# Creutzfeldt-Jakob Disease After the Second Dosage of The Novel Pfizer-Biontech Messenger Ribonucleic Acid (Mrna) COVID-19 Vaccination: A Case Report

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**Abstract**

Uncommon, rapidly progressing, and eventually fatal neurological condition called human prion disease. While most occurrences are sporadic, many can be acquired or inherited. In the current study, we focus on the case of a 63-year-old man who initially had vision problems then exhibits difficulty using his right side for daily activities and who begins to experience frequent falls with gait instability about a week after receiving the second dosage of the novel Pfizer-BioNTech messenger ribonucleic acid (mRNA) COVID-19 vaccination. Confidential findings confirmed the fatal diagnoses of sporadic Creutzfeldt-Jakob disease following a thorough study.

Keywords: Creutzfeldt-Jakob disease, COVID-19, Pfizer-BioNTech, mRNA, vaccine, prion disease.

## 1. Introduction

Human prion disease fall into one of three classifications: sporadic, hereditary, or obtained by infections. They were initially identified in the early 1920s [1]. Fatal insomnia, Creutzfeldt-Jakob disease (CJD), and variable protease-sensitive prionopathy are examples of the sporadic form [2]. About ninety percent of prion disease instances are sporadic CJD, which may be further classified into five categories according to clinical traits, histological observations at autopsies, and aberrant proteins molecular structures. The prevalence of sCJD is extremely low, with around 1-2 incidences per million people [3].

While there are many different types of symptoms associated with sJCD, the most common ones involve cognitive changes (such as dementia), behavioural and attitude abnormalities, problems with movements and coordination, vision problems, and constitutional symptoms [4]. Cognitive issues, which frequently comprise moderate confusions, memory loss, and trouble focusing, organising, or thinking, are among the initial diagnosis of sJCD. Extrapyramidal complaints such bradykinesia, dystonia, and tremor, cerebellar abnormalities like gait or limbs ataxia, and later-stage symptoms like myoclonus are all examples of motor characteristics of sJCD (sudden jerking movements) [5]. Additional typical initial symptoms could be mild, although the cognitive and motor problems are frequently prominent. These include constitutional indications as well as behavioural or mental health difficulties (such as agitation, anxiety, depression, or other personality changes) (i.e., fatigue, malaise, headache, vertigo, lightheadedness, cough, etc.) [6]. Cortical blindness blurred or double vision, or other perceptual issues are common visual complaints that are caused by issues with visual data processing in the brain rather than retinal or cranial nerves disorders. apraxia (difficulty to perform taught motions owing to cortical dysfunctions), neglect, or Aphasia are other complaints that may also exist and could be presenting characteristics [7]. Because of the severity of the other indications (symptoms) in sJCD, sensory complaints like numbness, tingling, and/or pain are less well-recognized and are likely underestimated [8].

It could be difficult to diagnose Creutzfeldt-Jakob disease (CJD), especially in the COVID-19 pandemic period. The majority of individuals with the condition experience sadness, anxiety, nervousness, autonomic problems, disruptions of sleep-

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wakefulness pattern, gait changes, ataxia, and myoclonus during the condition's earliest stages [9]. Status epilepticus is uncommon but nevertheless feasible in the early stages of the disease; seizures are not a frequent symptom [10]. It might be challenging to distinguish non-epileptic encephalopathies from non-convulsive status epilepticus (NCSE) in individuals with confusion, which could result in an incorrect diagnosis [11]. The current study reported a 63-year-old man who initially had vision problems then exhibits difficulty using his right side for daily activities and who begins to experience frequent falls with gait instability about a week after receiving the second dose of the novel Pfizer-BioNTech messenger ribonucleic acid (mRNA) COVID-19 vaccination. The possibility that the Pfizer-BioNTech COVID-19 vaccine caused sCJD is investigated in the current study.

## 2. Materials and Methods

### Study design and duration

This was a case report study performed from December 2021 to November 2022.

### Study setting

This study was conducted at IABFH, MNGHA-Dammam, Saudi Arabia.

