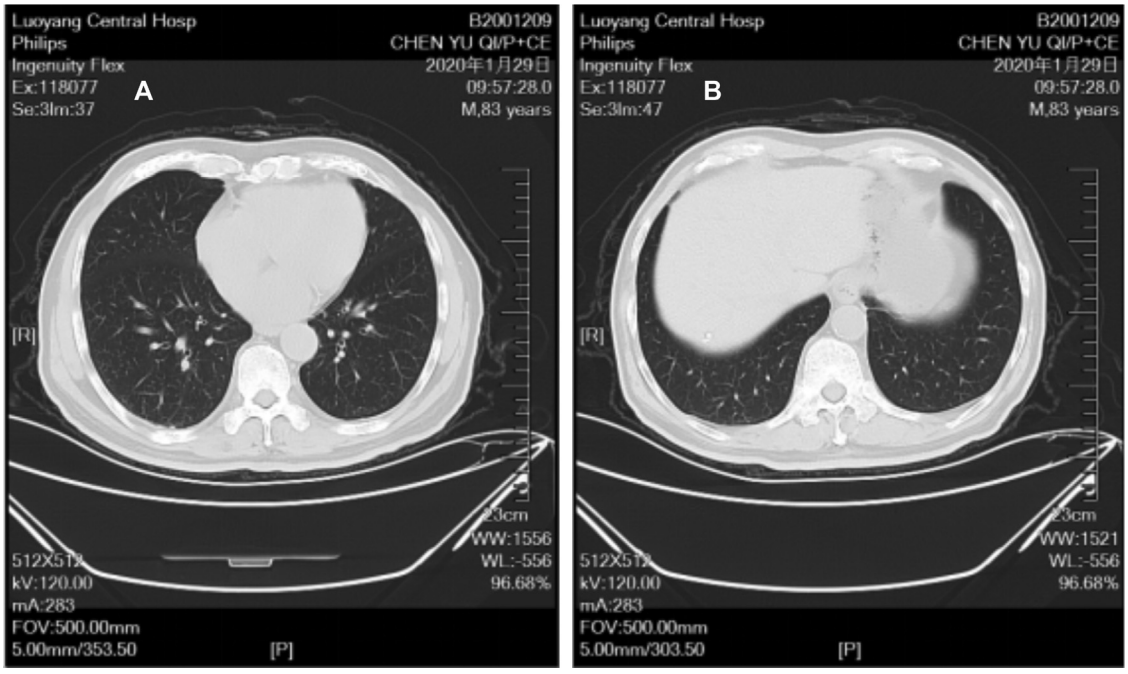

Fig. 2. A and B. On January 29, computerized tomography (CT) scan images revealed no acute intrathoracic abnormalities.

