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MISDIAGNOSIS OF A FULMINANT CASE OF PRIMARY CNS LYMPHOMA DUE TO OF COVID-19 OVERDIAGNOSIS

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ABSTRACT

Background: Novel coronavirus disease 2019 (COVID-19) is a pandemic infection that appeared in December 2019, in Wuhan, China. It has been considered as a multi-systemic disease that could involve central nervous system. We intend to report a case of fulminant primary CNS lymphoma (PCNL) misdiagnosed as COVID-19 infection and led to a delay in treatment. **Case presentation:** A 75-year-old female was admitted in our hospital due to altered mental status and mild fever. She had a history of tiredness, headache, and low-grade fever presented within two weeks. Her chest CT scan was apparently compatible with pulmonary involvement seen in COVID-19 and she was treated accordingly. Brain CT scan and MRI showed periventricular hyper-dense changes, diffuse brain edema and periventricular enhancing lesions. CSF analysis and brain biopsy confirmed the diagnosis of PCNL. **Conclusions:** It can be concluded that the in the outbreak of COVID-19 some manifestations of other diseases can be confused and assumed as the signs and symptoms of the pandemic disease and overdiagnosis of COVID-19 may result in missing the others. Although this infection has several faces with the ability to involve multiple organs, it always should be differentiated from the other possible illnesses to prevent devastating complications.

KEYWORDS: Brain tumor, Cancer, COVID-19, CNS, Lymphoma, PCNL.

INTRODUCTION

COVID-19 is known as a multi-systemic disease responsible for hundreds of thousands of deaths till now.[1] Its major clinical manifestations include anosmia or hyposmia, and dysgeusia as well as fever, cough, hypoxemia, dyspnea, respiratory distress, lymphopenia, and cytokine release syndrome.[2] Moreover, COVID-19 may involve the structures in central nervous system (CNS) in different forms. Neurological features of COVID-19 could be due to viral encephalitis, infectious toxic encephalopathy, acute necrotizing encephalopathy[3], and acute cerebrovascular disease.[4] Several mechanisms have been described for neurologic damages. One possible mechanism can be injury to cerebral tissue as a result of chronic inflammation due to immune system hyper-activation.[3,5] CNS symptoms depend on the extent and type of involvement and include headache, dropped level of consciousness, symptoms of meningoencephalitis, etc.[4]

In this study, we intend to report a case of fulminant primary CNS lymphoma (PCNL) in whom overdiagnosis of COVID-19 infection led to misdiagnosis and delayed treatment.

CASE PRESENTATION

A 75-year-old female with a history of controlled hypertension and diabetes mellitus (DM) was admitted to our hospital with altered mental status and mild fever during the pandemic of COVID-19. Patient was good until 2 weeks before admission, when tiredness, headache and low-grade fever started. The pattern of her lung CT scan (patchy ground-glass infiltration) (Figure 1) led the physicians to diagnosis of COVID-19 and pulmonary infection. Treatment was started despite negative RT-PCR amplification test of respiratory specimen. A rapidly progressive headache and generalized tonic seizure developed followed by decreased level of consciousness. Body temperature of 38.5℃, oxygen saturation (SPO2) of 90% despite oxygen therapy with facial mask, blood pressure of 140/90 mmHg, heart rate of 100 bpm, respiratory rate of 15 breaths/minute were other clinical findings. Her eyes were open and she obeyed orders with her hands but she was aphasic. No papilledema was seen in fundoscopy and there was no hemiparesis.

