Bilateral Infiltrates: Not Only COVID-19

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During December 2019 dozens of pneumonia cases with an unknown etiology were reported from the Hubei province of the Republic of China. These cases turned out to be the initial presentation of the coronavirus disease-2019 (COVID-19) epidemic [1]. As of 1 May 2020, according the World Health Organisation, there were more than 3 million confirmed cases and more than 200,000 deceased worldwide from the disease. The global implications are massive in terms of public health, psychological effects, economic damage, and uncertainty. The epidemic has affected people's lives around the globe.

The presenting symptoms of COVID-19 are vague. They include fever, cough, and fatigue [2]. Other less frequent symptoms are headache, diarrhea, and dyspnea [2]. Blood counts of COVID-19 patients usually show leukopenia and lymphopenia and typical findings on chest imaging are bilateral infiltrates [2]. Thus, the clinical presentation of COVID-19 is not easily differentiated from other diseases that can exhibit similar symptoms.

One of these diseases with similar presentation is microscopic polyangiitis (MPA), a member of the antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) syndromes. The clinical characteristics of MPA are varied and may involve multiple organ damage. The initial presentation is usually nonspecific, including signs of systemic inflammation such as weight loss, loss of appetite, and low-grade fever. One of the possible acute presentations of MPA is diffuse alveolar hemorrhage (DAH), which can manifest as non-specific respiratory complaints. In a review paper that analyzed several retrospective studies, Villiger and Guillevin [3] found that the kidneys were affected in nearly all patients. Other organs affected included the lungs, gastrointestinal tract, skin, nervous system, and heart.

PATIENT DESCRIPTION

We present the case of a 64-year-old female with known myeloperoxidase (MPO)-ANCA-associated vasculitis, diagnosed in May 2018. After diagnosis, she completed induction therapy with pulse steroids followed by eight courses of intravenous cyclophosphamide (500 mg/m^2) and went into remission. Her maintenance therapy consisted of azathioprine (100 mg/day) and prednisone (5 mg/day). Other medical conditions include essential hypertension and dyslipidemia.

The patient presented to the emergency department with worsening symptoms of cough, dyspnea, and hemoptysis within the previous 3 weeks. She had no additional complaints and was not aware of any contact with suspected or confirmed COVID-19 patients.

On presentation, her vital signs were within normal ranges, except for low oxygen saturation of 91%, without supplementary oxygen. Physical examination revealed crackles over both lung fields.

Laboratory workup showed elevated white blood cell (WBC) count of 13.6×m^3/µl (normal range 4.8–10.8×m^3/µl), low absolute lymphocyte count of 0.48×m^3/µl (normal range 0.90–5.20×m^3/µl), low hemoglobin level of 7.5 gr/dl (normal range 12–16 gr/dl), compared to a previously documented value of 12.1 gr/dl from 6 months earlier, hematocrit 22% (normal range 37–47%), platelets 371×m^3/µl (normal range 130–400×m^3/µl), urea of 90 mg/dl (normal range 17–43 mg/dl), sodium 132 mEq/L (normal range 135–145 mEq/L), potassium 3.3 mEq/L (normal range 3.5–5.1 mEq/L), and impaired renal function with creatinine level of 1.45 mg/dl (normal range 0.5–0.95 mg/dl). Other laboratory findings, including venous blood gas, were all within normal limits. Chest X-ray showed multiple bilateral alveolar infiltrates [Figure 1].

In light of the global COVID-19 outbreak, and given the patient's respiratory complaints, lymphopenia, and suspicious chest X-ray, pneumonia associated with COVID-19 infection was suspected. A nasopharyngeal swab specimen was obtained, and the patient was admitted to a contact isolation unit in an internal medicine department according to the hospital new COVID-19 emergency working guidelines.

