Case Report: Sporadic Creutzfeldt-Jakob Disease after Receiving the Second Dose of the Pfizer-BioNTech COVID-19 vaccine

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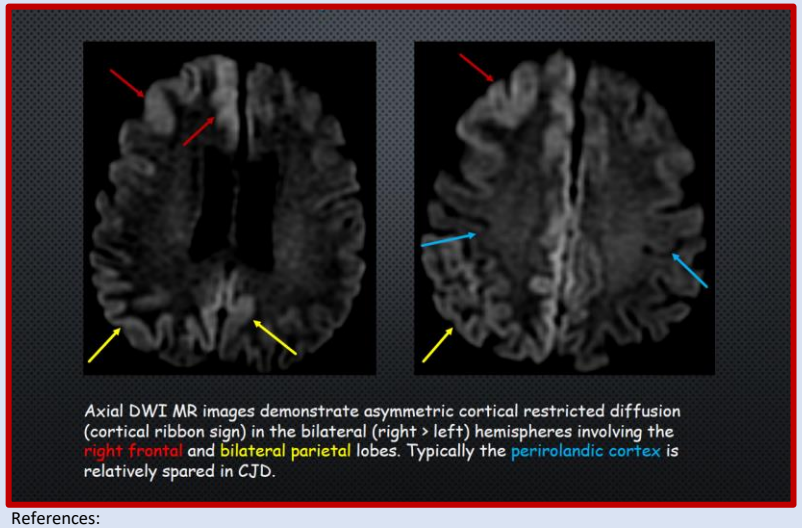
Introduction: Human prion disease is a rare, highly progressive neurodegenerative disease that is ultimately fatal. The majority of cases are sporadic Creutzfeldt-Jakob disease (sCJD). Although any association between the novel Pfizer-BioNTech COVID-19 vaccine and sCJD would not outweigh its benefit and importance, this case serves as an vital part of adverse event monitoring during phase IV of the vaccine trial.

Case Presentation:

- 64-year-old woman with a past medical history of bipolar depression and anxiety presents with rapidly progressive dementia, behavioral changes, headaches, and gait disturbance approximately one week after receiving the second dose of the Pfizer-BioNTech COVID-19 vaccine on April 25, 2021
- Physical exam was essentially unremarkable except for confusion and significant distress regarding her condition
- Initial labs, toxicology screening, and imaging were unremarkable except for a mildly increased white blood cell count
- Psychiatry and neurology were consulted
- Magnetic resonance (MR) imaging of the brain showed cortical diffusion restriction involving the bilateral frontal lobes, bilateral parietal lobes, and paramedian bilateral occipital lobes
- Lumbar puncture and extensive cerebral spinal fluid analysis
  - Positive via the newest, highly sensitive real-time quaking-induced conversion (RT-QuIC) testing
  - T-tau protein measured at 38,979 (reference < 0-1,149)
  - 14-3-3 protein was positive, neuron-specific enolase resulted at 16.3 (reference < 8.9)
- Exhibiting progressively worsening pyramidal and extrapyramidal symptoms, as well as akinetic mutism
- Based on the Center for Disease Control and Prevention's diagnostic criteria, the findings place her case as probable sporadic CJD with a definitive diagnosis to be made by a proper autopsy with neuropathological studies

Although the importance of vaccinations during the COVID-19 pandemic is undebatable, it is also the medical community's responsibility to continue to document and share information on the potential side effects. Reporting cases such as this will serve as significant references to consider in the instance that mass vaccination production is needed to defend against future unprecedented pandemics.



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Discussion:

- Normal prion protein is converted into an infectious, auto-enzymatic protein that aggregates in the brain tissue destroying neuronal cells leading to extensive neurodegeneration
- Human prion protein (PrP), is encoded by the PrP gene, *PRNP*, which is located on the short arm of chromosome 20
- Expressed primarily within the nervous system
- Conversion to the diseased prion protein, termed PrPSc, is determined by *PRNP* polymorphism involving methionine (Met) or valine (Val) at codon 129 and prion strain (type 1 PrPSc or type 2 PrPSc)
- Etiology has been thought to be a mostly sporadic disease with no known specific cause
- Retrospective case-control study in the United Kingdom found that all sporadic Creutzfeldt-Jakob disease (sCJD) cases from 1990 - 1998 lived close together, suggesting plausible precipitating factor
- mRNA contained in the Pfizer-BioNTech COVID-19 vaccine has the potential to bind to specific proteins and cause pathologic misfolding
- Various portions of the COVID-19 mRNA Pfizer-BioNTech vaccine to have a high affinity for cytoplasmic proteins such as TAR DNA binding proteins (TDP-43) and Fused in Sarcoma (FUS)
- Spike protein, which is translated by the mRNA, can increase intracellular zinc, which has been shown to cause the conversion of TDP-43 into its pathological prion
- Kuo et.al demonstrated how TDP-43 binds to mRNA transcripts with long UG-repeats
- Pfizer-BioNTech's COVID-19 vaccine contains many of these specific sequences
- Tetz and Tetz identified a prion-like domain found in the receptor-binding domain of the S1 region of the SARS-CoV-2 spike protein
- Case report of a previously healthy 60-year-old man who developed sudden onset sCJD with concurrent onset of symptoms of COVID-19
- Case of a patient with sCJD whom also had positive serum neuronal antibodies to the voltage-gated potassium channel complex (VGKC complex) and glycine receptor (GlyR) antibodies