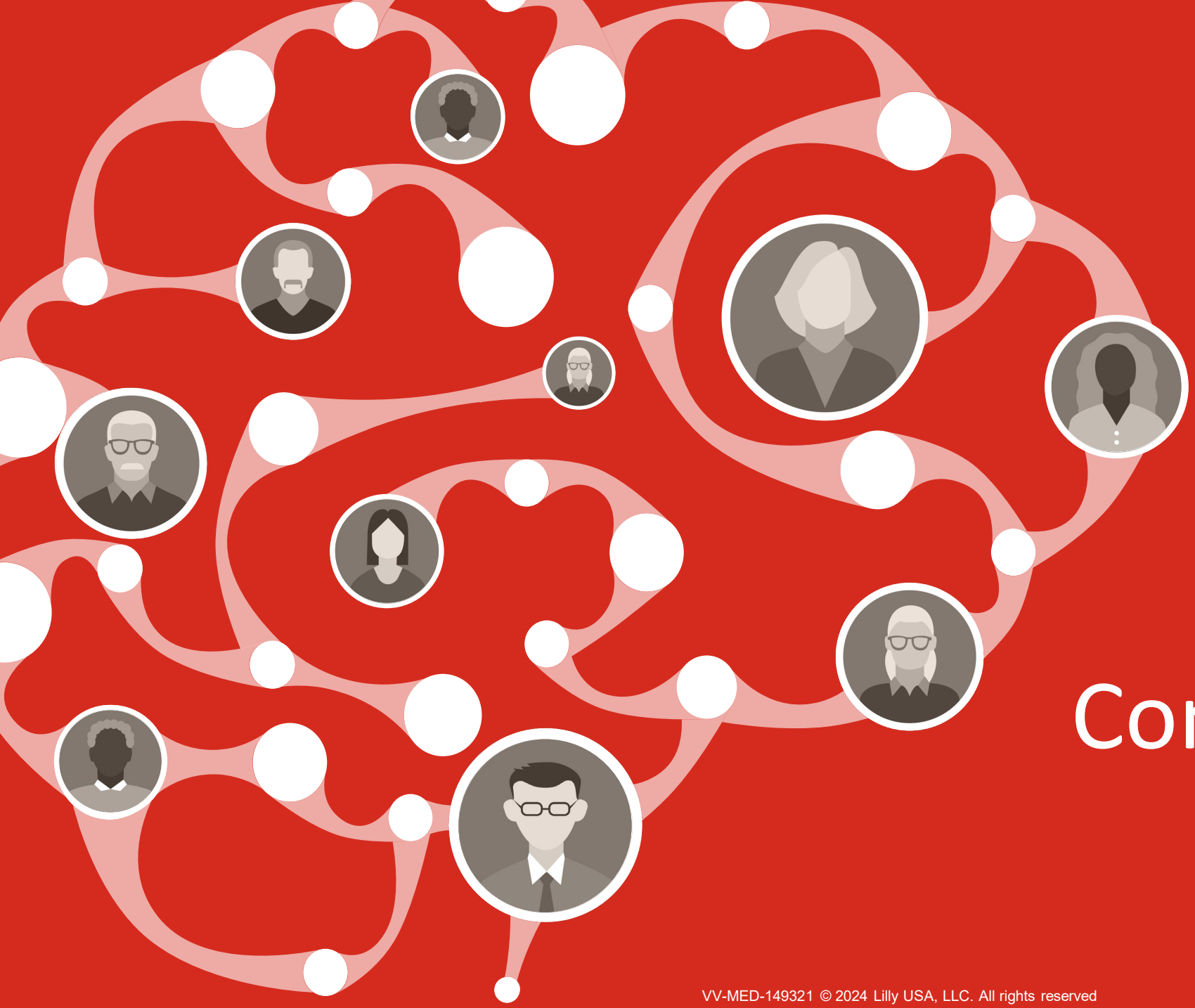


ConnectAD™

Welcome to ConnectAD™, a clinical case series created by the Eli Lilly and Company Neuroscience medical education team. This series is intended to connect healthcare professionals to resources that help them detect, diagnose, and manage Alzheimer's disease.