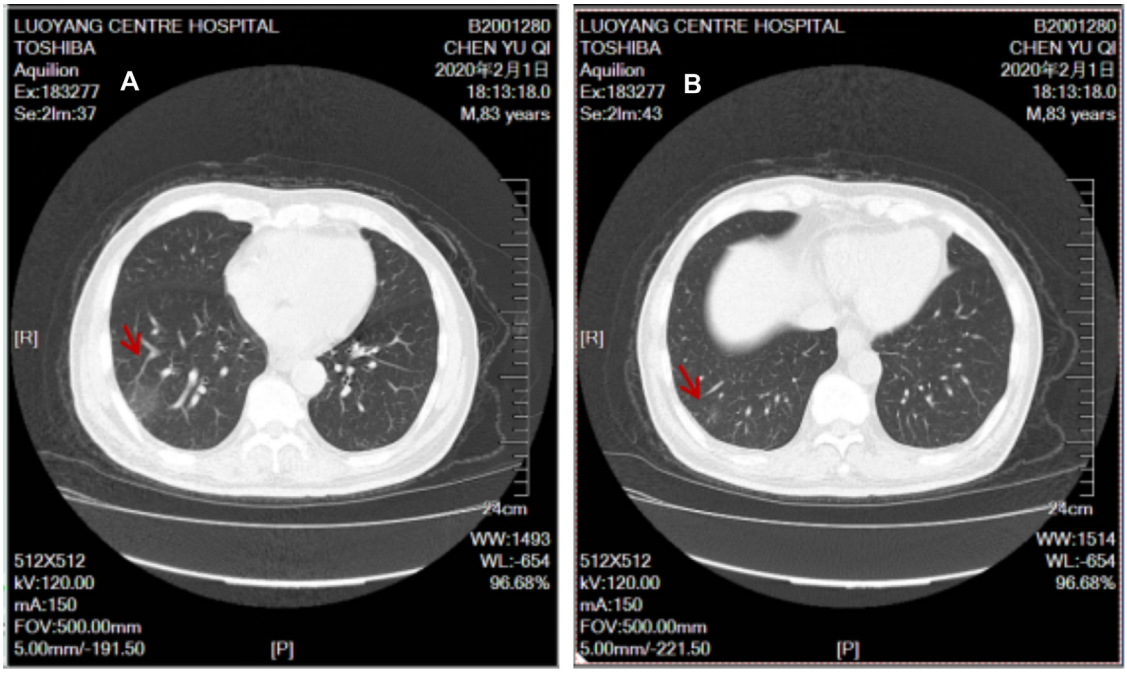

Fig. 3. A and B. On February 1, computed tomography (CT) scan images revealed a single ground-glass opacity in the right lower lung lobe.

3. Discussion

The patient was an 83-year-old man who developed hematochezia three days after indirect contact with individuals returning from Wuhan. Nine days later, he developed fever and lung inflammation with throat swabs that tested positive for SARS-CoV-2. As such, he was diagnosed with COVID-19. No source of bleeding was identified by colonoscopy or abdominal CT scan and as such, we considered the possibility that hematochezia might be secondary to infection with SARS-CoV-2 pathogen. Unfortunately, we did not determine whether SARS-CoV-2 could be detected in stool specimens, which may have provided further direct evidence in this case. At this writing, there are several reports of diarrhea associated with the presentation of SARS-CoV-2 infection [4], but to the best of our knowledge, this is the first report of hematochezia as the presenting symptom and chief complaint.

Upon diagnosis, the patient was transferred to the first affiliated hospital of Henan University of Science and Technology, and as such we have no additional follow-up information.

Six days after the patient left our hospital (February 7, 2020), another 63-year-old male patient – who had been on the same ward with underlying diagnoses of intestinal obstruction and postoperative recurrence of rectal carcinoma – developed fever and was also diagnosed with COVID-19. The ward was emptied and sterilized repeatedly; the Center for Disease Control (CDC) collected samples from numerous surfaces including the desktop, bed sheets, and quilt covers. SARS-CoV-2 was detected on these surfaces even after repeated attempts at sterilization. These results suggest that these patients may have carried high viral loads.

Taken together, our findings with respect to this case patient suggest that fever and respiratory findings may not be the only presenting signs and symptoms of SARS-CoV-2 infection. Presentations including diarrhea and hematochezia may be secondary to an alternate point of entry. This point needs to be clarified as quickly as possible.

Human and animal rights

The authors declare that the work described has been carried out in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans as well as in accordance with the EU Directive 2010/63/EU for animal experiments.

Informed consent and patient details

The authors declare that this report does not contain any personal information that could lead to the identification of the patient(s) and/or volunteers.

Disclosure of interest

The authors declare that they have no competing interest.

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Author contributions

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

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Une spondylodiscite à *Aspergillus* chez un patient traité par ibrutinib

Aspergillus spondylodiscitis in a patient treated with ibrutinib

INFO ARTICLE

Mots clés :
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1. Introduction

L'ibrutinib est un inhibiteur de *Bruton's tyrosine kinase* (BTK) ayant récemment révolutionné la prise en charge des syndromes lymphoprolifératifs B indolents, au premier rang desquels la leucémie lymphoïde chronique (LLC) [1]. L'emploi de ce traitement est associé à une augmentation du risque infectieux global et plus particulièrement à la survenue d'infections fongiques invasives (IFI) [2]. Nous rapportons un cas de spondylodiscite à *Aspergillus fumigatus* chez un patient traité par ibrutinib pour une leucémie lymphoïde chronique.