### Data collection

According to current clinical practice, the patient had all treatments and diagnostic techniques considered essential. Relatives of the patient has provided written, informed consent to take part in the research. Upon creating this report, we adhered to the CARE checklist to collect the data [12].

### Case report

This is a 63-year-old male with past medical history is notable for Hypertension, Diabetes mellitus, Dyslipidemia, previous stroke.

The condition started 2 months ago as he had a history of recurrent blurring of vision and was diagnosed with cataract then he had a sudden transient vision loss. However, his vision came back to baseline following that he developed depressive symptoms associated with irritability and a fixed belief that he had lost his vision.

One month later, he was present with rapidly progressive dementia, behavioral changes, and inability to use his right side in his daily living activities and recurrent falls with gait instability approximately a week after receiving the second dose of the Pfizer-BioNTech COVID-19 vaccine.

The physical examination revealed little of note other than uncertainty and severe concern at his condition.

Initial labs, toxicological screening, and radiology did not reveal anything noteworthy besides mild hypokalemia on the day of admission and his blood gas showed picture of mild respiratory acidosis. Initial CT-brain was unremarkable and repeated CT 3 days after admission was non-significant.

His CSF analysis was clear with increase of CSF protein and glucose with negative culture and negative HSV 1 and 2 PCR. CSF protein 14.3.3 was sent to reference lab which later on came positive.

ALL autoimmune profile and paraneoplastic serology were negative.

MRI brain Bilateral asymmetrical gyriform cortical abnormal signal intensity of bilateral cerebral hemisphere (concerning for CJD or post ictal changes).

EEG showed picture of slow diffuse activity and second EEG 3 days later confirmed clinical and electrical seizures in the right Frontal. Psychiatry and neurology were consulted.

After 48 hours of admission his condition started to deteriorate, and he developed generalized convulsion with drop of his GCS to 4.

During this admission he also developed an acute kidney injury which was contributed mostly due to Acyclovir crystallization. His renal failure improved with hydration and returned to baseline.

Patient was transferred from our hospital to a tertiary hospital with a history of rapid altered level of consciousness, status myoclonic epilepsy and visual hallucination, in addition to Right sided spasticity. Additionally, Intubation and continuous sedation and analgesia were commenced. A repeated Brain MRI showed Bilateral asymmetrical gyriform cortical abnormal signal intensity of bilateral cerebral hemisphere (concerning for CJD or post ictal changes). He also received pulse steroid therapy, and 7 sessions of therapeutic plasma exchange.

He was investigated and LP done again, MRI and EEG (mentioned above) and the diagnoses keeping with a probable sCJD. 14-3-3 Protein came positive, but the RT-QuIC was not done as the sample was bloody

He is on Lacosamide 200 mg BID, Topiramate Tablet 150 mg BID, Valproic Acid 1250AM/1500PM mg , CloBAZam 20 mg BID and LevETIRAcetam 1500 mg BID for his myoclonus. A

Patient has high PSA level and the PET scan showed signs of prostatitis, for that he was started on Ciprofluxacin for 4 weeks, his blood culture also showed candida and ID involved and they suggested to start Fluconazol for total of 14 days, opthalmololgy consulted to rule out endophtalmitis.

General body PET scan revealed diffuse symmetrical decrease metabolism in frontal and parietal and to a lesser extent occipital cortices with sparing of medial temporal cortex and basal ganglia. There was no evidence of FDG avid malignancy.

Patient failed trials of pressure support, he was transferred to Long term care to have tracheostomy, and Peg tube insertion. Injection of botox in masseter muscle for Bruxism.

His case is classified as likely sporadic CJD

depending on the diagnostic criteria of the Centers for Disease Control and Prevention, and a full autopsy with neuropathological tests was required to make a final diagnosis.