Disclaimer

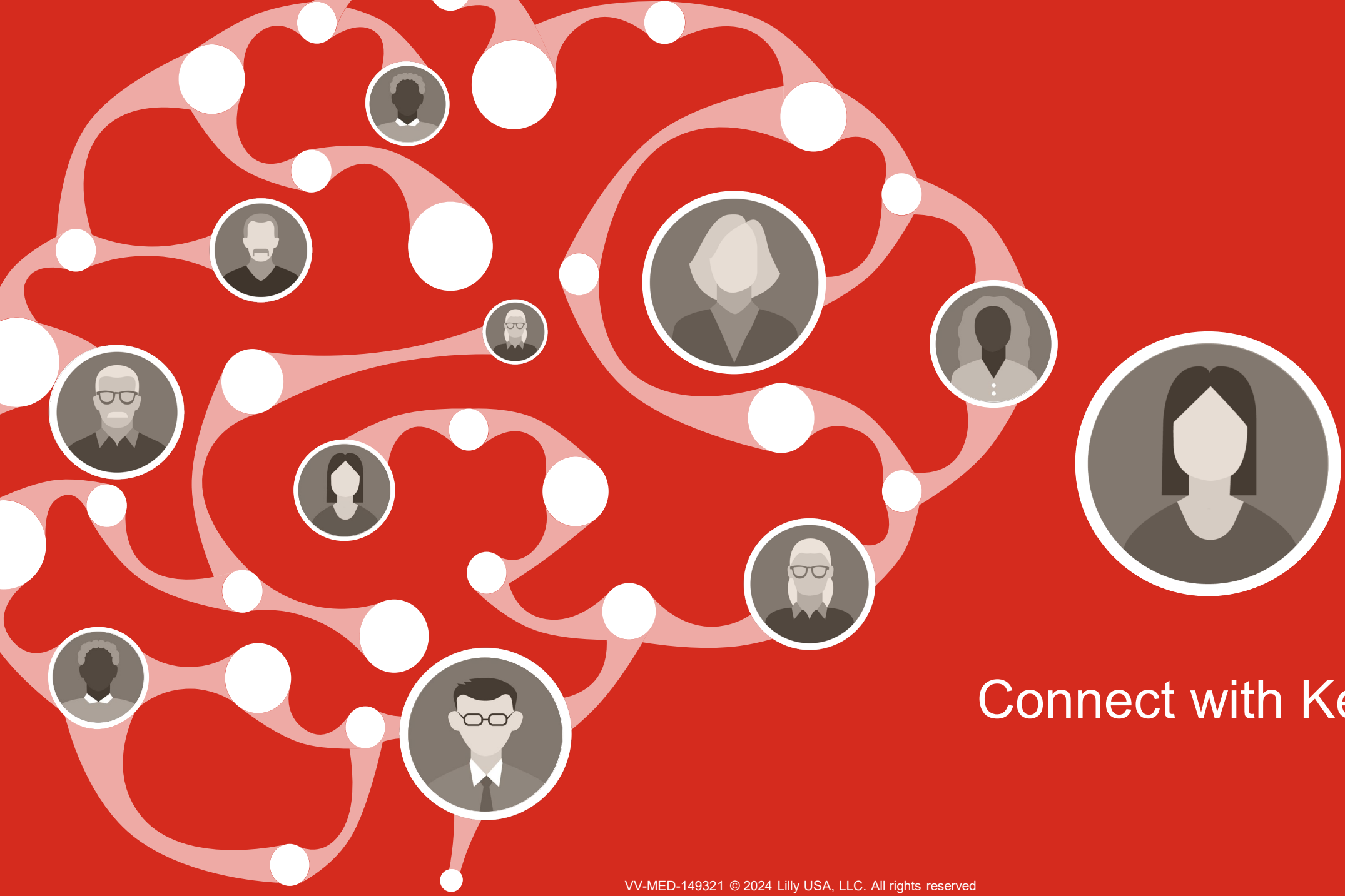
The content for this case was created by Eli Lilly and Company and is inspired by scenarios clinicians may encounter while caring for patients with Alzheimer's disease.