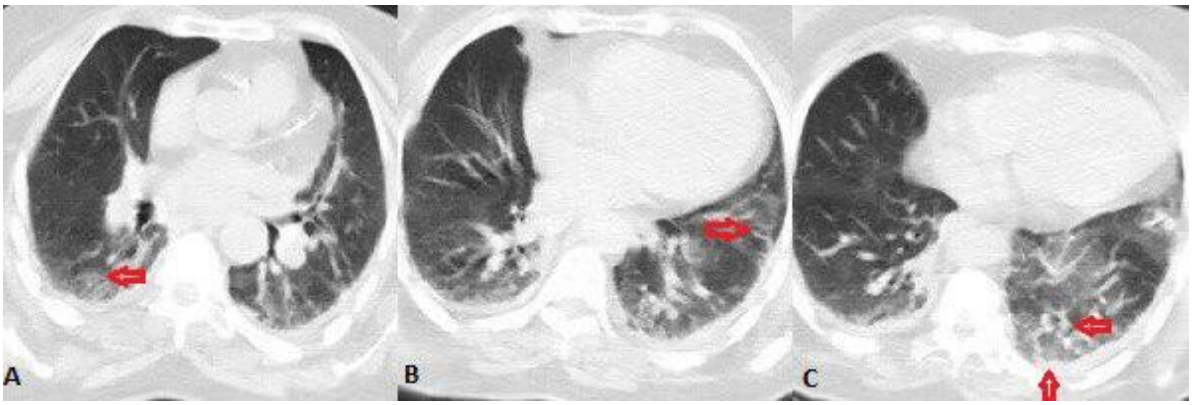

Figure 1: Spiral lung CT scan reveals patchy ground-glass infiltrations in favor of senile pattern which are similar to pattern of COVID-19 (A, B, C, red arrows)

The laboratory tests showed: raised leukocytes (19.0 x 10^9/L), dropped lymphocytes (500 per mm3), normal erythrocyte sedimentation rate (ESR, 29 mm/hour) and elevated C-reactive protein (CRP, 132 mg/L). The second RT-PCR amplification test of SARS-Cov-2 virus nucleic acid was negative again. In the emergency department, brain computed tomography (CT) scan showed diffuse cerebral edema in association with periventricular hyperdensity. Brain MRI showed isointense periventricular edematous lesions in T1-weighted and T2-weighted images, which were homogenously enhanced with an intense thick pattern after contrast injection, typically characteristic of the CNS lymphoma. This can also be misdiagnosed as an inflammatory process by a naive reviewer (Figure 2).

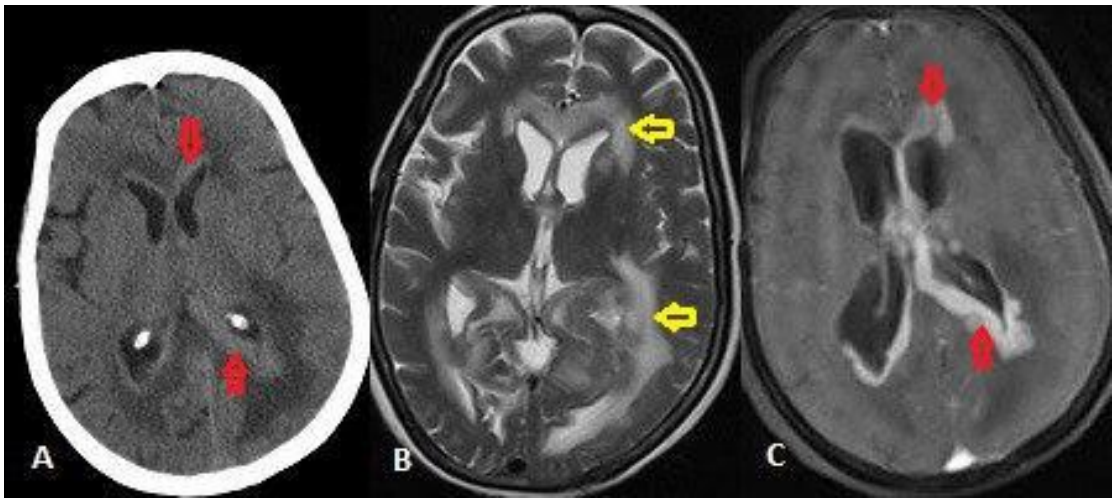

Figure 2: Axial CT scan shows periventricular hyperdense signal changes (A, red arrows), T2-weighted imaging points out the periventricular hyper-intensity in T2 suggesting cerebral edema (B, yellow arrows), T1-weighted imaging after contrast shows the diffuse thick periventricular homogenous enhancement that had surrounded whole lateral ventricles in both hemispheres (C, red arrows).