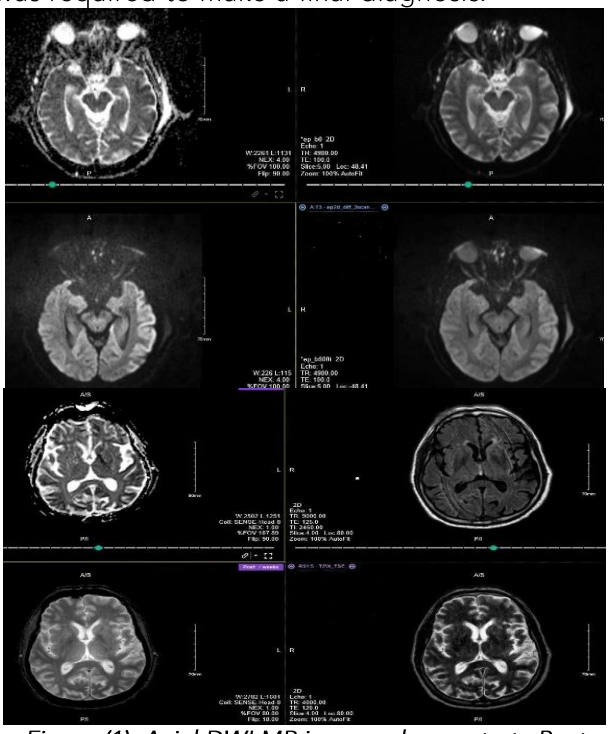

*Figure (1): Axial DWI MR images demonstrate Post siezure: Subtle asymmetric gyriform restricted diffusion involving the left parieto-occipital and temporal region with a subtle FLAIR hyperintense correlate. This could represent postictal change, however, differential possibilities include Creutzfeldt Jacob disease.*

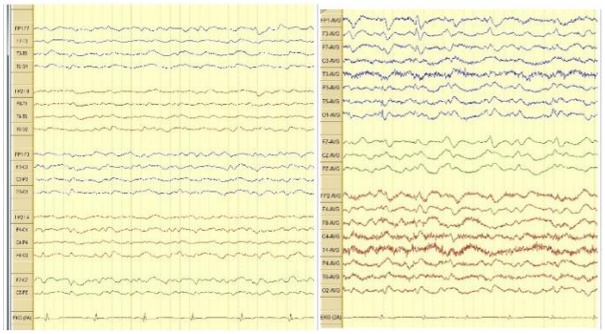

*Figure (2): the first EEG on the left slow diffuse activity while on midazolam infusion and the second EEG on the right showed active epileptic discharges from left frontal area F3 (Left frontal) with clinical seizure of right shoulder twitching followed by generalized periodic discharges GPDS.*

## 3. Discussion

Prion diseases (PrDs) are a collection of neurodegenerative illnesses that are all deadly and brought on by the transformations of an endogenous proteins termed PrP (prion-related proteins) into misconfigured proteins known as the *prion* [13]. Nucleic acids, a constituent of viruses, was found not to be present in the infectious agent. Moreover, treating prion-contaminated items with techniques that rendered viruses and other micro - organisms inactive failed to stop the experimental transmissions of these disorders; however, techniques that denatured or destructed proteins did, firmly establishing the idea that the causative agent was a protein [14]. The discovery of the humans PrP genes, or PRNP, as well as its mutations in people with inherited prion diseases provided additional evidence in favor of the prion hypotheses [15].

Even though $PrP^{Sc}$ has the same amino acids sequences in all instances, sporadic JCD may manifest rather differently; this is due, in part, to the fact that multiple strains of $PrP^{Sc}$ exist, each with somewhat distinct physicochemical and biological characteristics [16]. Such prions strains variety results in variations in tissue tropism, host affinities, and clinical manifestations from a clinicopathological perspective [17].

It is unknown how prions propagate all through the brains, but at least two hypotheses—the refolding theory and the seeding model—have been put forth and are not necessarily exclusive [18]. It is significant that mice lacking $PrP^{C}$ are unable to contract or spread prions. The explant also exhibits substantial $PrP^{Sc}$ accumulations and neurodegenerations when it is transplanted into a $PrP^{C}$ knockout mouse and injected with prions, yet the host brain tissues exhibit minimal toxic effects despite having $PrP^{Sc}$ produced from the grafts [19]. These investigations offer conclusive proof that the prion illness requires $PrP^{C}$. Additionally, it has been demonstrated that nearby cellular cofactors are partially connected to the ability of various prion strains to spread [20].

