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LETTER TO THE EDITOR

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Acceleration of sporadic Creutzfeldt–Jakob disease progression by COVID requires evidence from appropriately designed studies

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Abstract

The aim of this letter to the editor is to discuss the influence of SARS-CoV-2 infection on the progression of sporadic Creutzfeldt–Jakob disease (sCJD). A 73-year-old male was diagnosed with sCJD based on the clinical presentation, cerebral MRI, FDG–PET, and elevated 14-3-3 in cerebrospinal fluid. One month earlier he had suffered a slight COVID-19 infection. It was concluded that COVID-19 can lead to accelerated pathogenesis and exaggerated manifestations of sCJD.

Keywords SARS-CoV-2, COVID-19, Creutzfeldt–Jakob disease, Prion disorder, Neurodegeneration

To the Editor

Introduction

We read with interest the article by Alloush et al. about a 73-year-old male with sporadic Creutzfeldt–Jakob disease (sCJD) beginning 1 month after mild SARS-CoV-2 infection [1]. The diagnosis of sCJD was based on the clinical presentation, cerebral MRI, FDG–PET, and positive 14-3-3 test [1]. It was concluded that COVID-19 can lead to accelerated pathogenesis and exaggerated manifestations of sCJD [1]. The study is appealing but raises concerns and comments.

Main text

The major limitation of the study is that the diagnosis sCJD was not confirmed by autopsy. Clinical diagnostic criteria of sCJD include a combination of characteristic neuropsychiatric symptoms and signs, elevated cerebrospinal fluid (CSF) proteins 14-3-3, high CSF tau protein, EEG, MRI, and real-time quaking-induced conversion (RT-QuIC) [2], but the definite diagnosis is made by autopsy. The sensitivity and specificity of the tests used do not exceed 92% and 95%, respectively [3].

A second limitation of the study is that the CSF was not tested for SARS-CoV-2 by PCR. A negative nasopharyngeal swab test does not rule out cerebral SARS-CoV-2 infection. A negative PCR for SARS-CoV-2 in the CSF would have ruled out infectious SARS-CoV-2 encephalitis. Immune encephalitis caused by SARS-CoV-2 infection could have been excluded by the absence of antibodies associated with immune encephalitis and normal CSF levels of cytokine, chemokines, and glial factors.

We disagree with the statement that there was a rapid deterioration as the patient died 4 months after the disease onset [1]. The average duration of symptoms in patients with sCJD is 4 months of disease duration [4], so there is no acceleration or worsening of neurological deterioration or shortened survival. At the same time, the study design (case report) is not suitable for the conclusion that when a sCJD patient is infected with SARS-CoV-2, neurological decline is accelerated, worsened and, consequently, overall survival is shortened [1]. From a single patient and the lack of a control group, such conclusions remain unsupported. Whether SARS-CoV-2

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infection actually worsens and accelerates that sCJD needs to be investigated by a multicentre design in patients with autopsy-confirmed sCJD.

Conclusions

Overall, the elegant study has several limitations that put the results and their interpretation into perspective. Addressing these issues would strengthen the conclusions and could improve the status of the study. Before a supportive relationship between SARS-CoV-2 and sCJD can be established, appropriate studies with a prospective, multicentre design need to be conducted. The diagnosis of sCJD must be confirmed by an autopsy.

Abbreviations

CJD	Creutzfeldt–Jakob disease
CSF	Cerebrospinal fluid
MRI	Magnetic resonance imaging
PET	Positron emission tomography

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Declarations

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Consent for publication
Not applicable.

Competing interests
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