A Case of Creutzfeldt-Jakob Disease Presenting With Depression and Anxiety

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INTRODUCTION

Psychiatric complaints are common reasons for presentation to the Emergency Department (ED). Several reports estimate the incidence of such visits at 4-5% of all ED visits.[1,2] Many patients presenting with psychiatric complaints are otherwise healthy; however, it is common practice for the ED to determine if a patient is medically stable for psychiatric admission.

CASE REPORT

ANXIETY AND DEPRESSION WITH SUICIDAL IDEATION

- A 53-year-old male presenting to the ED with the above chief complaint.
- Reports vivid images of standing in the street waiting to be hit by a car.
- His anxiety and depression have been affecting his daily activities and relationships.
- He describes difficulty concentrating and angry outbursts.
- He recently quit his job of 28 years as a bakery manager at a local super market due to inability to concentrate, follow directions, and mood swings.
- Six days prior to presentation, the patient drove through a red light and ran off the road but did not have any recollection of why or how this happened. He was uninjured and he hit nothing. However, this car accident worsened his anxiety. He no longer drives.
- His second wife, who is present with him today, states that he has started talking to himself. In addition, wife reports that he has periods where he seems distant, absent for several seconds and he does not communicate.
- Patient started noticing progressively worsening depression over the past 4 months.
- His family doctor has steadily increased his sertraline over the past five months without improvement.
- His abusive father recently died further worsening his anxiety and depression.
- Patient has never had any hospitalizations for anxiety or depression in the past or had any suicidal ideations in the past.

ROS

1. Chest pressure with radiation down arms
2. Decreased appetite and 20-pound weight loss in the last several months which he attributes to anxiety

PMHx

1. Insomnia
2. Gastroesophageal reflux disease (GERD)
3. Depression
4. Hyperlipidemia
5. Allergic rhinitis
6. Attention deficit disorder (ADD)

PSHx

1. Remote vasectomy
2. Cataract extraction with intraocular lens implant in 2016

MEDHx

1. Sertraline 150 mg
2. Atorvastatin 40mg
3. Fexofenadine 180 mg
4. Fluticasone propionate 50 mcg
5. Multivitamin

FMHx

1. History of depression and psychiatric illnesses on his mother's side
2. His father had diabetes and hyperlipidemia
3. No family history of cardiac or cerebrovascular disorders.

SOCHx

1. Previous tobacco use until 6 years ago, having smoked a pack a day for 30 years.
2. He rarely uses alcohol and denies ever using recreational drugs.

PHYSICAL EXAM

- Normal vitals signs.
- He is a thin, Caucasian male appearing disheveled although is normocephalic and atraumatic.
- Cranial nerves are intact; neurologic examination is normal other than slow, tangential speech.
- The heart has a regular rate and rhythm with intact distal pulses.
- Breath sounds and respiratory effort are normal.
- The abdominal examination is normal.
- There is no rash.
- The patient reports suicidal ideation with plan.

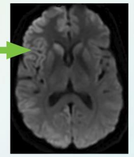

Figure 1: MRI Brain without Contrast
Diffusion- weighted image showing high signal intensity on the right caudate nucleus. See arrow.

TABLE 1: WHO CRITERIA FOR DIAGNOSIS

1. SPORADIC CJD

Rapidly progressive dementia; and at least two out of the following four clinical features:

1. Myoclonus
2. Visual or cerebellar signs
3. Pyramidal/extrapyramidal signs
4. Akinetic mutism

AND a positive result on at least one of the following laboratory tests:

- a typical EEG (periodic sharp wave complexes) during an illness of any duration; and/or
- a positive 14-3-3 cerebrospinal fluid (CSF) assay in patients with a disease duration of less than 2 years
- Magnetic resonance imaging (MRI) high signal abnormalities in caudate nucleus and/or putamen on diffusion-weighted imaging (DWI) or fluid attenuated inversion recovery (FLAIR)

AND without routine investigations indicating an alternative diagnosis.

Possible: Progressive dementia; and at least two out of the following four clinical features:

1. Myoclonus
2. Visual or cerebellar signs
3. Pyramidal/extrapyramidal signs
4. Akinetic mutism

AND the absence of a positive result for any of the three laboratory tests that would classify a case as "probable" (see tests a-c above)

AND duration of illness less than two years

AND without routine investigations indicating an alternative diagnosis.

2. IATROGENIC CJD

Progressive cerebellar syndrome in a recipient of human cadaveric-derived pituitary hormone; or sporadic CJD with a recognized exposure risk, e.g., antecedent neurosurgery with dura mater implantation.

3. FAMILIAL CJD

Definite or probable CJD plus definite or probable CJD in a first degree relative; and/or Neuropsychiatric disorder plus disease-specific PrP gene mutation.