A variety of cognitive and diagnostic tests can reasonably be used in the detection and diagnosis of Alzheimer’s disease. Inclusion of specific cognitive and/or diagnostic tests in this case reflects the diversity of clinical preferences, and the use of particular diagnostic tools does not imply endorsement or recommendation by Lilly.

Learning Objectives

Through completing this course, you will have a deeper understanding of:

- The clinical presentation of Alzheimer's disease
- How to integrate clinical and biomarker assessments to make an accurate diagnosis of Alzheimer's disease in the earliest stages

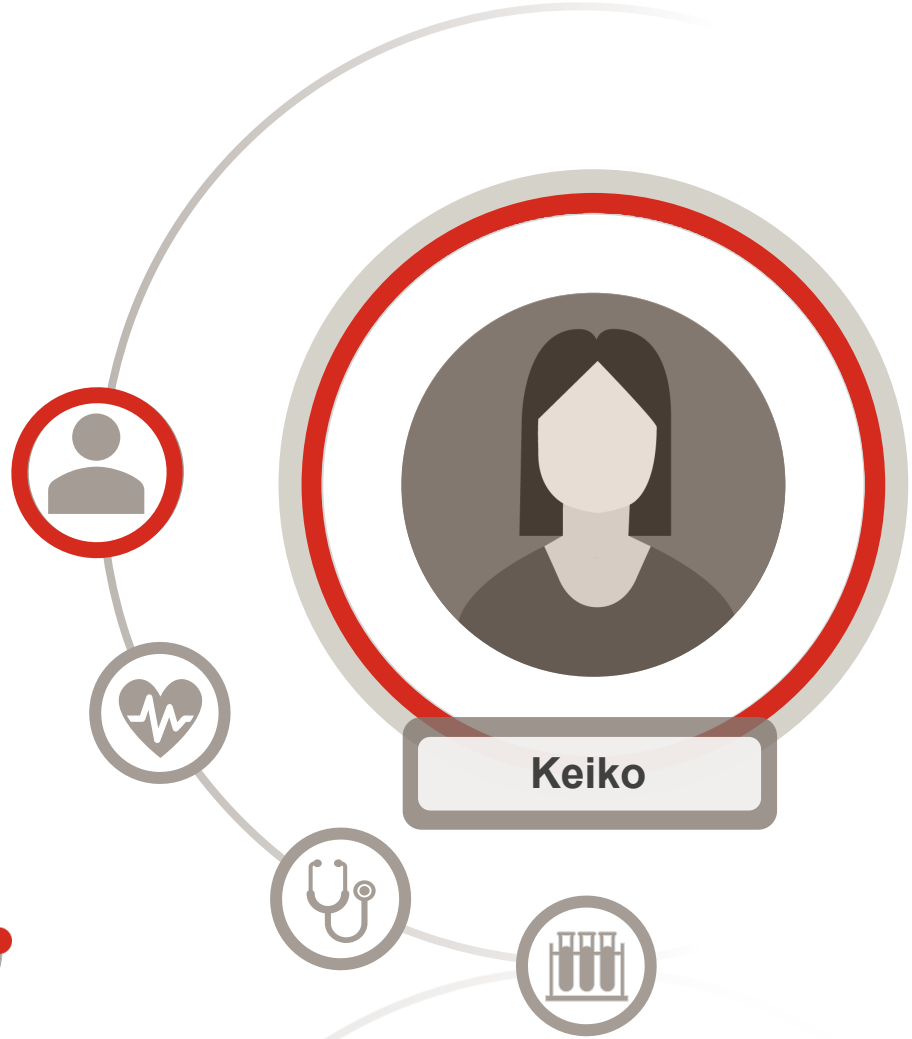


Connect with Keiko

Our Patient

Keiko

- 74 years old
- Female
- Asian
- Married, one child, 2 grandchildren
- College degree
- Registered nurse (retired)
- Family history
  - Depression
  - Anxiety



Clinical Information and History

Keiko has experienced recurrence of previously well-controlled depression over the past 3 years, with poor response to treatment.