The aberrant neurotransmissions, disrupted cerebral electric balance, and potential blood-brain injury that might result from this atypical presentations, according to our hypothesis, could all contribute to a lowered epileptic thresholds [21]. Previous research found the involvement of SARS-CoV-2 in promoting the start of proteins aggregations that lead to neurodegeneration and a connection between neurodegeneration and brain inflammation [22]. Furthermore, a number of neurodegenerative diseases, such as frontotemporal dementia , Parkinson's disease and Alzheimer's disease are associated with a rapid development when pro-inflammatory cytokines are present in higher quantities [23-25]. The greatest levels of IL-13 and TNF-α have been discovered to be connected with rapidly progressing varieties (rpAD) of Alzheimer's disease [26]. Comparable to other viral diseases like Ebola or Dengue fever [27, 28], COVID-19 is known for Cytokine storms with elevated levels of IL-1β, IL-6, IL-8, IL-10, and TNF- α [29], thus it might be assumed that higher cytokine amounts could be responsible for the quick development [30]. There are numerous neurologic abnormalities following COVID-19 infections, involving neurodegenerations. One of the key causes of neurodegenerations can be attributed to proteins aggregations in the brain. Heparin and heparin-binding proteins are bound by the SARS-CoV-2 Spike S1 proteins receptors binding domains

(SARS-CoV-2 S1 RBD) [30]. Additionally, the brain's abnormal amyloid proteins quickly assemble when heparins bind to them. In this study, we demonstrated that the SARS-CoV-2 S1 RBD interacts to several heparins-binding proteins that are prone to aggregating, such as TDP-43 RRM, Aβ, α-synuclein, prion and tau [30]. These associations imply that the heparins-binding site on the S1 proteins may facilitate the attachment of amyloid proteins to viral surfaces, which may start their aggregating and ultimately result in neurodegeneration in the brain. By focusing on this binding and aggregating mechanism, the findings will assist us in preventing future effects of neurodegeneration [30].

### mRNA vaccines

The two mRNA vaccinations now in use (Modera and BioNTech-Pfizer) are extremely comparable in terms of technology. They utilize the genuine signal sequence for its production and feature codon-optimized patterns for effective production of the full-length S proteins [31, 32]. Both designs have the two stabilizing alterations (K986P and V987P) in S2, which have been proven to inhibit the conformational transition of the pre-fusion into the post-fusion form of S [33].

The effects of SARS-CoV-2 invasions on the molecular genetics and gene expression patterns of the newly infected hosts are of utmost importance due to abnormal pathologic microRNA (miRNA) signatures, PrD, and SARS-CoV-2 infections, as well as the abundance, speciation, and difficulty of a small family of brain-enriched pathology-associated microRNAs (miRNAs) [33]. According to recent studies, dietary polyphenols may inhibit SARS-CoV-2 incursions by changing the host cells' miRNA expression profiles [34-36]. These ~ 22-nucleotide single-stranded RNAs (ssRNAs) contain a large number of inducible pro-inflammatory miRNAs, such as miRNA-146a-5p, miRNA-155-5p, and many others [34, 37, 38]. Since it was found to be highly upregulated in at least 12 subcategories of PrD in humans, ruminants, and rodents after infections by at least 18 neurotropic DNA and/or RNA viruses, including SARS-CoV-2, which affect the human nervous system, circulatory systems, respiratory, hepatic, lymphatic, CNS, and immune systems, the brains-enriched pathogenic miRNA-146a-5p has drawn a lot of attention [39]. All of the various PrD and infectious agents that promote inflammatory processes and/or specific neurological illness symptoms and/or syndromes that are inevitably deadly, progressive, incapacitating, insidious, and age-related are linked to miRNA-146a-5p and/or miRNA-155. There is strong evidence that miRNA-146a upregulates the ACE2R, which is recognized by the SARS-CoV-2 'S1' spike proteins [40]. Although prions lack detectable nucleic acids, they combined with viruses that contain DNA and/or RNA significantly and gradually activate miRNA-146a and/or miRNA-155 in the invader. However, it is unclear if this is a result of the host's innate or acquired immune responses or if it is a method by which the invading prion or virus is able to infect the host [41, 42].