2. Présentation du cas

Un patient de 70 ans était hospitalisé en avril 2018 pour un syndrome de compression médullaire (paralysie et anesthésie des membres inférieurs, troubles sphinctériens) dont les premiers symptômes (dorsalgies) avaient débuté deux mois auparavant. Il avait pour principal antécédent une LLC diagnostiquée en 2008 et traitée entre 2013 et 2017 par chloraminophène. En août 2017, le traitement avait été modifié pour de l'ibrutinib à la posologie de 420 mg/jour, associé à une seule perfusion initiale de rituximab. À l'admission, l'imagerie par résonance magnétique (IRM) du rachis objectivait une spondylodiscite T10–T11 avec épidurite compliquée de compression médullaire. Une laminectomie T10–T11 était réalisée en urgence. La culture mycologique du prélèvement osseux réalisé en peropératoire isolait *A. fumigatus* et l'examen histologique identifiait des filaments mycéliens aspergillaires. L'ensemble des autres examens microbiologiques réalisés sur le matériel opératoire était négatif. L'antigénémie aspergillaire était positive à 1,260 (pour un seuil de positivité de 0,5). Le bilan immunitaire mettait en évidence une hypogammaglobulinémie à 2 g/L, sans leucopénie ni lymphopénie, et la sérologie VIH était négative. Un traitement par voriconazole à la dose de 400 mg/jour en deux prises per os était instauré. Compte-tenu de l'interaction pharmacodynamique entre le voriconazole et l'ibrutinib, la posologie de ce dernier était réduite à un tiers. De plus, une substitution par immunoglobulines polyvalentes était associée au voriconazole. Secondairement, devant la persistance de la fièvre sous traitement, un scanner thoracique objectivait un épanchement pleural gauche cloisonné, contigu à l'atteinte vertébrale, sans lésions parenchymateuses pulmonaires pouvant faire évoquer une aspergillose pulmonaire. Le drainage de cet épanchement, dans lequel l'antigène aspergillaire était fortement positif (3,422) alors que la culture restait stérile, permettait la régression du syndrome infectieux. Le traitement par voriconazole était prescrit pendant 6 mois à dose curative puis poursuivi à dose prophylactique. Au terme du traitement curatif, l'évolution était favorable tant sur le plan infectieux que neurologique.

3. Discussion

L'ibrutinib est un inhibiteur irréversible de BTK, une enzyme impliquée dans la voie de signalisation du *B-cell receptor* (BCR). BTK joue ainsi un rôle physiologique important dans la prolifération et la survie des lymphocytes B en réponse à la reconnaissance de l'antigène. L'hyperactivation de cette voie BCR/BTK occupe une place centrale dans la physiopathologie de la LLC [3].

L'ibrutinib a démontré sa supériorité au cours de la LLC par rapport aux traitements standards de type chimio-immunothérapie, avec de plus un effet immunosuppresseur considéré comme moindre [1]. Néanmoins, une augmentation du risque infectieux sous ibrutinib est avérée [2]. Depuis la mise sur le marché de l'ibrutinib sont décrits plus spécifiquement des cas d'infections fongiques invasives et en particulier d'aspergilloses invasives. Une étude rétrospective conduite dans 16 centres français relevait, entre 2013 et 2017, 33 cas d'IFI chez des patients traités par ibrutinib, dont 27 cas (82 %) d'aspergillose invasive [4]. Ces cas d'aspergilloses concernaient principalement le poumon (25/27 soit 93 %) mais aussi, et de façon frappante, le système nerveux central (SNC) (11/27 soit 41 %). La majorité des patients présentait un ou plusieurs facteurs de risque d'aspergillose invasive associé (neutropénie, corticothérapie, chimiothérapie concomitante ou dans les six derniers mois). La survenue des IFI était précoce après l'instauration de l'ibrutinib (temps médian de 3 mois). Ruchlemer et al. ont décrit une cohorte de 28 IFI survenues sous ibrutinib, dont 18 aspergilloses invasives, avec une proportion élevée de localisation cérébrale (46 %). Le délai médian de survenue de l'infection était de 60 jours après l'initiation de l'ibrutinib [5].

L'analyse des cas rapportés montre qu'il n'existe pas d'attitude consensuelle quant à la poursuite ou l'arrêt de l'ibrutinib chez ces patients, bien que cette dernière attitude soit le plus souvent adoptée [4,5]. Après discussion avec l'hématologue en charge du patient, il a été décidé de poursuivre l'ibrutinib sous couvert d'une supplé-