Alice in Wonderland Syndrome as a Presenting Symptom in a Creutzfeldt-Jakob Disease Patient

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Patient Profile

A 71-year-old Thai female, right-handed, 4th grade education.

Housewife, lives in Bangkok. Previously independent with ambulation and activities of daily living (ADLs).

Chief Complaint

Abnormal vision for 1 month prior to admission

Present Illness

2 Months Prior to Admission

The patient experienced dizziness and unsteadiness without nausea or vomiting. She was diagnosed with BPPV and treated with medication. Dizziness improved, but she still needed to feel her way when walking indoors, without falls or collisions.

1 Month Prior to Admission

Family members noted the patient frequently fumbles when reaching for objects. The patient reported visual disturbances including objects appearing smaller or larger than their actual size and seeing colors more vividly. She describes seeing vehicles looking like “toy cars.” She can no longer read or write her name, and has difficulties recognizing neighbors. While still recognizing immediate family, the patient often asked why their faces looked distorted. She also experienced disorientation within her own house, inability to prepare meals, and difficulty dressing (e.g., buttoning clothes), requiring assistance with bathing and hair washing. Subsequently, the patient appeared slow, complained of constant daytime sleepiness, but her mood remained normal. The patient denied

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hallucinations (auditory or visual), weakness, fever, seizures, or incontinence. She experienced a 4-kilogram weight loss over 1 month.

Past History

Underlying diseases: hypertension, dyslipidemia

Deny trauma/head injury

Deny substance use, smoking, and alcohol consumption

Deny drug or food allergies

Deny similar symptoms in family members and family history of genetic or neurological disorders

Physical Examination

Vital signs: BT 36.4 °C, PR 65 bpm, RR 18/min, BP 138/75 mmHg

Height 149 cm, body weight 56.3 kg, BMI 25.36 kg/m²

General Appearance: Alert, elderly Thai female

HEENT: Anicteric sclera, non-pale conjunctiva, no thyroid enlargement, no lymphadenopathy

Respiratory: Normal chest expansion, equal breath sounds bilaterally, no adventitious sounds

Cardiovascular: No neck vein engorgement, regular and full pulse, normal S1 and S2, no murmur

Abdomen: Normal contour, soft, non-tender, normoactive bowel sounds, no palpable mass

Extremities: No limb or joint deformity, no joint swelling, no edema

Skin: No rash or wounds

Neurological Examination

Mental status: E4M6V5, well co-operative

Cranial nerves: intact

Motor system: No spasticity, rigidity, muscle atrophy, or fasciculations. Motor power grade 5 thoroughly.

Deep tendon reflexes: 2+

Babinski's sign: Absent bilaterally

Clonus: Negative bilaterally

Sensory: Intact pinprick sensation and proprioception

Cerebellar signs: Intact finger-to-nose, normal gait, no ataxia

Stiffness of neck: Negative

Cognitive assessment: Normal attention, disoriented to time and place, normal fluency and comprehension, no neglect. Naming impaired only when the object is presented in front of the patient, but the patient was able to identify the object when touching it. The patient cannot describe the large letter when tested with Navon Letters. Marked simultanagnosia when tested with the "Cookie Thief" picture. Optic ataxia was present without oculomotor apraxia.

Patient Discussion

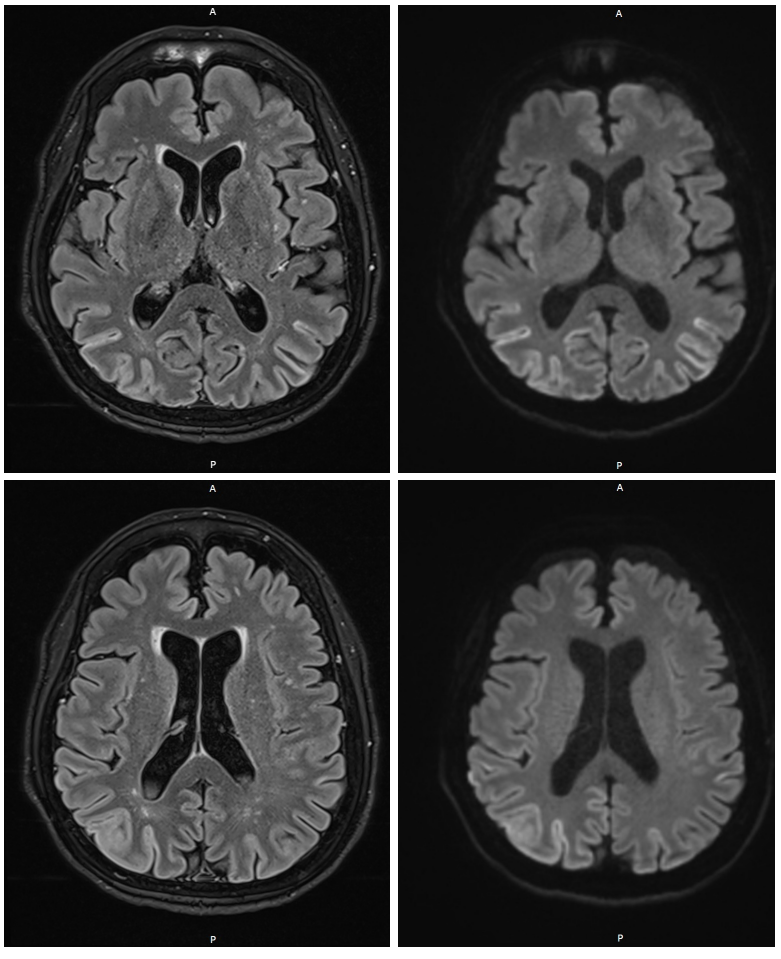
This is a 71-year-old Thai female presented with a two-month history of subacute, rapidly progressive cognitive decline and visual distortions. Her early symptoms of dizziness likely were the results of her visual abnormalities that could be defined as metamorphopsias (visual perceptual disturbances). The progression to visual agnosia and executive dysfunctions strongly suggested widespread cortical dysfunction.