## 4. Conclusion

To conclude, the current case highlights the connection between neuroinflammation and proteins misfolding and adds sCJD to the growing list of post-COVID-19 vaccination neurological disorders. To confirm SARS-true CoV-2's significance as a neurodegenerative initiator, additional preclinical and epidemiologic research is required.

## References

1. Asante, E.A., et al., A naturally occurring variant of the human prion protein completely prevents prion disease. Nature, 2015. 522(7557): p. 478-481.
2. Chen, C. and X.-P. Dong, Epidemiological characteristics of human prion diseases. Infectious diseases of poverty, 2016. 5(1): p. 1-10.
3. Bonda, D.J., et al., Human prion diseases: surgical lessons learned from iatrogenic prion transmission. Neurosurgical focus, 2016. 41(1): p. E10.
4. Liberski, P.P., et al., Kuru, the first human prion disease. Viruses, 2019. 11(3): p. 232.
5. Aguzzi, A., A.K. Lakkaraju, and K. Frontzek, Toward therapy of human prion diseases. Annual review of pharmacology and toxicology, 2018. 58(1): p. 331-351.
6. Schmitz, M., et al., Hereditary human prion diseases: An update. Molecular neurobiology, 2017. 54(6): p. 4138-4149.
7. Baiardi, S., et al., Recent advances in the histo-molecular pathology of human prion disease. Brain Pathology, 2019. 29(2): p. 278-300.
8. Parchi, P. and P. Gambetti, Human prion diseases. Current opinion in neurology, 1995. 8(4): p. 286-293.
9. Watson, N., et al., Impact of the COVID-19 pandemic on Creutzfeldt–Jakob disease surveillance and patient care in the United Kingdom. European Journal of Neurology, 2022. 29(4): p. 1222-1226.
10. Nasiri, E., et al., Is there a link between COVID-19 and Creutzfeldt-Jakob Disease? a Case Report. Journal of Research in Clinical Medicine, 2021. 9(1): p. 26-26.
11. Watson, N., et al., 048 Impact of the COVID-19 pandemic on Creutzfeldt-Jakob disease surveillance and patient care in the UK. Journal of Neurology, Neurosurgery & Psychiatry, 2022. 93(9): p. e2.
12. Gagnier, J. and G. Kienle, altman DG, Moher D, Sox H, Riley D, et al. The CaRe Guidelines: consensus-based clinical case reporting guideline development. Glob adv Health Med, 2013. 2: p. 38-43.
13. Wang, Z., G. Jansen, and S. Sabourin, Prion and Prion-like Diseases in Humans. 2014.