During the following days, external ventricular drainage (EVD) was inserted after neurological deterioration due to hydrocephalus and CSF sample was also obtained, which was negative for COVID RT-PCR, while the

cytological study confirmed CNS lymphoma. Despite these results, we decided to carry out an open biopsy in the following days. Unfortunately, the patient passed away after a week and brain autopsy revealed primary CNS lymphoma (PCNL) (Figure 3). No evidence of COVID-19 infection was found in autopsy.

Figure 3: pathologic findings of the brain tissues obtaining via autopsy.

DISCUSSION

Primary CNS lymphoma (PCNL) is a rare malignant neoplasm with poor prognosis. Although median overall survival in this type of non-Hodgkin lymphoma (NHL) is estimated to be about 25 months, elderly patients survive for less than 7 months with higher rate of early death (death in less than 4 months).[6]

The prevalence of primary CNS lymphoma (PCNL) rises dramatically in immunosuppressive disorders such as acquired immunodeficiency syndrome (AIDS) or in patients who receive immunosuppressive therapies. The risk is highest in patients older than 60 years, like our case, and aging is known as a predisposing factor to this malignancy.[6,7]

PCNL presents with different manifestations including focal neurologic deficits, psychiatric disorders, etc. In addition, seizure and B symptoms such as weight loss, nocturnal diaphoresis and fever can be seen but these manifestations are relatively uncommon.[6,8] Low-grade fever was evident in this case.

Novel challenging coronavirus was first emerged in December 2019, in Wuhan, China. World health organization (WHO) named it as severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) and the disease was referred to as COVID-19 (2). As COVID-19 was spreading in all countries of the world one by one, new features of this infection were identified. In fact, physicians diagnosed COVID-19 patients who presented not only by respiratory system characteristics but also by multi-system involvement.

Although the immune system is known as a very useful supporting system to resolve the infections, uncontrolled hyper-inflammatory innate responses and impaired adaptive ones could play the role of a foe, which is capable of injuring neural tissues locally or systemically.[9] Accordingly, smelling and taste disturbances, stroke, vessel diseases and encephalitis could occur subsequently.[10]

PCNL symptoms could be mistaken by neurologic findings of the COVID-19 at the early stages. In our patient, fever and headache in association with suspicious lung CT scan pattern obliged internist to treat her as COVID-19 while this case was not infectious. It could be a result of the COVID-19 pandemic that physicians prefer to overdiagnosis it rather than missing it. Hence, overdiagnosis of COVID-19 may lead to miss the main illness, probably resulting in wasting the golden time for treatment.

On the other hand, the pattern of involvement in the brain CT scan and MRI could also mislead a naive physician. Periventricular edema and enhancement can be misinterpreted as an infectious and inflammatory process, while this is only a misdiagnosis. Thick periventricular enhancement in MRI and hyperdense solid intervening mass between ventricles and periventricular edema in CT scan can be considered as strong evidence in favor of lymphoma. Thick and irregular periventricular enhancement is typical for primary central nervous system lymphoma. On the contrary, in infectious ependymitis thin enhancement of the ventricular margin occurs. Classic imaging appearance for primary CNS lymphoma is of a CT hyperdense avidly enhancing mass.[11]

Our case illustrates the fact that neurological manifestations associated with COVID-19 infection are not specific and may be misleading. When looking for evidence of COVID-19 infection in patients presenting with neurological illness, one should consider other possible CNS pathologies with similar imaging characteristics.[12]

CONCLUSIONS

Overdiagnosis of COVID-19 may lead to missing the diagnosis of other probable diseases. Although this infection has several manifestations and is able to involve multiple organs, it always should be differentiated from the other possible problems to prevent devastating complications.

Conflict of interest

The authors declare no conflict of interest.

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