Her neurological exam, which showed intact cranial nerves, normal motor/sensory systems, and no cerebellar signs, localized the pathology to higher cortical functions, especially visual processing and executive domains. Considering the patient's

prominent visual distortions, it is highly suggestive of Alice in Wonderland Syndrome, which indicates a visual perceptual dysfunction (dorsal stream) and visuo-spatial deficits (ventral stream). Hence, the lesion can be localized at the temporo-occipital and parieto-occipital cortices.

The rapid progression from visual symptoms to severe cognitive impairment in two months is alarming and requires prompt investigations for any secondary cause. Etiology of the disease could be subacute infectious, inflammatory (e.g. autoimmune, paraneoplastic), or space-occupying lesions (e.g. tumor, mass-forming infection). There is also a possibility of degenerative diseases with rapid course such as prion diseases.

Investigation



(Front cover)

The MRI study reveals FLAIR/T2-hyperintensity change with restricted diffusion at bilateral cerebral cortices; more on parietal, occipital, and posterior/basal temporal cortices, as well as faint restricted diffusion at bilateral basal ganglia.

CSF analysis: clear color, protein 40, glucose 67, WBC 3 (mono 100%), RBC 0

CSF RT-QuIC for prion protein: positive

Discussion

Alice in Wonderland Syndrome (AIWS) is a perceptual disorder marked by distorted visual perception (metamorphopsias), such as micropsia or macropsia, body schema, and time experience. Its pathophysiology involve dysfunction in the temporo-parietal-occipital junction area, which integrates visual and spatial sensory input. This phenomenon can be found in many diseases including migraine, epilepsy, encephalopathy, psychiatric disorders, or medication and substance use. Visual distortions and AIWS can also be early signs of a prion disease called Creutzfeldt-Jakob disease (CJD).

Prion diseases, also known as transmissible spongiform encephalopathies (TSEs), are rare, rapidly progressive, and fatal neurodegenerative disorders. They're caused by the accumulation of misfolded prion protein (PrPsc) in the brain, which acts as a template to misfold normal prion protein (PrPc), leading to widespread neuronal death. Prion diseases can be sporadic, genetic, or acquired.

Creutzfeldt-Jakob disease (CJD) is the most prevalent human prion disease. Its variable clinical manifestations can mimic other neurological conditions, making diagnosis challenging. A recent study from the Neurological Institute of Thailand found that cognitive impairment is the most frequent initial symptom of sporadic CJD (sCJD), followed by ataxia and visual disturbances. sCJD typically affects individuals over 60 and progresses rapidly to death within months. Known sCJD subtypes include the Heidenhain variant (initial visual distortions), the Stern variant (sleep disturbances and thalamic dysfunction), and the Brownell-Oppenheimer variant (predominantly ataxic).

Magnetic resonance imaging (MRI) studies in sCJD typically shows abnormal FLAIR hyperintensity and restricted diffusion (DWI) in the bilateral cortical gyri (cortical ribboning), caudate, basal ganglia, specifically the caudate head and putamen, and thalamus, while sparing the peri-rolandic area. The Heidenhain variant may show more pronounced abnormalities within the occipital lobes, correlating with its early visual symptoms. Pulvinar sign or double hockey stick in FLAIR may be atypical for sCJD but could be seen in Variant CJD (vCJD).

Cerebrospinal fluid (CSF) analysis is crucial in supporting a CJD diagnosis, though it's usually normal. Nowadays, Real-Time Quaking-Induced Conversion (RT-QuIC) is used for diagnosis of probable CJD in addition to progressive neuropsychiatric syndrome. The assay is highly sensitive (>90% for sCJD) and specific (near 100%). It uses protein amplification technique that mimics the prion misfolding process and enables the detection of extremely small quantities of disease-associated prion protein in human CSF.

Currently, there is no cure or disease-modifying treatment for CJD or other prion diseases. Management is solely supportive and palliative, focused on symptom control and maintaining the patient's quality of life as the disease progresses.

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