From https://www.cdc.gov/prions/cjd/diagnostic-criteria.html

CLINICAL COURSE

- Initial laboratory testing including toxicology is unremarkable.
- Due to the chest discomfort, the patient was medically cleared after two negative troponins, normal ECG, and normal chest X-ray.
- He signed a voluntary commitment for psychiatric treatment and was admitted to the behavioral health unit for psychiatric treatment.
- Over the next few days, the patient continues to experience depression and anxiety. He no longer endorses suicidal ideation, but now experiences paranoia. This progresses over the next few days to the point where the patient requires constant redirecting. He grows increasingly disoriented, answering unrelated to questions but speaking clearly. He receives several different antidepressants and antipsychotics without any improvement in symptoms.
- Due to the progression of illness, the patient is seen by the medical team, though there is no significant change in his examination, and it is felt that his neurologic status is related to his psychiatric illness. Neurology is consulted after staff observes brief episodes where his arm dropped, and he was staring without responding. His wife notes episodes prior to this admission including twitching like movements in his arms. The patient's speech progresses to confabulation. A Magnetic Resonance Imaging (MRI) brain with and without contrast and Electroencephalogram (EEG) are ordered. At this point the patient is cooperative, but has limited speech and frequently fails to answer questions. Strength and sensation remain intact, though the patient now has mildly increased tone.

CASE CONCLUSION

- MRI demonstrates DWI high signal intensity/restricted diffusion in bilateral cerebral cortices and basal ganglia, more pronounced on the right. This finding can be seen with Creutzfeldt-Jakob (CJD) disease, encephalitis, and toxic/metabolic processes, and unlikely diagnosis of hypoxic/ischemic injury. Recommendation is made for correlation with clinical history, EEG and CSF. See MRI image.
- The EEG is abnormal and shows slowing over the right hemisphere with some anterior rhythmic slowing that are consistent with a diffuse encephalopathy.
- CSF demonstrates large amount of T-tau protein and is positive for CJD protein 14-3-3.
- These tests confirm the diagnosis of Creutzfeldt-Jakob disease.
- The patient continues to decline cognitively, eventually becoming delirious, with incoherent speech and lack of communication. The patient is moved to hospice and eventually expires.

DISCUSSION

CJD is one of the major causes of rapid progressive dementia.[3] CJD is a fatal neurodegenerative disease affecting humans and animals. It is caused by an abnormal accumulation and/or metabolism of prion proteins. The mutation in the prion protein results in the production of protease-resistant prion protein, which causes nerve damage.[3] It is believed that the protein may cause small vacuoles in neuronal cell bodies, axons, dendrites which may be the cause of nerve damage resulting in the various clinical presentations. One person is affected per one million per year. There are no gender biases. It typically occurs in people in their 5th–7th decades, average age 60 years. CJD can be transmitted by sporadic, familial, iatrogenic, and variant means. CJD occurring without a known source is called sporadic CJD which is the most common cause.[3] Iatrogenic CJD may be related to cornea transplantation, dural grafts, application of infected electrode injections of growth hormone or gonadotropin obtained from cadavers. Variant type of CJD is characterized by psychiatric symptoms at an earlier stage with a longer clinical deterioration and death at a younger age. Our patient may have had this variant /sporadic form. Nearly one third of cases of variant CJD start with depression, emotional lability, behavioral changes, loss of appetite, and insomnia.[4,5]

The differential diagnosis for altered mental status and abnormal neurologic examination is quite extensive. Many causes of altered mentation are reversible or can be improved with appropriate diagnosis and treatment such as heavy metal toxicity, thyroid disorders, viral or bacterial encephalopathies and vitamin deficiencies.[6] Diagnosis will rarely be completed in the emergency room. However, it is crucial to note the rapidly progressing dementia symptoms and to begin work-up in consultation with other specialties including neurology.[6,7]

When evaluating a patient with suspected CJD or other rapidly progressive dementia, the work up should include a complete blood count (CBC), comprehensive metabolic panel (CMP), thyroid function and computed tomography (CT) of the brain. In consultation with neurology, other diagnostic studies may be warranted.[8] Those may include serology for neurosyphilis, paraneoplastic antibodies, limbic encephalitis. MRI of the brain, with axial DWI diffusion weighted imaging, FLAIR- fluid attenuated inversion recover, EEG, CSF, CJD 14-3-3, S100b, abeta and tau proteins may be ordered.[5,9]

CJD anomalies on MRI are often patchy, extensive, but should involve more than one cortical region/area that is not vulnerable to artefactual signal change.[10] Thalamic signal change may be diffuse or have emphasis in dorsal/medial aspects. MRI is more than 90% effective in the diagnosis of sporadic CJD. DWI often shows hyper densities basal ganglia. However, other areas may be affected depending on clinical presentation.[10]

EEG anomalies in CJD often include lateralized or focal periodic sharp waves representing cerebral dysfunction.[10] Lumbar puncture is used to evaluate CSF for specific proteins.[5,11] But the cost and availability of these tests, limit the ability to rapidly obtain them.[11] Rapid clinical progression occurs from normally functioning to death in approximately one year for most diagnosed CJD patients. The patient in this case, expired in approximately 7 months from his worsening anxiety and depression. This is a 100% fatal disease. Definitive diagnosis still involves prion protein identification in post mortem brain tissue.[11]

CONCLUSION

This case is important to the ED because it highlights the importance of the history of the present illness. In this case, the rapid loss of ADLs with behavioral changes should increase suspicion for a medical etiology for the patient's symptoms. Although the physical exam was benign initially, there was a progressive decline in neurologic status in the HPI. In the event of any neurologic symptoms and/or rapid loss of functioning of ADLS, it is important to consider the many causes of rapid progressive dementia and to initiate the work-up in consultation with neurology. Ultimately, the outcome for the patient was unchanged; however, the diagnosis was possibly delayed by being in a psychiatric unit. Many of the other causes of rapidly progressive dementia can be reversed or slowed with appropriate treatment.

The authors have no conflicts or financial interest to disclose.

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