14. Hughson, A.G., et al., Inactivation of prions and amyloid seeds with hypochlorous acid. PLoS pathogens, 2016. 12(9): p. e1005914.
15. Windl, O., et al., Genetic basis of Creutzfeldt-Jakob disease in the United Kingdom: a systematic analysis of predisposing mutations and allelic variation in the PRNP gene. Human genetics, 1996. 98(3): p. 259-264.
16. Takada, L.T., et al., Genetic prion disease: experience of a rapidly progressive dementia center in the United States and a review of the literature. American Journal of Medical Genetics Part B: Neuropsychiatric Genetics, 2017. 174(1): p. 36-69.
17. Bartz, J.C., Prion strain diversity. Cold Spring Harbor perspectives in medicine, 2016. 6(12): p. a024349.
18. Ayers, J.I., B.I. Giasson, and D.R. Borchelt, Prion-like spreading in tauopathies. Biological psychiatry, 2018. 83(4): p. 337-346.
19. Arshad, H. and J.C. Watts, Genetically engineered cellular models of prion propagation. Cell and Tissue Research, 2022: p. 1-18.
20. Fernández-Borges, N., et al., Cofactors influence the biological properties of infectious recombinant prions. Acta neuropathologica, 2018. 135(2): p. 179-199.
21. Dolatshahi, M., et al., Longitudinal alterations of alpha-synuclein, amyloid beta, total, and phosphorylated tau in cerebrospinal fluid and correlations between their changes in Parkinson's disease. Frontiers in neurology, 2018. 9: p. 560.
22. Khatoon, F., K. Prasad, and V. Kumar, Neurological manifestations of COVID-19: available evidences and a new paradigm. Journal of neurovirology, 2020. 26(5): p. 619-630.
23. Prasad, K., et al., Brain disease network analysis to elucidate the neurological manifestations of COVID-19. Molecular neurobiology, 2021. 58(5): p. 1875-1893.
24. Ezzat, K., et al., The viral protein corona directs viral pathogenesis and amyloid aggregation. Nature communications, 2019. 10(1): p. 1-16.
25. Tavassoly, O., F. Safavi, and I. Tavassoly, Heparin-binding peptides as novel therapies to stop SARS-CoV-2 cellular entry and infection. Molecular pharmacology, 2020. 98(5): p. 612-619.
26. Clausen, T.M., et al., SARS-CoV-2 infection depends on cellular heparan sulfate and ACE2. Cell, 2020. 183(4): p. 1043-1057. e15.
27. Kim, S.Y., et al., Characterization of heparin and severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) spike glycoprotein binding interactions. Antiviral research, 2020. 181: p. 104873.
28. Wang, X., et al., PharmMapper 2017 update: a web server for potential drug target identification with a comprehensive target pharmacophore database. Nucleic acids research, 2017. 45(W1): p. W356-W360.
29. Yan, Y. and S.-Y. Huang, Pushing the accuracy limit of shape complementarity for protein-protein docking. BMC bioinformatics, 2019. 20(25): p. 1-10.
30. Idrees, D. and V. Kumar, SARS-CoV-2 spike protein interactions with amyloidogenic proteins: Potential clues to neurodegeneration. Biochemical and biophysical research communications, 2021. 554: p. 94-98.
31. Vogel, A.B., et al., BNT162b vaccines protect rhesus macaques from SARS-CoV-2. Nature, 2021. 592(7853): p. 283-289.
32. Corbett, K.S., et al., SARS-CoV-2 mRNA vaccine design enabled by prototype pathogen preparedness. Nature, 2020. 586(7830): p. 567-571.
33. Heinz, F.X. and K. Stiasny, Distinguishing features of current COVID-19 vaccines: knowns and unknowns of antigen presentation and modes of action. npj Vaccines, 2021. 6(1): p. 1-13.
34. Winkler, E.S., et al., Human neutralizing antibodies against SARS-CoV-2 require intact Fc effector functions for optimal therapeutic protection. Cell, 2021. 184(7): p. 1804-1820. e16.
35. Dicks, M.D., et al., A novel chimpanzee adenovirus vector with low human seroprevalence: improved systems for vector derivation and comparative immunogenicity. PloS one, 2012. 7(7): p. e40385.
36. van Doremalen, N., et al., ChAdOx1 nCoV-19 vaccine prevents SARS-CoV-2 pneumonia in rhesus macaques. Nature, 2020. 586(7830): p. 578-582.
37. Voysey, M., et al., Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. The Lancet, 2021. 397(10269): p. 99-111.
38. Logunov, D.Y., et al., Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia. The Lancet, 2020. 396(10255): p. 887-897.
39. Logunov, D.Y., et al., Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia. The Lancet, 2021. 397(10275): p. 671-681.
40. Duan, L., et al., The SARS-CoV-2 spike glycoprotein biosynthesis, structure, function, and antigenicity: implications for the design of spike-based vaccine immunogens. Frontiers in immunology, 2020. 11: p. 576622.
41. Bos, R., et al., Ad26 vector-based COVID-19 vaccine encoding a prefusion-stabilized SARS-CoV-2 Spike immunogen induces potent humoral and cellular immune responses. npj Vaccines, 2020. 5(1): p. 1-11.
42. Lukiw, W.J., et al., SARS-CoV-2 invasion and pathological links to prion disease. Biomolecules, 2022. 12(9): p. 1253.