As mood symptoms worsened over the past year, she has also experienced progressive cognitive difficulties:

- Difficulty recalling recent events and conversations
- Challenges handling medications and appointments

Clinical history

- Depression
- Anxiety

General health

- Heart rate: 76 bpm
- Blood Pressure: 130/80

Current medication (class)

- Selective serotonin reuptake inhibitor (SSRI)

bpm=Beats Per Minute.

Initial Clinical Assessment

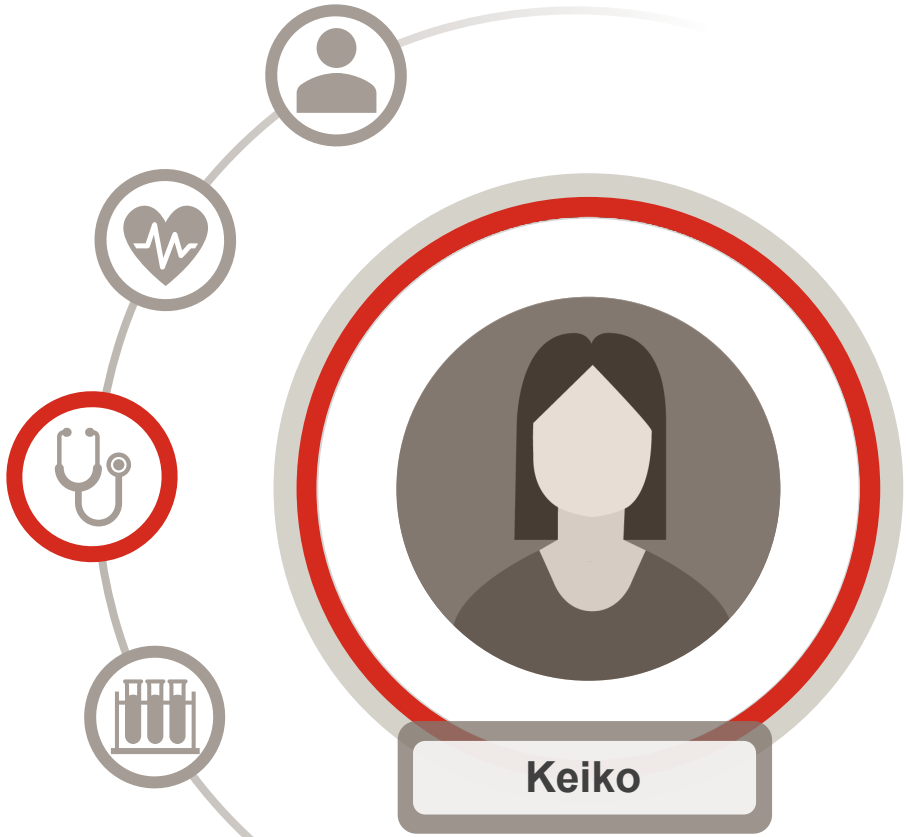
General neurological exam: Normal

Mental status

- Alert, insightful, good effort on testing
- Instrumental activities of daily living: Dependent (medications, appointments)

Cognition

- MoCA: 24/30 (normal ≥26)
  - Word recall: 0/5
  - Figure copy: 0/1
- Geriatric Depression Scale-15 items (GDS-15): 10/15 (moderate depression)



MoCA=Montreal Cognitive Assessment.

Additional Findings

Blood work within normal limits, including:

- Complete blood count (CBC)
- Electrolytes
- Glucose
- Creatinine
- Thyroid stimulating hormone (TSH)
- Vitamin B12

Brain MRI

- Mild diffuse cortical atrophy, with superimposed moderate temporal atrophy (left side more affected than right)

CSF assay

- $A\beta_{42}/A\beta_{40}$: Low
- P-tau: High
- T-tau: High

Aβ=Amyloid Beta; CSF=Cerebrospinal Fluid; MRI=Magnetic Resonance Imaging; P-tau=Phosphorylated Tau; T-tau=Total Tau.