After the patient's admission to the isolation unit, a possible diagnosis of diffuse alveolar hemorrhage was suspected due to her medical history. The next diagnostic step would usually include chest computed tomography (CT) scan. However, due to her hemodynamically stable condition and to protect the staff from a possible COVID-19 contagion, it was decided to postpone the CT scan until COVID-19 was ruled out. Meanwhile, she was treated with 125 mg methylprednisolone and one unit of packed red blood cells. During her stay in the isolation unit she completed a urinalysis, which revealed massive proteinuria.

Figure 1. Initial chest X-ray showing bilateral alveolar infiltrates

A COVID-19 swab test result came back negative, and therefore the patient completed a chest CT scan that demonstrated extensive bilateral areas of ground glass opacities consistent with the diagnosis of alveolar hemorrhage. She was then treated with high dose intravenous methylprednisolone pulse therapy (1 g\day) for 3 days, one dose of rituximab (1 gram) and an additional unit of packed red blood cell. She showed clinical improvement and an increase in hemoglobin level. After 5 days of hospitalization in our department she was discharged in a general good condition for further ambulatory surveillance.

COMMENT

Diffuse alveolar hemorrhage (DAH) is a severe clinicopathologic manifestation of many conditions, including ANCA-AAV. It can be serious and even life-threatening in up to 30% of cases and therefore should be diagnosed and treated early. Presentation of DAH is non-specific and may resemble other conditions such as pneumonia or pulmonary edema. Typically, the signs and symptoms of DAH include dyspnea, hemoptysis, cough, hypoxia, and anemia. Initial imaging evaluation usually includes a chest radiograph demonstrating bilateral infiltrations. Further investigations include CT scan, fiberoptic bronchoscopy, and bronchoalveolar lavage. In the setting of AAV high-dose corticosteroids and intravenous cyclophosphamide or rituximab are the main treatments [4].

After the outbreak of the COVID-19 pandemic, great efforts were made and large resources were allocated to quickly identify affected patients, both to provide them with suitable treatment and to isolate them from other people to prevent further spreading of the infection. These measures led to dramatic changes in health systems throughout the world. Elective procedures were canceled, non-emergency clinics were closed, and hospitals established new working protocols for suspected and confirmed COVID-19 patients. Isolation wards were prepared, and medical staff members started working in shifts to reduce the possibility of medical personnel infecting each other. These changes affected the admission patterns of all patients, and particularly patients whose symptoms resembled those of COVID-19. Using the experience gained during the pandemic, it will thus be useful to refine the admissions protocols to improve the diagnosis of these patients.

In this report, we describe a patient with known AAV who presented to the hospital with DAH. Due to her respiratory complaints, she was referred to a special area in the emergency department dedicated to suspected COVID-19 patients. She was evaluated by medical staff members who were fully protected. The possible diagnosis of COVID-19 infection was supported by lymphopenia and presentation on X-ray. A nasopharyngeal swab for the detection of the virus was sent to the laboratory and she was admitted into a contact isolation unit intended for suspected COVID-19 patients until test results are obtained. At the time, the isolation unit lacked advanced monitoring systems. It also maintained minimal contact protocols between patients and medical staff to reduce the risk of medical personnel being infected. Thus, the unit lacked the appropriate monitoring capacities for a patient with DAH who is in critical condition and should be monitored and observed frequently.

Furthermore, the uncertainty of COVID-19 status delayed additional diagnostic procedures such as CT scan or bronchoscopy, which delayed adequate early treatment with high-dose intravenous corticosteroids.

The possible implications of delayed diagnosis and therapy for DAH could be fatal and healthcare professionals should consider alternative diagnoses even during an epidemic such as COVID-19.

There is no doubt of the importance of identifying suspected COVID-19 cases as early as possible avoid further contagion. Meanwhile, it is imperative to address the complaints adequately without endangering the staff and other patients [5].

CONCLUSIONS

Our case highlights that, beyond the direct effects of the COVID-19 outbreak, medical staff members should be aware of the possibility of adverse indirect effects on non-COVID patients, in particular patients whose symptoms resemble those of COVID-19. These patients may receive less efficient treatment than usual protocol due to the extra measures taken to prevent the spread of COVID-19 and public insecurity surrounding the situation.

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