Rapidly Progressive Young-Onset Dementias

Neuropsychiatric Aspects

Rajeet Shrestha, MD[a,b], Timothy Wuerz, DO[a], Brian S. Appleby, MD[a,b,c,*]

KEYWORDS

• Rapidly progressive dementia • Young onset dementia • Early onset dementia • Presenile dementia • Neuropsychiatry • Prion disease • Creutzfeldt–Jakob disease • Neuropsychiatric symptoms

KEY POINTS

- Rapidly progressive dementia (RPD) is roughly defined as progression to dementia or death within 2 years.
- Many RPDs demonstrate neuropsychiatric symptoms, especially at initial presentation.
- The differential diagnosis for RPD in younger patients is broad. Diagnostic workup includes blood work, brain MRI, electroencephalogram (EEG), lumbar puncture, and body CT.
- Creutzfeldt–Jakob disease is diagnosed clinically by assessing a clinical syndrome as well as the use of EEG, cerebrospinal fluid 14-3-3 proteins, and brain MRI findings.
- Clinical management should employ nonpharmacologic interventions first, followed by pharmacologic treatments if necessary. Neuropsychiatric symptoms should be reassessed frequently and medications adjusted as necessary.

INTRODUCTION

Rapidly progressive dementias (RPDs) are a unique and important population of patients of which psychiatrists should be aware. Many RPDs occur in younger

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[a] Department of Neurology, Case Western Reserve University School of Medicine & University Hospitals, 3619 Park East Drive, Suite 211, Beachwood, OH 44122, USA; [b] Department of Psychiatry, Case Western Reserve University School of Medicine & University Hospitals, 3619 Park East Drive, Suite 211, Beachwood, OH 44122, USA; [c] Department of Pathology, Case Western Reserve University School of Medicine & University Hospitals, 3619 Park East Drive, Suite 211, Beachwood, OH 44122, USA
* Corresponding author. 3619 Park East Drive, Suite 206, Beachwood, OH 44122.
E-mail address: bsa35@case.edu

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Abbreviations

AD	Alzheimer's disease
APOE	Apolipoprotein E gene
CJD	Creutzfeldt–Jakob disease
CSF	Cerebrospinal fluid
EEG	Electroencephalogram
FTLD	Frontotemporal lobar degeneration
PRNP	Prion protein gene
PrP^c	Native cellular prion protein
PrPSc	Pathologic scrapie prion protein
rpAD	Rapidly progressive Alzheimer's disease
RPD	Rapidly progressive dementia
RT-QuIC	Real-time quaking-induced conversion
sCJD	Sporadic Creutzfeldt–Jakob disease
vCJD	Variant Creutzfeldt–Jakob disease
YOAD	Young-onset Alzheimer's disease
YOD	Young-onset dementia

patients, in which sense they overlap with young-onset dementias (YODs). Both groups frequently exhibit a clinical presentation in which neuropsychiatric symptoms are prominent. For the purposes of this discussion, YOD refers to cases in which signs and symptoms of dementia start to occur before the age of 65. RPD is roughly defined as cases in which severe dementia or death occur within 2 years of symptom onset. This article discusses the differential diagnosis, workup, and management of this population with emphasis on certain patient groups.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of RPD is extensive and includes neurodegenerative, inflammatory/autoimmune, infectious, toxic–metabolic, and neoplastic causes, among others (**Box 1**). The most common etiology for RPD is neurodegenerative diseases, which do not have disease-modifying treatments. Prion diseases are usually high in the differential diagnosis when evaluating a patient with RPD, but other etiologies must be considered. Other neurodegenerative diseases typically have a slow progression, but they can sometimes be rapidly progressive.

Non-neurodegenerative causes of RPD can be treated potentially and their course halted or reversed to varying degrees. If undiagnosed or untreated, a number of these conditions may progress rapidly and be fatal. Therefore, it is paramount to investigate comprehensively and expeditiously any presentation of a rapid deterioration in cognitive, behavioral, and motor functioning. Among nondegenerative etiologies, autoimmune diseases form a major diagnostic group that includes encephalopathies associated with antineuronal antibodies, steroid responsive encephalopathy with associated autoimmune thyroiditis, central nervous system lupus, multiple sclerosis, and others. A number of infectious diseases can also affect the brain and can be difficult to diagnose clinically if there are no other obvious clinical signs of infection. Various vitamin deficiencies, endocrine and metabolic disorders, and toxicities should also be considered in cases of RPD. Finally, primary central nervous system neoplastic causes should be ruled out.[1]

EPIDEMIOLOGY

The epidemiologic characteristics of RPD are highly variable because of the diverse etiologic conditions that can lead to them. Individuals with AD and dementia with