Given the patient information presented, what is the diagnosis?

1. Generalized anxiety
2. MCI due to AD
3. Mild dementia due to AD
4. Major depressive disorder
5. Other

AD=Alzheimer's Disease; MCI=Mild Cognitive Impairment.

Given the patient information presented, what is the diagnosis?

Option 3:

Mild dementia due to AD

AD=Alzheimer's Disease.

Justification for Diagnosis

Why is Keiko diagnosed with mild dementia due to AD?

Keiko is presenting with clinical symptoms that include both mood and cognitive impairment. Clinical assessment also uncovered symptoms of functional dependence.

Several features of mood symptoms (chronic, progressive worsening, non-responsive to treatment) suggest an underlying neurodegenerative disorder as the cause, rather than isolated depression.[1]

MRI findings confirmed suspicion for underlying neurodegeneration.

CSF testing provided neuropathological confirmation of an AD diagnosis.

AD=Alzheimer's Disease; CSF=Cerebrospinal Fluid; MRI=Magnetic Resonance Imaging.

1. Tetsuka S. *Aging Dis.* 2021;12(8):1920-1934.

Key Learnings in Keiko's Case (1 of 2)

Depression and dementia often co-exist in the same individual.[1] If mood symptoms are identified, clinicians should not be discouraged from exploring a simultaneous diagnosis of dementia in the appropriate clinical setting

- Mood impairment (especially depression) may precede the development of cognitive symptoms in neurodegenerative disorders[2]
  - Data suggest that 38% of elderly patients diagnosed with depression eventually receive a diagnosis of dementia[3]
- If the following clinical characteristics are seen in patients with mood symptoms, it may be indicative of dementia[4]:
  - Chronic course; identifiable with onset and progression over months to years
  - Resistance to antidepressant treatment
  - Associated progressive cognitive difficulties
- Evaluation of dementia in the presence of mood symptoms should include assessment of neuropathological biomarkers[5]

1. Leung DKY, et al. *Int J Geriatr Psychiatry*. 2021;36(9):1330-1344. 2. Marrie RA, et al. *Rev Neurol (Paris).* 2024;180(3):125-140. 3. Connors MH, et al. *Psychol Med*. 2019;49(5):727-737. 4. Tetsuka S. *Aging Dis.* 2021;12(8):1920-1934. 5. Liguori C, et al. *Front Aging Neurosci*. 2018;10:38.

Key Learnings in Keiko's Case (2 of 2)

The CSF biomarker assay can be used to confirm the presence of pathology consistent with AD[1]

CSF assays

- Quantitatively measure the levels of Aβ and tau protein within the fluid of the lumbar sac[2]
- Reflect the rates of Aβ and tau protein production and clearance[2]
- Advantages include:
  - Less expensive than PET by 10-15-fold[3]
  - Simultaneous information on Aβ and tau biomarkers[4]
- Limitations include:
  - CSF is obtained via lumbar puncture; this is invasive and can be uncomfortable for patients[5]
  - Limited availability outside of specialized clinics[6]
  - Do not detect regional Aβ or tau deposition[2,3]

Aβ=Amyloid Beta; AD=Alzheimer's Disease; CSF=Cerebrospinal Fluid; PET=Positron Emission Tomography.

1. https://alz.org/media/Documents/scientific-conferences/Figures-and-Tables-Clinical-Criteria-for-Staging-and-Diagnosis-for-Public-Comment-Draft-2.pdf.(Accessed January 2024). 2. Jack CR Jr, et al. *Alzheimers Dement*. 2018;14:535-562. 3. Hansson O, et al. *Alzheimer's Res Ther*. 2019;11(1):34. 4. Dubois B, et al. *Lancet Neurol*. 2021;20(6):484-496. 5. Lee JC, et al. *Exp Mol Med*. 2019;51(5):1-10. 6. Zetterberg H, et al. *Alzheimer's Dement (Amst)*. 2019;784-786.

Thank you for connecting with Keiko